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INDEX

JUDICIOUS WORK

With great joy and after careful work, we present to our readers the second 2024 edition of the Revista Brasileira de Ultrassonografia (RBUS), Revista Azul. Once again, we believe we have achieved the objective of contributing significantly to the scientific dissemination and continuous updating of Brazilian sonographers, which directly reflects on the achievement of more humanized and quality care provided to our patients.

We invite you, a sonographer and science enthusiast, to join us on this journey towards the knowledge and advancement of ultrasound in Brazil. The future of Ultrasonography depends on each one of us!

ANTONIO GADELHA DA COSTA
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ORIGINAL ARTICLE

UNRAVELING MIXED GONADAL DYSGENESIS: CHALLENGES IN PRENATAL DIAGNOSIS AND CLINICAL MANAGEMENT

EDUARDO DE FREITAS KELSCH [1], MIRIAN FRANCINE FAVERO [1], THIAGO MENEZES CÉZAR [1], ISABELLA KAPCZINSKI MÜLLER [1], JORGE ALBERTO BIANCHI TELLES [2], RAFAEL FABIANO MACHADO ROSA [1]

ABSTRACT

OBJECTIVE: The aim of this study is to report a case of mixed gonadal dysgenesis (MGD) diagnosed during pregnancy, highlighting the importance of prenatal diagnosis, clinical management, and genetic counseling.

CASE REPORT: The patient was a 20-year-old woman referred due to a fetal ultrasound showing evidence of renal abnormalities. At the 30-week ultrasound, a dysplastic right kidney with multiple cysts and ambiguous genitalia suggestive of a disorder of sexual development was observed. Fetal magnetic resonance imaging (MRI) revealed a dysplastic kidney with multiple cysts. There was an image suggestive of a hypoplastic scrotum and an undefined genital tubercle. The fetal karyotype showed a chromosomal constitution of mosaicism 45,X[28]/46,XY[2], consistent with the diagnosis of MGD. On neonatal clinical examination of the genitalia, there was a phallus measuring 3 cm with hypospadias but no urethral opening, and a palpable gonad in the left labioscrotal swelling. The right gonad was intra-abdominal, and the urethra opened into a wide urogenital sinus. Micrognathia, a single left palmar crease, clinodactyly of the fifth fingers, and hypoplastic nails were also observed. The abdominal ultrasound showed a right kidney with multiple cysts of varying sizes.

DISCUSSION: MGD is a complex condition that can manifest in various ways. The discussed case highlights the importance of a multidisciplinary approach in the management of gonadal dysgenesis cases, considering not only aesthetic aspects but also the functionality and health of the patient. The choice of gender assignment should be made after careful evaluation and in collaboration with the parents, taking into account emotional and social implications.

CONCLUSION: Early diagnosis and proper follow-up are crucial for the management of MGD. Collaboration between different medical specialties and the involvement of the parents in decision-making are essential to ensure appropriate and informed treatment. This case highlights the need for continuous support and careful planning for the child's future.

KEYWORDS: DISORDERS OF SEXUAL DIFFERENTIATION, MIXED GONADAL DYSGENESIS, PRENATAL DIAGNOSIS, POLYCYSTIC RENAL MALFORMATION, MOSAICISM, GENDER ASSIGNMENT

INTRODUCTION

Prostate ultrasound is commonly requested by doctors for male patients over 40 years old, both for diagnostic and screening purposes. The accurate determination of prostate volume is important for determining the degree of hyperplastic enlargement, the resulting tendency for urinary tract obstruction, and the preferred option for surgical treatment. The literature available for transabdominal prostate ultrasound instructs that the scan should be performed with a full bladder and the transducer tilted 15° towards the feet[1].

An enlarged prostate can result in voiding dysfunction due to static (mechanical) or dynamic (smooth muscles of the bladder neck and prostatic urethra) obstruction. Although classical literature is controversial regarding the direct relationship between prostate size and voiding dysfunction in patients with benign prostatic hyperplasia (BPH) and its implications for management and outcomes, some recent studies have highlighted the role of predominant secondary changes in the bladder in small-sized prostates, including a high bladder neck, increased smooth muscle tone in the bladder neck/prostate, and increased prostatic urethral angle, in contrast to the primary obstructive component in large glands[2].

Therefore, the cause of voiding dysfunction in patients with BPH should be established before undergoing surgery to improve the patient's condition, as management strategies differ in bladder outlet obstruction due to small and large prostates. The assessment of post-void residual urine is considered by many urologists to be an important test in patients with benign prostatic hyperplasia. Residual urine is found more frequently in these patients than in the healthy population. However, it does not always correlate with uroflowmetric findings.

Therefore, the objective of this study is to evaluate if

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there is a correlation between prostate volume and post-void residual urine volume.

METHODS

This is a retrospective cross-sectional observational study conducted with male patients using data from January to July 2023. The sample size was determined by temporal convenience, and the data were analyzed using Excel. The research was submitted to the Ethics Committee through the Brazil platform, respecting the ethical principles regulating research in human subjects (resolution 466/12).

The variables related to ultrasound findings were: patient age, prostate weight, and post-void residual urine volume.

For the statistical analysis, the Pearson correlation test was applied, where 1 = perfect correlation; 0.75 = strong correlation; 0.5 = moderate correlation; -0.5 = no correlation. Additionally, the Kolmogorov-Smirnov test and Spearman correlation were used.

For the abdominal prostate ultrasound examination, it is essential to have a full bladder. Patients should drink a large volume of water (5 cups) one hour before the procedure. Once ready, the patient lies down in a supine position, and the transducer is used with gel for visualizing the prostate in the pelvic region. Two measurements are taken with the transducer in the longitudinal plane and one in the transverse plane to calculate the volume (transverse x anteroposterior x longitudinal x 0.52), as shown in figure 1. The initial bladder volume is also calculated in the same way at this time. Afterward, the patient empties their bladder to calculate the post-void residual volume.

The reference values for post-void residual urine (PVR) in the study are: absent (no residue), negligible (0 to 40 ml), moderate (40 to 100 ml), and significant (> 100 ml), as shown in figure 2.

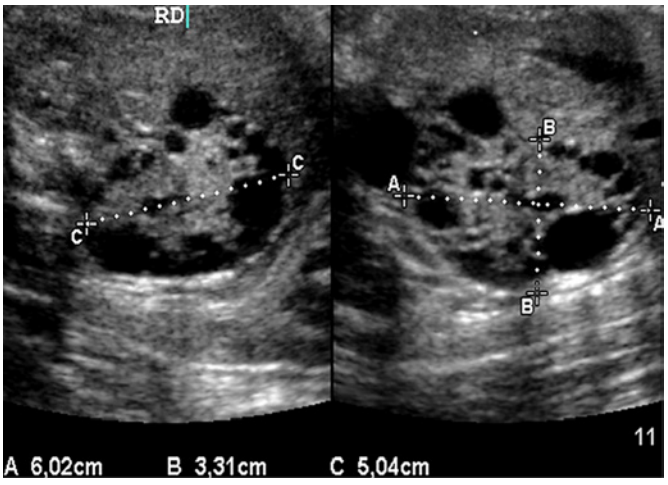


Figure 1: Fetal ultrasound performed at 30 weeks of gestation showing the right kidney (RK) dysplastic with multiple cysts.

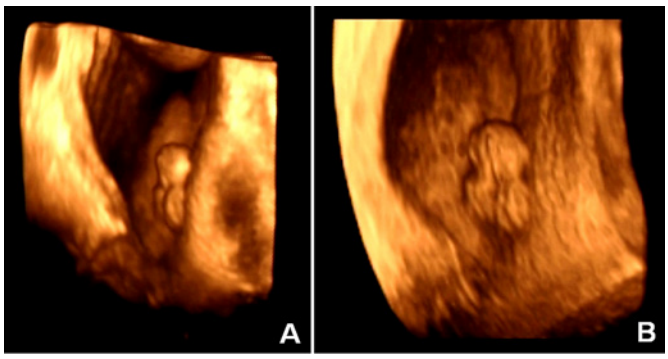
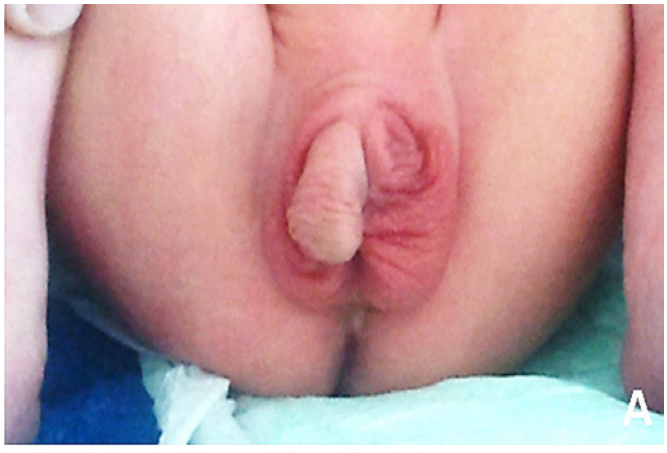


Figure 2: Image obtained through three-dimensional ultrasound showing genital abnormality, suggestive of ambiguous genitalia or a disorder of sexual differentiation (DDS) (A and B).

The supplementary evaluation through fetal magnetic resonance imaging showed an image suggestive of an undefined genital tubercle and an apparent hypoplastic scrotum. The fetal karyotype, obtained through amniocentesis, revealed the presence of a mosaicism 45,X[28]/46,XY[2], which, along with the prenatal findings, indicated the diagnosis of MGD. The fetal echocardiography was normal.

The baby was born at 40 weeks of gestation via cesarean section due to cephalopelvic disproportion, weighing 3180g, measuring 48cm, with a head circumference of 35cm, and Apgar scores of 9 at both the first and fifth minutes. Physical examination revealed the following findings: micrognathia, a single left palmar crease, bilateral clinodactyly of the fifth fingers, hypoplasia of the nails on the hands and feet, and genitalia with a phallus measuring approximately 3 cm with a urethral opening at its base, associated with rough and fused labioscrotal prominences, as well as a palpable left gonad located in the labioscrotal swelling (Figure 3).



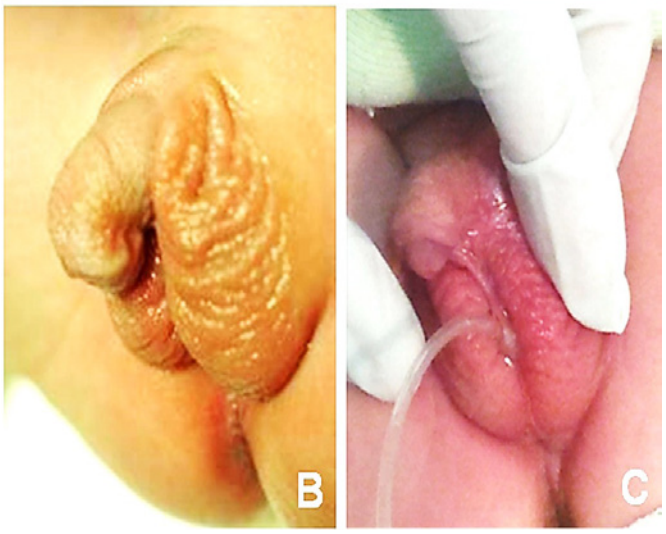


Figure 3: Appearance of the patient's external genitalia observed after birth. Note that the phallus measures approximately 3 cm, with a urethral opening at its base, associated with fused and rough labioscrotal prominences. The urethral catheter indicates the location of the urethral opening.

The right gonad was not located. Upon evaluating the set of findings, the patient's genitalia were classified as Prader stage IV. The Prader scale has five stages, ranging from typical female genitalia to typical male genitalia, with various forms of genital ambiguity in between[3].

Prader Classification[3]:

Grade I: The external genitalia is mostly female with mild clitoral hypertrophy. There is a slight increase in clitoral size, with normal labia and vagina, indicating virilization occurring after 20 weeks of intrauterine life (IUL).

Grade II: More pronounced clitoral hypertrophy. There is slight fusion of the labia, but a separate vaginal opening from the urethra is still visible, indicating virilization starting at 19 weeks of IUL.

Grade III: More complete fusion of the labia majora, forming a "scrotal pouch" appearance. The clitoris is enlarged, resembling a small penis. The urethra and vagina open together into a urogenital sinus, creating a single opening, indicating virilization at [14-15] weeks of IUL.

Grade IV: The clitoris is significantly enlarged, resembling a penis with a single opening for both the urethra and vagina (urogenital sinus). Labial fusion is nearly complete, forming a scrotal-like appearance, but no testicles are present. This degree corresponds to ambiguous genitalia, where it is harder to distinguish between sexes, as the external genitals resemble male genitalia without testes. It indicates virilization at [12-13] weeks of IUL.

Grade V: The external genitalia is completely male, with full fusion of the labia into a scrotal sac and advanced clitoral enlargement so that the organ resembles a penis. There may be a urethral opening at the level of the glans, similar to a typical penis, but the absence of testicles is a distinguishing feature, indicating virilization at [11] weeks of IUL.

The postnatal abdominal ultrasound showed that the right kidney had multiple cysts of varying sizes, with some enlarged. The inguinal ultrasound demonstrated a topical left gonad with a minimal associated hydrocele. The right gonad could not be identified.

The child's hormone levels revealed total testosterone at 0.2 ng/mL, androstenedione at 2.19 ng/mL, and alpha-fetoprotein levels above 300 ng/mL. Abdominal and pelvic video laparoscopy showed the presence of a long urogenital sinus, measuring approximately 7 to 8 cm, with no urethral meatus identified. There were testicular vessels on the left entering the left inguinal canal, associated with a hernia without internal content. No structure resembling a uterus was visualized. The right gonad was found near the right iliac vessels, and the respective vas deferens was not identified. A biopsy of the intra-abdominal right gonad revealed testicular hypoplasia.

For the evaluation and management of the case, a multidisciplinary meeting was held with the parents. Based on the observed findings and the parents' impressions, the consensus was to adjust the external genitalia to male anatomy. Since there was a possibility that the gonad located in the left labio-scrotal prominence could be functional and potentially able to promote spontaneous puberty, the decision was to preserve it, with regular and frequent follow-up due to the risk of gonadal malignancy.

DISCUSSION

Embryonic development of the reproductive system is a complex event that begins around the 7th week of gestation and requires a cascade of events involving the sequential and synchronized activation and suppression of various genes. For the differentiation of the indifferent gonad into a testis, the presence of the Y chromosome is essential, specifically the SRY gene. This gene triggers the production of the testis-determining factor, which leads to the formation of Leydig cells that produce testosterone, the male hormone. Testosterone, in turn, initiates the sequence of changes that results in the virilization of the external genitalia and, consequently, the development of a phenotype consistent with the male sex. Additionally, testosterone preserves the Wolffian duct and stimulates the migration of the gonads, differentiated into testes, to the labio-scrotal swellings. Through the peripheral conversion of testosterone into dihydrotestosterone (by the action of the enzyme 5-alpha-reductase), these swellings fuse and form the scrotal sac [4].

Another important hormone produced by the testis is the Müllerian inhibiting factor, which acts locally on the Müllerian ducts, preventing their development. If the SRY gene is not present, the gonads continue to develop as ovaries, leading the fetus to assume a female phenotype, with the preservation of the Müllerian ducts, which will later form the fallopian tubes, uterus, and the proximal portion of the vagina, along with the regression of the Wolffian ducts [4].

I see! Here's the translation of your text into English:

Sexual differentiation disorders (SDDs) consist of a group of alterations that occur at some point in this cascade of events, resulting in ambiguous phenotypes that can vary greatly and cannot be clearly classified as either female or male. This situation is referred to as ambiguous genitalia or genital ambiguity4. More objectively, some authors propose clinical parameters to consider its presence. For example, Lee et al.4 consider the diagnosis of ambiguous genitalia when the following criteria are present: 1) clear genital ambiguity; 2) when an apparently female genitalia presents with an enlarged clitoris and fusion of the labia majora; and 3) in the presence of genitalia that appears male with bilateral cryptorchidism, hypospadias, or micropenis.

The prenatal diagnosis of ambiguous genitalia, which affects approximately 1 in every 4,500 live births, presents challenges in various areas and has significant implications, including management of the pregnancy and planning for the baby's birth, as well as decisions regarding the sex of rearing and genetic counseling [5].

Currently, the assessment of genitalia through fetal ultrasound (FUS) is divided into two stages: early and later. The early assessment, conducted from 13 weeks of gestation, has an accuracy of nearly 100% and evaluates the angle between the ventral portion of the fetus and the axis of the genital tubercle. A male classification is given when this angle is greater than 30º, and a female classification is given when it is less than 10º. In the later stage of pregnancy, from 16 weeks onwards, direct visualization of the fetal genitalia is possible. In males, this is represented by a semicircular structure, the scrotum, with a penis in the midline; in contrast, a female genitalia appears as parallel echogenic lines representing the labia majora and minora[6]. Other findings to consider that assist in this identification include the presence of gonads within a structure compatible with a scrotum (indicative of testes), an enlarged phallus (suggestive of a penis), and the presence of a uterus, as well as the measurement of the rectovesical portion, also known as the anogenital distance6. However, factors such as maternal obesity, amniotic fluid volume, proximity of the umbilical cord to the genitalia, and an unfavorable fetal position for visualization can influence the accuracy of the examination.

The possibility of ambiguous genitalia should be considered whenever the sex of the fetus/infant cannot be determined through ultrasound evaluation [7]. Features such as a phallus with a rounded tip, abnormal curvature, and reduced size are suggestive of hypospadias [8]. Additionally, the observation of echogenic lines corresponding to the remnants of the prepuce, as well as the ventral deflection of the urinary stream (which can be visualized using color Doppler), support this diagnosis. The "tulip sign," which describes the appearance of a ventrally curved phallus between two labio-scrotal folds, is also noted [8].

Evaluation through three-dimensional ultrasound can also provide better visualization of genital structures due to its greater clarity and improved differentiation of structures. This also facilitates the visualization of the genitalia by parents and other members of the multidisciplinary team, helping in understanding the findings and development [9].

Additionally, fetal magnetic resonance imaging (MRI) can be used in prenatal diagnosis to provide detailed information about structures within the pelvis, such as internal genitalia, the urinary tract, or the rectum. It has the advantage of not being limited by maternal body composition, fetal position, or the presence of oligohydramnios. However, its main disadvantage is the long duration of the examination [6].

Thus, the identification of a potential genital abnormality in the fetus allows for its evaluation to begin during the prenatal period, through imaging tests, as previously discussed, as well as laboratory tests like fetal karyotyping. This test can be performed by obtaining material through invasive procedures such as amniocentesis and cordocentesis, and provides information about the fetal chromosomal composition, indicating whether it is typically female or male, or if there are any abnormalities [4].

After birth, various aspects need to be considered during the physical examination of the baby. These include the size and shape of the phallus, which helps in identifying conditions such as micropenis or clitoromegaly; the location of the urethral meatus, which may be found in different positions along the midline and ventral side of the penis, potentially indicating hypospadias; the presence of fusion of the labio-scrotal folds, which can suggest ambiguous genitalia; the location and size of the gonads, which may be small or absent, either in the abdomen, along the inguinal canal, or in the labio-scrotal fold; and the presence of inguinal masses, which may contain gonads or other structures, such as fallopian tubes or even a uterus [7].

In addition, laboratory tests are recommended to address any doubts regarding the function of the identified structures. These tests may include measurements of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, dihydrotestosterone, and androstenedione, depending on the clinical suspicion. It is important to note that, especially if the fetal karyotype has not been performed, it should be done, as its result is crucial for diagnosis. In particular cases, especially if there is uncertainty about the prenatal results or a need for confirmation, the importance of repeating the test should be evaluated [4].

Regarding the choice of gender for rearing, the birth certificate, which is currently issued shortly after birth, includes an option labeled "unknown" in the sex designation section. This allows for the newborn's registration to proceed even if the determination of the rearing gender takes additional time, considering the complexity of the cases. This option is also important due to the time typically required for a thorough evaluation [4].

Ambiguous genitalia is actually a finding that can be related to different etiologies. For instance, some authors categorize these causes into three groups based on the karyotype

results: the first, 46,XX (with congenital adrenal hyperplasia causing more than 90% of cases); the second, 46,XY (associated with various causes such as androgen insensitivity syndrome, pure gonadal dysgenesis XY, and 5-alpha-reductase deficiency); and finally, abnormalities of sex chromosomes, with or without the presence of mosaicism (such as Turner syndrome and DGM, which is associated with mosaicism 45,X/46,XY, as observed in our patient)[4].

The patient presented with a multicystic dysplastic kidney on the initial evaluation through ultrasound, which led to referral and further investigation at a specialized fetal medicine center. However, additional findings of abnormalities in the development of the external genitalia observed at this tertiary center, including what appeared to be hypospadias without associated urethral opening and seemingly fused and rugose labio-scrotal prominences, with the presence of a gonad on the left side, raised the suspicion of a disorder of sexual development (DSD). Therefore, it was recommended to perform fetal karyotyping during the prenatal period, which revealed the presence of mosaicism 45,X/46,XY.

In this case, the presence of ambiguous genitalia in the fetus, combined with the karyotype result showing mosaicism involving a sex chromosome alteration, categorizes the case into the third category of disorders of sexual development (DSD) previously described. Mosaicism 45,X/46,XY can present clinically in various ways and with different manifestations. Its spectrum can range from a seemingly normal man or one with infertility, a boy with short stature who may or may not have hypospadias and/or cryptorchidism, an individual with ambiguous genitalia, to a patient with Turner syndrome or a woman with secondary amenorrhea. However, it is only when mosaicism 45,X/46,XY is associated with ambiguous genitalia that it is classified as gonadal dysgenesis (GD). Within the spectrum related to this mosaicism, the presentation as MGD constitutes only a small fraction of cases, with the majority being individuals with a normal male presentation [1].

Some minor dysmorphic features or stigmata (including micrognathia, bilateral clinodactyly of the fifth fingers, and nail hypoplasia), as well as the renal abnormalities observed in our patient, can be explained by the 45,X lineage, as these findings are part of the clinical spectrum observed in Turner syndrome.

In discussing the issue of choosing the sex of rearing, a multidisciplinary meeting was held, considering the parents' perspective. It is crucial to emphasize the importance of collaborative work among specialists from different fields due to the complexity of the case and the need for informed and appropriate decisions in such situations. This search involves not only aesthetic considerations but also extremely relevant aspects concerning functionality. To seek more objective and concrete alternatives, various existing tools were utilized to further substantiate the decision made. Decisions regarding the baby's sex are only made after birth, as a more accurate and definitive assessment can only be conducted at that time. This consideration must include the expectations and understanding of the parents, who will provide their opinions on the case and, eventually, on the patient themselves. Three concepts must be considered in these cases: legal sex, where in this case, the patient has ambiguous genitalia but a decision was made to adapt it to male genitalia; sex of rearing, which refers to how the patient will be raised and treated by the parents; and gender, which refers to how the individual will perceive themselves in society, encompassing biopsychosocial aspects that may not necessarily align with the legal sex10. Therefore, the genitalia and the way it is reared do not define the patient's gender.

An example of this was the result observed using the Prader scale, a classification system initially created to assess the degree of virilization of the external genitalia in patients with congenital adrenal hyperplasia and a chromosomal constitution of 46,XX. The scale ranges from I to V. Upon examining the patient, it was noted that the characteristics, such as the size of the penis and the degree of labio-scrotal fusion with its roughness, were consistent with the level IV on this scale. This indicated a significant degree of virilization, which, as observed, was reflected in the parents' own perception of their child as a boy.

According to the masculinization score developed by Ahmed et al[2]. and applied by Cools et al.11, a patient with DGM, which considers findings related to external genitalia and ranges from 0 to 12, our patient had a score greater than 7. This was due to the fact that the patient had a phallus size within two standard deviations of the mean for their age, the presence of hypospadias, fusion of the labio-scrotal swellings (which were also rugose), and a palpable gonad in the scrotal sac with another visible in the abdominal cavity (both ovoid and with characteristics resembling those of a testicle). Additionally, the evaluation of internal sexual organs through laparoscopy did not reveal the presence of a uterus or fallopian tubes but did show testicular vessels on the left and a left vas deferens entering the inguinal canal on the same side. According to the management proposed by Cools et al.[11], it is recommended to perform orchiopexy of the gonad, with regular examinations of it, as well as annual ultrasound starting from puberty due to the possible risk of malignancy. A biopsy of the gonad should be performed before and after puberty to assess the risk of tumors, and in cases of precancerous changes or in situ neoplasia, the patient should undergo gonadectomy. The risk of malignancy of the gonad appears to be inversely related to the masculinization score of Ahmed et al.[2], meaning that a higher score (or greater virilization) is associated with a lower risk of neoplasia[11].

The gonad present alongside the labioscrotal prominence has the potential to be functional, and its preservation may allow the individual to produce hormones on their own, thus inducing and maintaining spontaneous puberty (i.e., without the need for medications to induce puberty)[11]. Therefore, in such cases, the risk (of gonadal malignancy) and the potential benefit (the development of spontaneous puberty) must be evaluated. It is important to highlight some points related to the choice of gender assignment, which we consider rel-

evant: 1) as mentioned previously, this choice involves not only aesthetic considerations but, more importantly, functional aspects, with the parents' impression being something that should be strongly taken into account; 2) the presence of a male lineage associated with mosaicism does not determine the choice of male gender assignment, as this option is complex and depends on other variables; 3) currently, some groups, based on the principle of autonomy, have proposed that the choice of gender assignment should be made by the individual with ambiguous genitalia when they are at an age where they possess the maturity and conditions to do so11, however, in our context, gender assignment is usually made primarily based on functional characteristics, expected surgical outcomes, and the family's perspective. Therefore, these decisions are not simple, and it is recommended that these cases be evaluated by multidisciplinary teams, particularly those experienced in such situations; 4) the choice of prophylactic orchiectomy should not influence the decision regarding gender assignment, as the choice to perform gonadectomy due to the risk of malignancy does not necessarily mean that the male option should be ruled out; and finally, 5) it is important to remember that there are different types of sex, such as anatomical sex, sex related to sexual activity, and gender identity, with the latter potentially differing from the one adopted. Nevertheless, as mentioned before, this decision is highly complex and challenging, weighing the benefits and potential risks, with the chosen option ultimately seeking to ensure the best well-being and quality of life for both the patient and their family[4,10,11].

CONCLUSION

Dealing with cases of ambiguous genitalia in the prenatal period presents great challenges for all parties involved, whether it be the family or the medical team, who must be aligned in the search for alternatives that prioritize the health of the individual, both physically and mentally. Multidisciplinary and collaborative work, aimed at finding the best alternatives, is therefore essential in these cases. Within this context, prenatal diagnosis is of significant importance, as it not only allows certain evaluations and tests to be carried out early on, but also facilitates the preparation of the family and the approaches to be adopted after birth. This complexity, due to the number and importance of the aspects to be considered in cases of genital ambiguity, makes them a real challenge for everyone who faces such a situation.

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ORIGINAL ARTICLE

ULTRASONOGRAPHIC EVALUATION OF THE ANTERIOR AXILLARY RECESS IN THE NORMAL SHOULDER

LENA PARI GALINDO [1], SILVIA LUCIA MAYANGA [2], MONRES JOSÉ GOMES [3]

ABSTRACT

OBJECTIVES: The objectives of the study were to demonstrate the usefulness of ultrasound to estimate the thickness of the anterior axillary recess (AAR) in the shoulder, determine if the thickness of the anterior axillary recess is altered with the patient's position, the degree of arm abduction, gender and laterality; compare the thickness of the anterior axillary recess obtained with the normal value reported in current scientific literature.
MATERIAL AND METHODS: Descriptive, longitudinal, prospective study, carried out in 32 normal volunteers aged between 18-60 years, excluding people who had a history of inflammatory and traumatic pathology of the rotator cuff, rheumatic diseases, diabetics and hypothyroid patients. An ultrasound evaluation protocol was designed considering the variables patient position, arm position in abduction of 90º, 60º and 45º, laterality and gender. The descriptive statistical analysis of the quantitative variables was carried out by calculating the mean, standard deviation, error of the mean and confidence intervals; The variation of AAR according to position, laterality and gender was analyzed with one-way ANOVA. The thickness AAR by ultrasound and MRI was compared with the t-student test for a single sample; after determining normality with the Shapiro-Wilk test.
RESULTS: Of 32 normal volunteers, 20 (62.5%) women and 12 (38.5%) men, obtaining 64 cases. The thickness of the anterior axillary recess without discriminating the patient's position or the degree of abduction was 2.07 mm, (SD ± 0.34mm), 95% CI [2.03 – 2.11 mm]. No statistically significant difference was found in the anterior axillary recess according to the patient's position, arm abduction (p=0.055) or laterality (p=0.085). According to gender, the ARR is thicker in men, 2.38mm, 95% CI [2.16 – 2.58 mm], the difference was significant (p=0.00). When comparing the thickness of the anterior axillary recess obtained with the normal value reported in current scientific literature, a statistically significant difference was found (p=0.00).
CONCLUSIONS: Ultrasound allows the evaluation of the anterior axillary recess of the shoulder, the thickness is not altered with the patient's position or the degree of arm abduction, but it is thicker in men than in women and the average thickness obtained differs from the normal reference value.

KEYWORDS: ANTERIOR AXILLARY RECESS, ULTRASOUND, SHOULDER.

INTRODUCTION

In joints, recesses are folds or extensions of the joint capsule composed of two layers of synovium and a small amount of synovial fluid that extend outside the joint space. In the shoulder, the anterior axillary recess (AAR) reflects the integrity of the joint capsule[1]. For this reason, several studies consider that thickening of the AAR indicates a significant structural change and serves as a key radiological sign in the diagnosis of adhesive capsulitis[2,3].

Currently, imaging evaluation of the AAR can be performed using magnetic resonance imaging (MRI) and ultrasonography. MRI has higher sensitivity and specificity, and it also allows for the assessment of the entire joint to detect other abnormalities. Ultrasonography, on the other hand, is also widely used for shoulder evaluations, particularly for the rotator cuff tendons[6,7]. Although the standard protocol does not include an evaluation of the AAR, as joint capsule pathology is rare, it is suggested that in patients with suspected adhesive capsulitis (AC), the evaluation be extended to the axilla to assess the AAR[3].

The thickness of the anterior axillary recess (AAR) is considered normal if it measures less than 4 mm, as reported in the current scientific literature[8,10]. However, this value was obtained from arthro-MRI studies and extrapolated as a reference for ultrasonography. In this regard, some studies on adhesive capsulitis using ultrasonography have used the thickness of the AAR as a parameter, finding that in normal shoulder controls, the AAR thickness ranged from 1.6 ± 0.72 mm^2 to 2.2 ± 0.16 mm[3,11].

Ultrasonographic evaluation of the shoulder is generally performed in a seated position[6,7], and in some cases, it can be done in the supine position, especially when there is

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suspicion of an inflammatory process in the joint capsule, as the shoulder relaxes, allowing access to the axilla. For the ultrasonographic evaluation of the AAR, it is recommended that the arm be in abduction and external rotation (ABER position), as this position exposes the AAR, facilitating its identification and characterization. However, in adhesive capsulitis (AC), there is a limitation in arm abduction, and the AAR should be assessed within the degrees of abduction permitted by the patient[8].

The advantages of ultrasonography over magnetic resonance imaging, besides its accessibility and lower cost, include the fact that it does not require the use of intra-articular contrast, allows the patient and arm to be moved to evaluate different positions[1], and can be used as a guide for minimally invasive treatments[10]. Therefore, it is important to demonstrate the usefulness of ultrasonography in estimating the thickness of the anterior axillary recess by proposing a simple and easily reproducible ultrasound technique, applied to the shoulders of healthy volunteers. The objective is to determine whether the thickness of the AAR changes with patient position, degree of arm abduction, gender, and laterality, and finally, to compare the AAR thickness obtained with the normal values reported in the current scientific literature.

Anatomical Reminder

The glenohumeral joint is a ball-and-socket joint formed by the convex surface of the humeral head and the glenoid cavity of the scapula. Its articular surfaces are covered with hyaline cartilage, and the glenoid margin is surrounded by a fibrocartilaginous tissue called the labrum, which forms a ring that complements and deepens the glenoid cavity. The structures that fix and stabilize both bones are the joint capsule and the coracohumeral and glenohumeral ligaments[1].

The joint capsule is composed of loose fibrous tissue and is covered by the synovial membrane on its deep surface. It extends from the scapula to the humerus, encompassing the entire joint. It has two openings: a superior opening for the passage of the long head of the biceps tendon in the rotator interval and for communication with the subscapular recess; in the inferior portion, the joint capsule is loose and redundant, forming a fold known as the anterior axillary recess[1]. See Fig. 1.

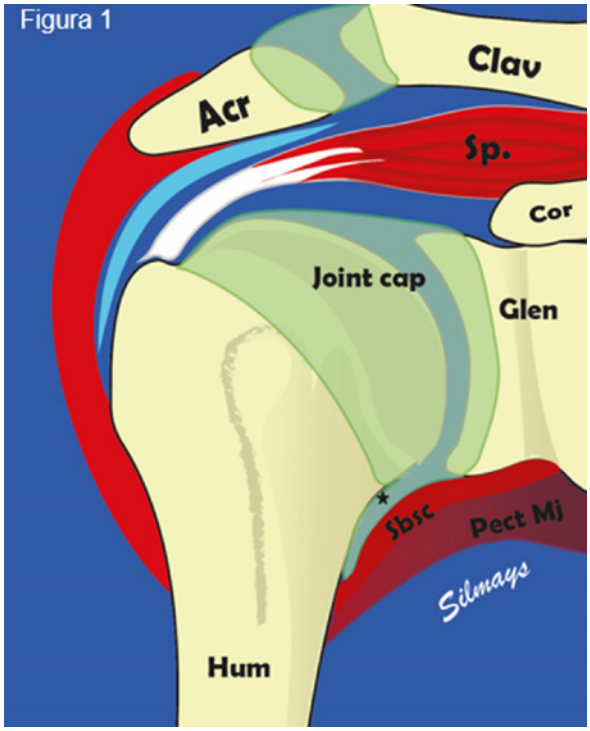


Figure 1. Schematic representation of the shoulder joint.
Joint Cap: Joint capsule; black asterisk: Anterior axillary recess; Sbsc.: Subscapularis muscle; Pect Mj: Pectoralis major; Glen: Glenoid cavity; Acr: Acromion; Clav: Clavicle; Cor: Coracoid; Hum: Humerus.

MATERIAL AND METHODS

This descriptive, longitudinal, prospective study was conducted with 32 healthy volunteers aged between 18 and 60 years, excluding individuals with a history of inflammatory and traumatic rotator cuff pathology, rheumatic diseases, diabetes, and hypothyroidism.

Ultrasonographic Evaluation Protocol

The ultrasonographic evaluation was performed by two radiologist doctors specializing in musculoskeletal imaging, applying a simple and easily reproducible ultrasound technique to assess the AAR in the axilla, using a high-resolution multifrequency linear transducer of 10-16 MHz in grayscale. Gain and focus were adjusted according to the patient's anatomy.

Ultrasonographic Technique

- The ultrasonography was initiated with the person seated in a swivel chair, with the physician facing the shoulder to be evaluated. When the person was in the supine position, the physician positioned themselves adjacent to the shoulder being assessed.

- The arm's position in abduction and external rotation (ABER position) and the degrees of arm abduction established for the study were 90°, 60°, and 45°, which were measured using a universal goniometer (Fig. 2).

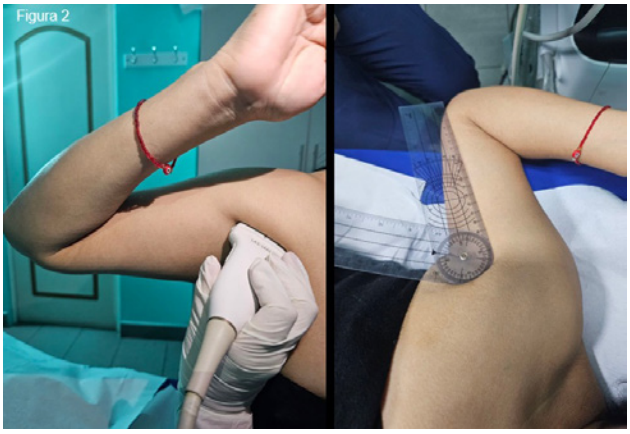


Figure 2: Ultrasonographic technique: Patient in a seated position (A) and in the supine position (B); a universal goniometer was used to determine the angle of arm abduction at 90° (A) and 60° (B).

- In the ABER position, the anterior axillary line was identified, and the ultrasound transducer was positioned with its orientation directed toward the arm, following the long axis of the humerus. The ultrasound transducer was adjusted at different angles according to the degree of arm abduction while maintaining reference to the long axis of the humerus (Fig. 3A).

- In the ultrasound image, the anatomical structures were identified: in the deep plane, the profile of the humerus can be recognized, with the head and anatomical neck represented by a hyperechoic line with posterior acoustic shadowing. Immediately above, the hyperechoic folds that form the AAR were observed, followed by the muscular plane formed by the inferior border of the subscapularis muscle and the pectoralis major muscle in the more superficial plane, just below the skin (Fig. 3B and 3C).

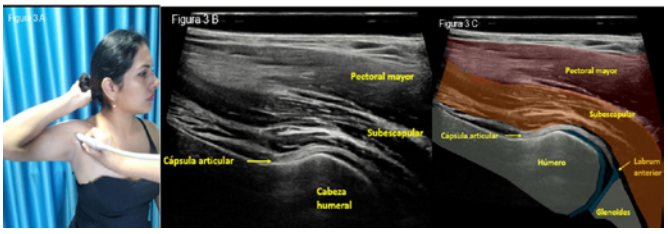


Figure 3. Ultrasonographic technique of the AAR in the axilla. A. Ultrasound transducer positioned on the anterior axillary line following the profile of the humerus. B. Ultrasound image of the joint capsule and the AAR. C. Color-coded identification of the anatomy.

- The measurement of the thickness of the anterior axillary recess was performed from the superficial border of the humeral periosteum, located immediately distal to the anatomical neck, to the superficial border of the capsule beneath the subscapularis muscle, preferably at its thickest portion (Fig. 4A). In a normal shoulder, the AAR is usually collapsed or presents a thin anechoic line due to synovial fluid; the thickness of the two echogenic layers of the recesses was measured (Fig. 4A and 4B). The AAR should not be confused with the folds of the muscle fascia or the subscapularis muscle, which at this level has its lower bundles inserting into the humerus. To avoid this confusion, the echogenic image of the capsule should be followed to the joint cavity to verify its continuity (Fig. 5A and 5B).

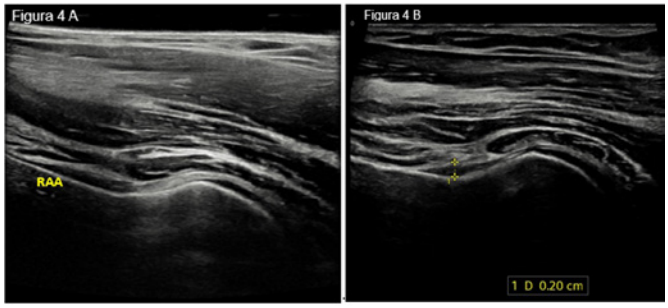


Figure 4. Measurement of the AAR in the axilla. A. Collapsed AAR, showing two hyperechoic lines. B. Open AAR with a linear anechoic synovial fluid.

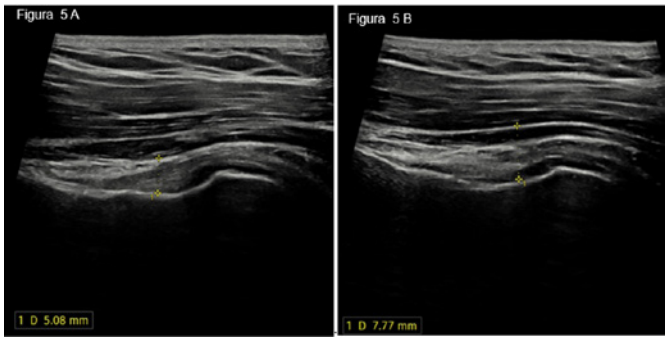


Figure 5. Measurement errors of the AAR. A. The AAR is confused with the recess of the subscapularis muscle fascia. B. The AAR is confused with the lower bundle of the subscapularis muscle.

Statistical Analysis

Descriptive statistical analysis of the quantitative variables was performed by calculating the mean, standard deviation, standard error of the mean, and confidence intervals. The analysis of the variation in anterior axillary recess (AAR) thickness based on position (sitting and supine), degrees of arm abduction (ABER 90° - 60° - 45°), laterality, and gender was conducted using the one-way ANOVA test. To compare the obtained AAR thickness with the normal reference value (4 mm), a one-sample t-test was performed after determining normality with the Shapiro-Wilk test. A 5% probability of error was considered ($p < 0.05$). The data were processed using SPSS v.27 for Windows 10, and the tables and graphs were represented in Excel.

RESULTS

Ultrasound was performed on 32 healthy volunteers, of whom 20 (62.5%) were women and 12 (37.5%) were men. Both shoulders were assessed, resulting in a total of

64 cases. The mean age of the volunteers was 40.77 years (range: 18-60 years).

The mean thickness of the anterior axillary recess (AAR), regardless of patient position and degree of abduction, was 2.07 mm (SD ± 0.34 mm), with a 95% confidence interval [2.03 – 2.11 mm].

Considering the position and degree of arm abduction, the greatest thickness of the AAR was obtained in the supine position with ABER at 90º, with a mean of 2.18 mm, 95% CI [2.07 – 2.29 mm]. The smallest thickness of the AAR was observed in the sitting position with ABER at 45º, with a mean of 1.98 mm, 95% CI [1.88 – 2.08 mm]. When comparing the means across all positions and degrees of ABER, no statistically significant difference in AAR thickness was found (p=0.055). See Table 1 and Graph 1.

Position - ABER	Mean	Standard Deviation	Standard Error	95% Confidence Interval		ANOVA
				Lower Limit	Upper Limit	
Decúbito 90º	2.18	0.38	0.43	2.07	2.29	
Decúbito 60º	2.10	0.32	0.38	2.01	2.20	
Decúbito 45º	2.05	0.33	0.39	1.95	2.14	p = 0.055
Sentado 90º	2.11	0.41	0.05	2.01	2.22	
Sentado 60º	2.00	0.39	0.05	1.91	2.10	
Sentado 45º	1.98	0.40	0.05	1.88	2.08	
Total	2.07	0.41	0.02	2.03	2.11	

Table 1: Comparison of AAR Means According to Position - ABER

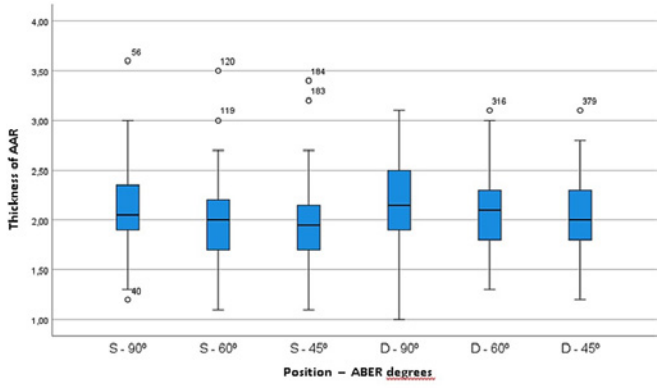
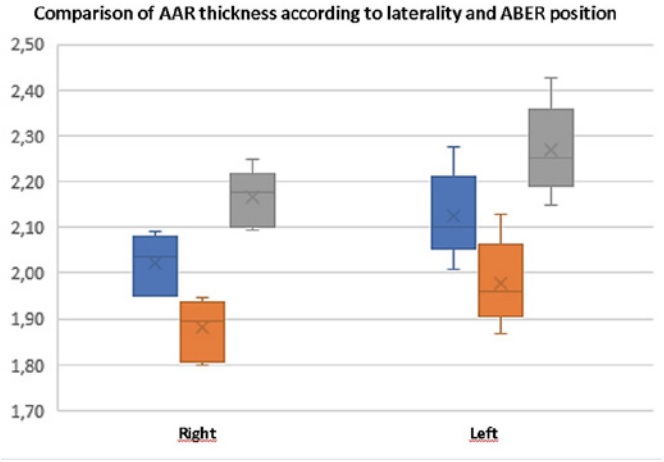


Table 2: Comparison of Anterior Axillary Recess (AAR) Means According to Laterality and Position – ABER 90º, 60º, 45º

Regarding laterality, no significant difference was found in the thickness of the anterior axillary recess between the right and left shoulders in either the supine or sitting position, nor with different degrees of arm abduction. See Table 2 and Graph 2.

Position - ABER		N	Mean	Standard deviation	Standard error	95% Confidence Interval		p-value
						Lower limit	Upper limit	
Sitting - 90º	Right	33	2.05	0.42	0.07	1.90	2.19	p= 0.173
	Left	31	2.19	0.40	0.07	2.04	2.33	
Sitting - 60º	Right	33	1.95	0.40	0.07	1.81	2.09	p= 0.235
	Left	31	2.07	0.38	0.07	1.93	2.21	
Sitting - 45º	Right	33	1.95	0.43	0.07	1.80	2.10	p= 0.569
	Left	31	2.01	0.38	0.07	1.87	2.15	
Supine - 90º	Right	33	2.09	0.44	0.08	1.93	2.25	p= 0.085
	Left	31	2.28	0.41	0.07	2.13	2.43	
Supine - 60º	Right	33	2.08	0.37	0.06	1.95	2.21	p= 0.537
	Left	31	2.14	0.40	0.07	1.99	2.28	
Supine - 45º	Right	33	2.03	0.38	0.07	1.89	2.16	p= 0.683
	Left	31	2.07	0.41	0.07	1.92	2.22	

Table 2: Comparison of Anterior Axillary Recess (AAR) Means According to Laterality and Position – ABER 90º, 60º, 45º

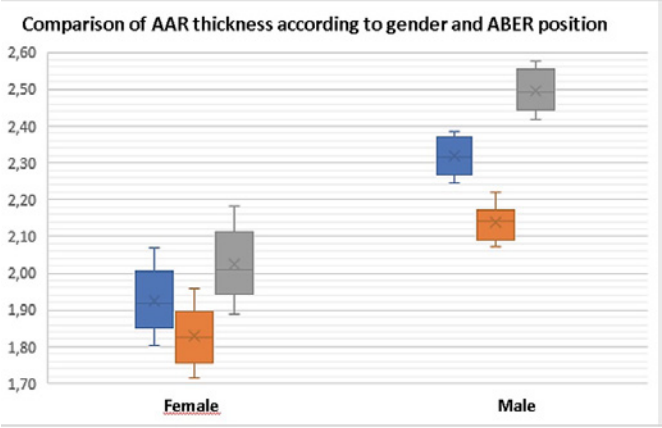


Graph 2: Comparison of AAR averages according to laterality and position – ABER 90º, 60º, 45º.

Regarding gender, it was found that the axillary recess is thicker in males than in females, remaining thicker in both positions and at all degrees of arm abduction; this difference was statistically significant. The maximum thickness was obtained for the male gender in the supine position at ABER-90º, with an average value of 2.38 mm, 95% CI [2.16 – 2.58 mm]. See Table 3 and Figure 3.

Position ABER / Gender		N	Mean	Standard deviation	Standard error	95% CI Lower limit	95% CI Upper limit	p-value
Sitting - 90º	Female	40	1.98	0.34	0.05	1.87	2.09	p= 0.001
	Male	24	2.33	0.44	0.09	2.15	2.52	
Sitting - 60º	Female	40	1.87	0.30	0.05	1.77	1.96	p= 0.000
	Male	24	2.25	0.41	0.08	2.07	2.42	
Sitting - 45º	Female	40	1.80	0.27	0.04	1.72	1.89	p= 0.000
	Male	24	2.28	0.42	0.09	2.10	2.45	
Supine - 90º	Female	40	2.07	0.35	0.06	1.96	2.18	p= 0.007
	Male	24	2.38	0.50	0.10	2.16	2.58	
Supine - 60º	Female	40	1.94	0.27	0.04	1.85	2.02	p= 0.000
	Male	24	2.38	0.39	0.08	2.22	2.55	
Supine - 45º	Female	40	1.90	0.31	0.05	1.80	1.99	p= 0.000
	Male	24	2.30	0.39	0.08	2.14	2.46	

Table 3: Comparison of average axillary recess thickness according to gender and position – ABER 90º, 60º, 45º



Graph 3. Box plot comparing AAR thickness according to gender and ABER position.

The thickness of the RAA obtained in this study differs from the reference mean value (4 mm). When comparing these data using the one-sample t-test, the result demonstrated that this difference is statistically significant; this result persisted with postural changes and different degrees of arm abduction. See Table 4.

	Test Value = 4					
	t	df	p - value	Mean Difference	95% CI Lower	95% CI Upper
Sitting - 90°	-36.48	63	0.000	-1.89	-1.99	-1.78
Sitting - 60°	-41.03	63	0.000	-1.99	-2.09	-1.90
Sitting - 45°	-39.97	63	0.000	-2.02	-2.12	-1.92
Supine - 90°	-33.65	63	0.000	-1.82	-1.93	-1.71
Supine - 60°	-39.57	63	0.000	-1.90	-1.99	-1.80
Supine - 45°	-39.95	63	0.000	-1.95	-2.05	-1.86

Table 4: Values of the One-Sample t-Test

DISCUSSION

The assessment of the anterior axillary recess at the shoulder joint has gained importance in recent years due to the increase in cases of adhesive capsulitis. Although the diagnosis of this pathology is strictly clinical and the European Society of Musculoskeletal Radiology does not recommend the use of ultrasonography as an imaging modality for diagnosis, articles have recently been published identifying the radiological signs of adhesive capsulitis with ultrasound. The thickening of the anterior axillary recess is considered a sign of adhesive capsulitis, with a sensitivity ranging from 68.9% to 100% and specificity between 90.2% and 98% [2,3].

In our study, the mean thickness of the anterior axillary recess (AAR) in healthy volunteers was 2.07±0.3mm. This result is in agreement with the study by Stella et al.[2], where the mean thickness of the AAR in the normal shoulder was 1.6mm; in the study by Do et al.[3], it was 2.6mm; and in the study by Moragues et al.11, the mean thickness of the AAR was 2.2mm. The thickness of the AAR increased in the supine position with 90º abduction, reaching a maximum value of 2.29mm (95% CI). The variation was not significant; likewise, the AAR did not show significant thickening when comparing the right shoulder with the contralateral side.

Contrary to the previously mentioned findings, when comparing the thickness of the anterior axillary recess (AAR) by gender, male participants exhibited a thicker AAR than female participants, reaching a maximum thickness of 2.58mm (95% CI) in the supine position with 90º abduction, and the difference was significant in all positions and degrees of abduction. The ultrasound results, considering the changes in position, abduction angle, and gender in this study, could not be compared with other publications, but we believe it is important to understand these characteristics during the evaluation of a pathological shoulder.

Stella et al.[2] published the ultrasound signs of adhesive capsulitis, comparing the thickness of the anterior axillary recess (AAR) in patients diagnosed with adhesive capsulitis and healthy volunteers or with the healthy contralateral shoulder. Ninety-three percent of patients with adhesive capsulitis had an AAR greater than 4mm, and the remaining 7%, although they did not have a thickness greater than 4mm, were found to be thickened by more than 60% when compared to the healthy contralateral shoulder. The interval found for the 7% of patients who had a thickness of less than 4mm showed AAR values between 3-4mm in the pathological shoulder.

Do et al.[3] evaluated the signs of adhesive capsulitis relating clinical deterioration and ultrasound parameters, with one of the parameters being the thickness of the anterior axillary recess (AAR), considered pathological if, when compared to the healthy contralateral side, the value obtained in the suspected shoulder exceeded 4mm. The ultrasound evaluation was performed with the patient in the supine position and with the arm at 90º, concluding that an AAR thickness greater than 4mm has a sensitivity of 68.9% and specificity of 90.2% for the diagnosis of adhesive capsulitis, and it was found to be thickened in all clinical stages of the disease. These results would have greater sensitivity and specificity if compared with the AAR of their healthy controls rather than with the normal average of 4mm.

In previous studies, the normal thickness of the anterior axillary recess (AAR) is considered to be less than 4mm, a value obtained from studies using arthro-resonance[8-10], and this value was extrapolated to ultrasound to define the AAR as thickened or not[2,3]. However, the results of this study showed that the thickness of the AAR measured by ultrasound has a significant difference compared to the reference average. This difference may be attributed to the bulging caused by the contrast agent in the AAR. On the other hand, ultrasound does not use contrast agents in the joint; therefore, the thickness of the synovium and the increase in intra-articular fluid must be considered solely and exclusively as a result of a pathological process of the articular capsule.

CONCLUSION

Ultrasonography allows for the evaluation of the anterior axillary recess (AAR) of the shoulder using a simple and easily

reproducible technique. In normal individuals, the thickness does not change with variations in patient position or the degree of arm abduction, but it is thicker in men than in women, and the average thickness obtained differs from the normal reference value.

We recommend ultrasonography for the evaluation of the anterior axillary recess (AAR) in the shoulder, differentiating the normal thickness of the AAR according to the imaging modality. It is important to consider that the normal thickness of the AAR for ultrasonography is 2.07 mm (SD ± 0.34 mm), without distinction of position and laterality; in men, a maximum normal thickness of 2.58 mm (95% CI) should be considered. Based on the results of this study and other publications, it would be advisable to reach a consensus to validate the ultrasonographic findings of normal AAR.

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ORIGINAL ARTICLE

ULTRASONOGRAPHIC FINDINGS IN PATIENTS WITH ENDOMETRIOSIS IN OVARIES AND ADNEXA – IMAGE COMPILATION

BIANCA CHACON DEZOTTI [1], ISABELLA FERREIRA CAPRA [1], LARISSA DA SILVA ALMEIDA [1], MARIA CAROLINA ROSSI PEGORER [1], REJANE MARIA FERLIN [1], LEONARDO DE SOUZA PIBER [1]

ABSTRACT

INTRODUCTION: Endometriosis is a condition in which endometrial tissue grows outside the uterine cavity, causing chronic inflammation and disabling pain, depending on its location and severity. Transvaginal ultrasonography is the preferred non-invasive diagnostic method due to its accessibility and low cost, and it is effective in identifying endometrial lesions and signs of pelvic involvement. Ovarian involvement, or endometrioma, is characterized by cystic lesions with dense and uniform content, associated with pelvic pain and infertility, and may also indicate the presence of other endometriotic lesions.

OBJECTIVE: To review and describe the ultrasonographic characteristics of endometriosis in the ovaries and adnexa.

METHODS: This narrative review focuses on compiling images from articles published in the last five years using the MEDLINE database via PubMed. The Medical Subject Headings (MeSH terms) in English used were "Endometriosis," "Diagnostic Imaging," and "Ultrasonography," in the following search strategy: (Endometriosis) AND (Diagnostic Imaging) OR (Ultrasonography).

RESULTS: The typical ultrasonographic finding of endometrioma is presented as a unilocular or multilocular cyst with homogeneous echogenicity and low echogenicity of its contents. However, it may also present anechoic characteristics, mixed echogenicity, or a "ground glass" appearance. Involvement of the adnexa can be evidenced by adhesions or deep infiltrative endometriosis foci on the tubal walls.

DISCUSSION AND CONCLUSION: Although there are several classic signs, the importance of a scanning protocol for endometriotic lesions is emphasized. Early detection of lesions is crucial to guide the surgical approach and plan a multidisciplinary strategy, which is essential for more accurate diagnosis and to reduce complication rates. Additional efforts are needed to improve physicians' knowledge of imaging criteria for the early detection of this debilitating disease, as endometriosis has a negative impact on women's lives in various stages and aspects.

KEYWORDS: ENDOMETRIOSIS, ENDOMETRIOMA, OVARIES, ULTRASONOGRAPHY, DIAGNOSTIC IMAGING.

INTRODUCTION

Endometriosis is characterized by the presence and development of endometrial stroma and glands outside the uterine cavity, resulting in a chronic inflammatory reaction. The exact cause is still unknown, but its likely etiology is multifactorial, related to early menarche and exposure to steroid hormones, body mass index between late childhood and early adolescence, family history of endometriosis, environmental factors, and lifestyle.[1]

Transvaginal ultrasonography is the non-invasive examination of choice due to its low cost and easy access, as well as its ability to identify both endometriotic lesions and indirect signs of pelvic involvement. It is performed in four stages, not necessarily in this order: evaluation of the uterus and adnexa, assessment of involvement of the pouch of Douglas, evaluation of the anterior and posterior compartments, and identification of "soft markers" (evaluation of ovarian mobility and areas with altered consistency). If any lesion is found, the examination report should include its location, size, distance from the anal verge, and whether it involves the intestines.[2]

Ovarian involvement in endometriosis, known as an endometrioma, is characterized by a cystic lesion with thick, homogeneous content and a "ground glass" appearance. It is important to always be aware of lesions suggestive of endometriomas in the adnexa, as they can cause intense pelvic pain and infertility issues and may also indicate the presence of other endometriotic lesions.[2]

OBJECTIVES

To review, identify, and describe the ultrasonographic characteristics of endometriosis in the ovaries and adnexa.

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METHODS

This is a narrative review focusing on the compilation of images. The database used was MEDLINE via PubMed. The Medical Subject Headings (MeSH terms) in English were "Endometriosis," "Diagnostic Imaging," and "Ultrasonography," in the following search strategy: (Endometriosis) AND (Diagnostic Imaging) OR (Ultrasonography). Studies included (clinical trials, pictorial essays, literature reviews, case reports, among others) addressed the topic, contained ultrasonographic images, met the research objective, and were available online in full text, published in the last five years, in English, Spanish, and Portuguese. A total of 272 articles were found and initially selected through title screening, from which 86 were excluded. Of the remaining 186 articles, 132 were chosen after abstract screening, and 73 were selected based on the presence of ultrasonographic images. Seven of these studies specifically addressed ovarian and adnexal endometriosis and were included in this review (see flowchart - Figure 1).

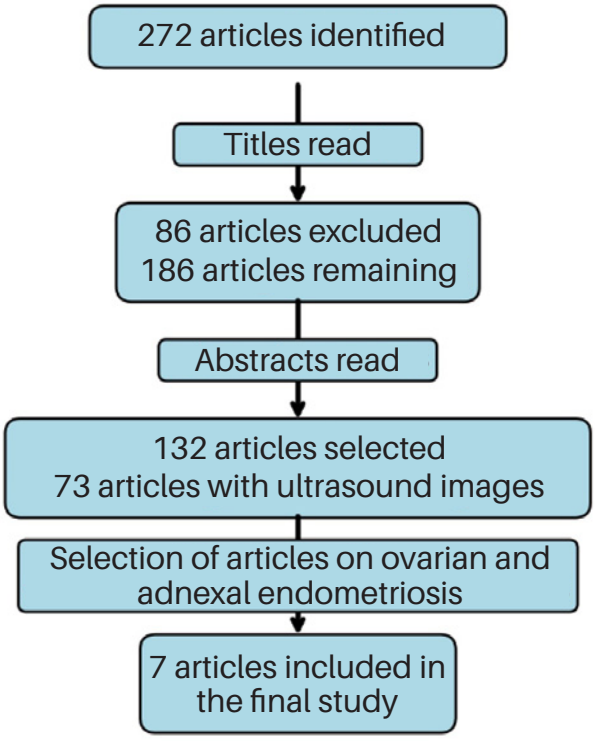

Figure 1. Flowchart - illustrates the article selection process as described.

RESULTS

Table 1 illustrates the selected studies for the research, highlighting the criteria and images used.

Articles	Author	Images Used	Important Data Used
Ultrasound imaging for ovarian and deep infiltrating endometriosis [3].	Exacoustos C, Zupi E, Piccione E. (2017)	4	Imaging characteristics of typical endometriomas: unilocular cyst with ground-glass echogenicity and analysis of the affected adnexa.
The sonographic spectrum of pelvic endometriosis: pearls, pitfalls, and mimics[4].	Jones LP, Morgan MA, Chauhan A. (2019)	1	The "kissing ovaries" sign characterizes the imaging of ovarian endometrioma.
Ultrasound of pelvic pain in the nonpregnant woman[5].	Patel MD, Young SW, Dahiya N. (2019)	1	Diagnostic specificity of using color Doppler in endometriomas.
Complete evaluation of anatomy and morphology of the infertile patient in a single visit: the modern infertility pelvic ultrasound examination[6]	Groszmann YS, Benacerraf BR. (2016)	2	Image analysis with color Doppler of ovarian endometrioma demonstrating internal flow.
Transvaginal US of endometriosis: looking beyond the endometrioma with a dedicated protocol [7].	Collins BG, Ankola A, Gola S, McGillen KL. (2019)	1	Color Doppler analysis of a unilocular endometrioma cyst.
The 'kissing ovaries' sign on ultrasound [8].	Chen F, Cernigliaro J, Desai M, Bhatt S. (2019)	1	Imaging characteristics of severe deep pelvic endometriosis.
Imaging evaluation of fallopian tubes and related disease: a primer for radiologists [9].	Revzin MV, Moshiri M, Katz DS, Pellerito JS, Gettle LM, Menias CO (2020)	1	Analysis of endometriotic implants in the fallopian tubes.

Table 1. Illustrates the main criteria used in the selected studies.

In the ultrasonographic evaluation of the pelvis, it is possible to trace ovarian involvement due to endometriosis, referred to as an endometrioma. Endometriomas are often associated with other lesions, such as deep infiltrative endometriosis and adhesions.[3]

The typical endometrioma can be visualized on ultrasonography as a unilocular or multilocular cyst with homogeneous low-level echogenicity of the cyst content. Alternatively, it may appear as a unilocular cyst with a ground glass echogenicity and no vascularization, or as a unilocular cyst with ground glass appearance, papillary projections, and no flow within the papillary projection, indicating an atypical endometrioma.[3] It is believed that echogenic wall foci occur due to cholesterol deposits.[4]

Figures 2 to 4 present characteristic endometriomas.

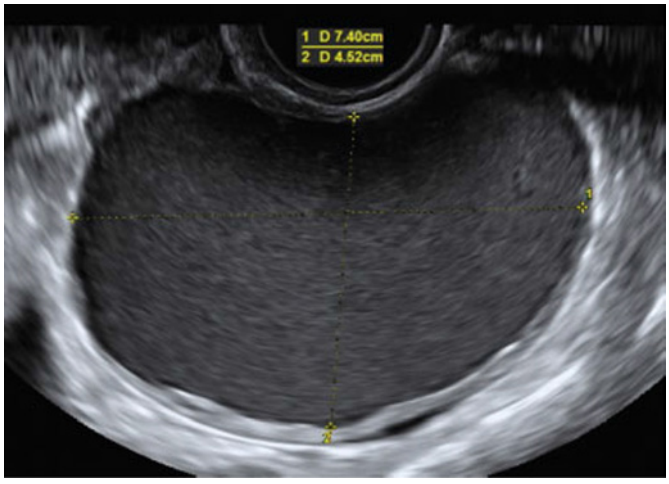

Figure 2: Typical ultrasonographic appearance of an ovarian endometrioma: unilocular cyst with ground glass echogenicity.[3]

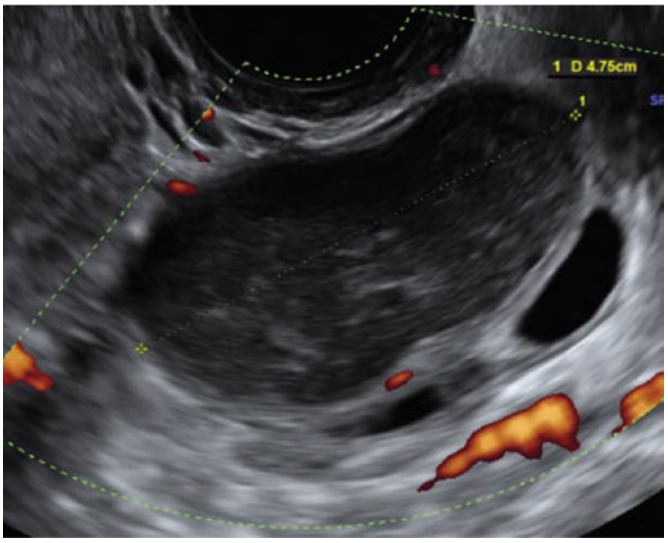

Figure 3: Ultrasonographic appearance of an ovarian endometrioma: a unilocular cyst with irregular ground glass echogenicity due to hyperechoic stripes and no vascularization in the hyperechoic internal tissue, consisting of fibrin densities from the blood content.[3]

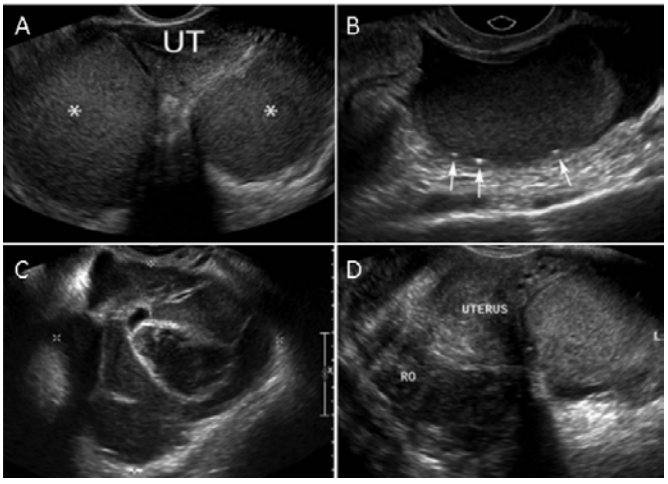

Figure 4: (A) Endovaginal image showing bilateral ovarian endometriomas characterized by diffuse low-level internal echoes. UT, uterus. (B) Endovaginal image of an endometrioma demonstrating diffuse low-level echoes and peripheral echogenic foci. (C) Endovaginal image showing a multilocular endometrioma. (D) Endovaginal image demonstrating bilateral endometriomas with adhesions to the uterus, producing the "kissing ovaries" sign.[4]

Studies show that nearly 50% of analyzed endometriomas had characteristics different from those of a typical endometrioma. Furthermore, the aspects of endometriomas between premenopausal and postmenopausal patients were divergent. In postmenopausal women, solid multilocular tumors and anechoic cyst fluid or cysts with mixed echogenicity were more frequently observed. In contrast, premenopausal women exhibited ground glass echogenicity, one to four follicles, and an absence of detectable blood flow in papillary projections.[3]

Figure 5 presents an endometrioma with a clot or fibrin simulating a papillary projection.

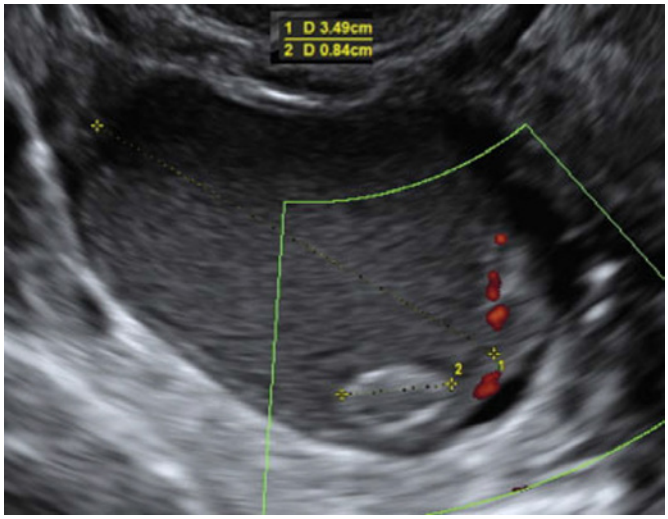

Figure 5: Ultrasonographic image of an atypical ovarian endometrioma: unilocular cyst with ground glass echogenicity, internal papillation (line 2), and absence of vascularization in the papillary projection. This is not true papillation but rather hyperechoic tissue consisting of blood clots or fibrin adjacent to the cyst wall.[3]

Color Doppler is used to demonstrate the absence of flow within the cystic component, which, along with the presence of echogenic wall foci, increases diagnostic specificity.[5] Figures 6 and 7 present endometriomas without flow on Doppler imaging.

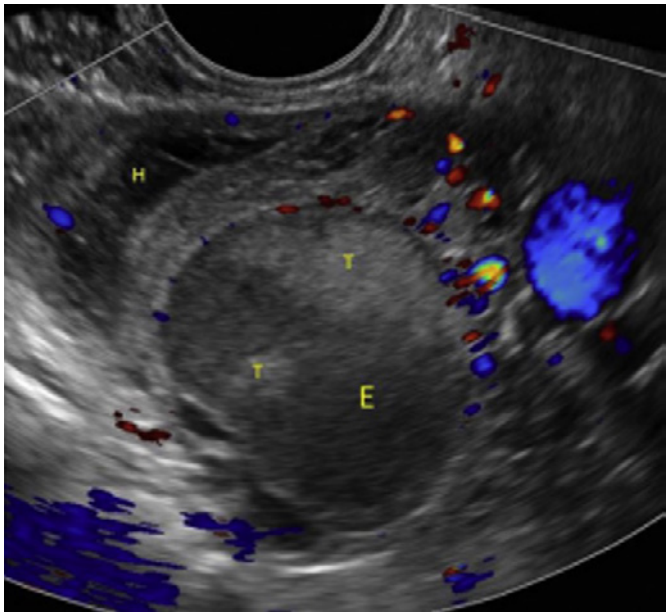

Figure 6: Color Doppler image of an ovarian endometrioma (E) with tumefactive debris (T). A hemorrhagic cyst is also present (H).[6]

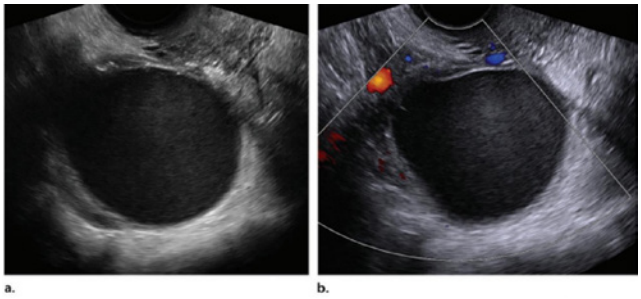

Figure 7: Transverse grayscale (a) and color Doppler (b) showing the presence of a unilocular cyst containing homogeneous low-level echoes and no internal vascularization on color Doppler.[7]

On the other hand, Figure 8 presents an endometrioma with the presence of flow without septation.

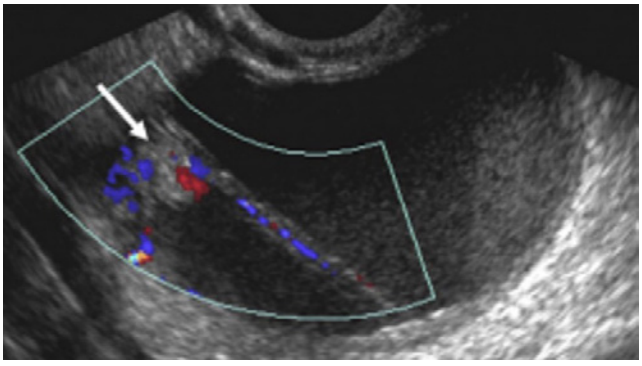

Figure 8: Color Doppler image of an ovarian endometrioma with a nodule and septation demonstrating internal flow (arrow). These nodules may be fibrotic or related to adjacent deformed ovarian parenchyma.[6]

The "kissing ovaries" sign, where the ovaries are juxtaposed, demonstrates the appearance of the ovaries when they are pulled toward the midline, joined due to pelvic adhesions (Figure 9). The imaging techniques that enable this visualization include computed tomography, magnetic resonance imaging, and ultrasonography. This sign can be observed in both pelvic endometriosis and pelvic inflammatory disease, representing an indicator of severity.[8]

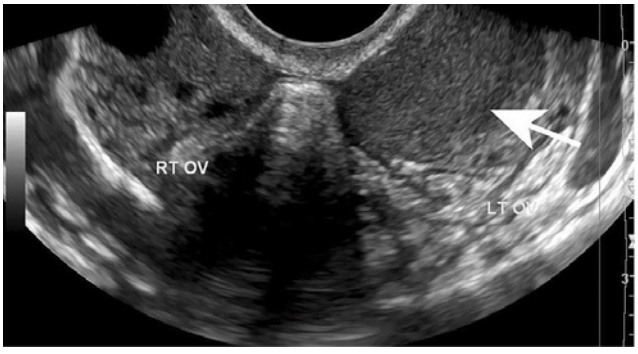

Figure 9: Grayscale transvaginal ultrasound of the pelvis. In the midline, both ovaries (RT OV and LT OV) are in close proximity. A complex cystic lesion is also seen in the left ovary (arrow), with diffuse low-level echoes, representing an endometrioma in this patient with deep pelvic endometriosis.[8]

Uterine tube involvement can occur through adhesions or by foci of deep infiltrating endometriosis of the tubal walls. Endometriosis of the uterine tube is characterized by dilation of the tube, thickening of the walls, and incomplete septa, with dense liquid content resembling an endometrioma, known as hematosalpinx. In cases of tubal obstruction due to adhesions or deep infiltrating endometriosis, with involvement of the distal part and fibrin, there is the presence of hydrosalpinx with a "string of beads" sign, characterized by hyperechoic mural nodules measuring 2-3 mm.[3] Figure 10 presents these characteristics.

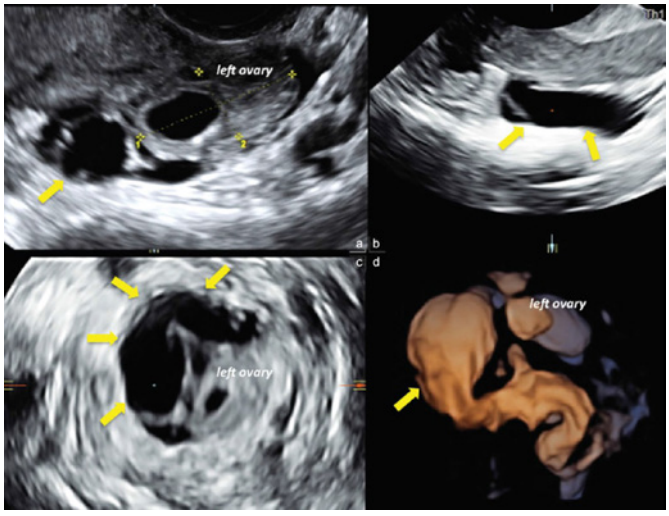

Figure 10: 3D ultrasound with multiplanar view of a hydrosalpinx (yellow arrows) adhered to the left ovary. Presence of a dilated uterine tube with liquid content, thin walls (c), incomplete septa (b), and small hyperechoic mural papulations in the transverse section (a). The 3D volume reconstruction clearly shows the typical flask-shaped tubular structure [3].

Approximately 30% of women with endometriosis have affected fallopian tubes. In these cases, endometriosis can be classified as extraluminal (when the implants are superficial non-invasive peritoneal lesions located on the surface of the serosa of the tubes) or intraluminal (when there is implantation along the mucosa of the tubes).[9]

Bleeding in intraluminal implants can lead to hematosalpinx, and ultrasound and magnetic resonance imaging (MRI) are the best imaging modalities for diagnosis.[9]

On ultrasound, a dilation greater than 5 mm in diameter is observed in the tube, filled with complex fluid. However, its wall does not show signs of thickening or hyperemia.[9] Figure 11 presents a dilated tube with liquid content.

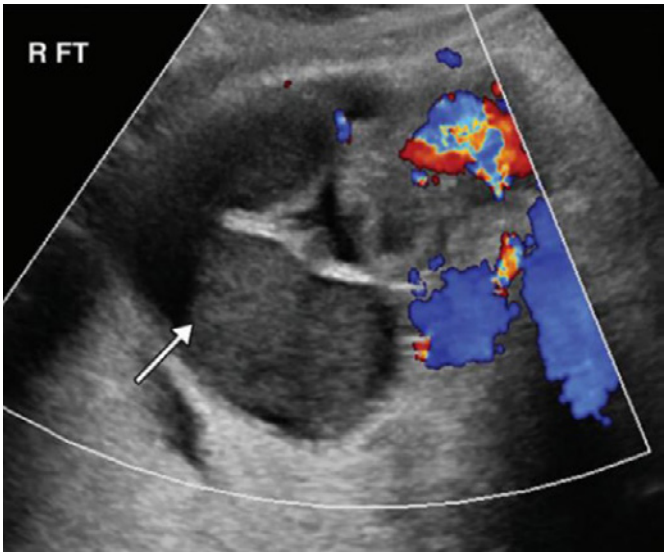

Figure 11: Color Doppler ultrasound shows a dilated tube containing debris and liquid fluid (arrow). Note the absence of thickening of the tube wall or hyperemia.[9]

CONCLUSION

While there are many classic indicators, the examination protocol for identifying endometriotic lesions deserves special attention. Early detection of these lesions is highly recommended, as it assists in choosing the appropriate surgical approach and developing a multidisciplinary team strategy, which is essential for more accurate diagnosis and reducing complication rates.

It is imperative that additional efforts be made to enhance physicians' understanding of imaging criteria for the early detection of this debilitating condition, as endometriosis negatively impacts women's lives in various areas and stages of their lives.

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ORIGINAL ARTICLE

PRENATA L ULTRASOUND DIAGNOSIS OF ICHTHYOSIS - IMAGE COMPILATION

MARIA CAROLINA ROSSI PEGORER[1], LARISSA DA SILVA ALMEIDA[1], BIANCA CHACON DEZOTTI[1], ISABELLA FERREIRA CAPRA[1], REJANE MARIA FERLIN[1], LEONARDO DE SOUZA PIBER[1]

ABSTRACT

INTRODUCTION: Genodermatoses are hereditary diseases that primarily affect the skin and are often associated with increased morbidity and mortality. Ultrasound is commonly used in the prenatal diagnosis of these conditions and can reveal findings that suggest their presence. Ichthyosis, a common genodermatosis, is characterized by skin hardening, a predisposition to infections, respiratory issues, and dehydration. Obstetric ultrasound can show signs such as facial abnormalities, underdeveloped hands and feet, and skin thickening.

OBJECTIVE: This study aims to review, identify, and describe fetal imaging characteristics associated with ichthyosis.

METHODS: This narrative review focuses on compiling images from articles published over the last five years, using the MEDLINE databases via PubMed and Google Scholar. The English MeSH terms used include "Skin Diseases," "Ultrasonography," "Prenatal," and "Prenatal Diagnosis." The search strategy used in Google Scholar was: ((Genodermatosis) AND (Ultrasound)). In the PubMed platform, the search strategy used was: ((Skin Diseases) AND (Ultrasonography, Prenatal) OR (Prenatal Diagnosis)).

RESULTS AND DISCUSSION: In cases of harlequin ichthyosis, the diagnostic hypothesis may arise based on findings such as abnormal extremities, growth restriction, echogenic amniotic fluid, and facial dysmorphisms, including a flat face and a wide mouth with thick lips, observed on three-dimensional ultrasound. Prenatal ultrasound findings in restrictive dermopathy may include a fetus with asymmetric growth restriction, separation of the chorioamniotic membrane, polyhydramnios or oligohydramnios, a small and continuously open round mouth, micrognathia, fixed flexion contractures of the upper limbs, and a varix of the fetal intra-abdominal umbilical vein.

CONCLUSION: Ichthyoses are rare genetic diseases with often poor prognoses. Imaging, being non-invasive and able to detect the disease even in the absence of a family history, plays a crucial role. Therefore, imaging professionals must be familiar with the distinctive imaging characteristics of these conditions, which can be identified through ultrasound. Prenatal ultrasound, especially 3D ultrasound, plays a key role in diagnosis, although the late manifestation of the disease poses challenges for timely detection and treatment.

KEYWORDS: DERMATOSES, GENODERMATOSES, ICHTHYOSIS, PRENATAL DIAGNOSIS, MEDICAL IMAGING.

INTRODUCTION

Fetal medicine is a subspecialty of Gynecology and Obstetrics that aims to promote the health of the mother-fetus duo through diagnostic and therapeutic procedures related to pregnancy. Ultrasound is the primary method used in this field, and through it, other exams, such as guided amniocentesis, can be performed, as well as the diagnosis of diseases like genodermatoses.[1]

Genodermatoses are hereditary, heterogeneous diseases that primarily or exclusively affect the skin [2], and some of them lead to increased morbidity and mortality. The main conditions in this group include epidermolysis bullosa, ichthyotic disorders, and pigmentation disorders, such as oculocutaneous albinism.[3]

Congenital ichthyoses are diseases caused by gene mutations that lead to keratinization disorders, affecting the skin barrier function and, consequently, the ability to protect against external aggressors.[4,5] This condition represents a group of heterogeneous diseases with hereditary genetic disorders. More than 50 genetic mutations involving various essential components for maintaining the epidermal barrier have been described in the literature.

The clinical manifestations include generalized xerosis, areas of scaling, and fissuring. In more severe cases, there can be thermal dysregulation with hypothermia, protein loss that increases nutritional requirements, and frequent infections.[4] This group is divided into various subtypes based on clinical presentation, histopathology, and genetics.[6] The two major subgroups of ichthyoses are non-syndromic, which affect only the skin, and syndromic, which involve both the skin and other organs impacted by the genetic mutation.

Non-syndromic ichthyoses can also be subdivided into different groups, which include vulgar ichthyosis, X-linked

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ichthyosis, autosomal recessive congenital ichthyoses, and keratinopathic ichthyoses. A severe form of autosomal recessive congenital ichthyosis is known as harlequin ichthyosis, characterized by a shiny membrane that envelops the fetus and peels off after birth. As new types of ichthyoses are discovered through advances in genetics, it becomes possible to address the specific mutation involved.[4]

Among the ichthyoses, vulgar ichthyosis is the most common form, with an incidence of 1 in 250 births, compared to X-linked ichthyosis, which has an incidence of 1 in 2,500 births and is more prevalent in males. Bullous ichthyosis of Siemens has an even lower prevalence, affecting fewer than 1 in 1,000,000 individuals.[7] Finally, in addition to being a severe and rare form, harlequin ichthyosis can be associated with serious complications and has a mortality rate of 5% in cases.[4]

Prenatal diagnosis for patients with hereditary conditions can be an important aspect of medical care, providing the opportunity to address potential problems in a timely manner. For the families of affected children, prior knowledge can facilitate better psychological and financial preparation, as well as guidance during the pregnancy.[3] Prenatal diagnosis is recommended for those fetuses at increased risk of developing genodermatoses. As this is a group of hereditary diseases, indications for prenatal diagnosis include having an affected family member or a previously affected child.[2,3]

In the past, when searching for prenatal diagnosis of genodermatoses, the only option available was fetal skin biopsy, an invasive procedure performed late in pregnancy, between 15 and 22 weeks of gestation. Subsequently, with the advent of new techniques, the fetoscope was phased out, and the procedure began to be guided solely by ultrasound. Currently, this examination is rarely used and has been replaced by fetal DNA analysis; however, in some situations, it remains an option, such as when DNA data are insufficient, like when the mutation cannot be identified or the causative gene is unknown.[2,3,8]

Over the years, with advances in medicine and the discovery of genes, DNA-based prenatal diagnosis has become a reality in clinical practice. However, invasive techniques for obtaining fetal cells remain necessary, such as amniocentesis, which is the most commonly used invasive procedure for prenatal diagnosis in the second trimester of pregnancy. Being invasive, it can lead to complications such as amniotic fluid leakage, vaginal bleeding, and the risk of fetal loss, which has drastically decreased over the years (to 0.5%).[3,8] On the other hand, chorionic villus sampling (CVS), which aspirates tissue from the placenta, is performed under ultrasound guidance using either a transcervical or transabdominal approach. This procedure has the advantage of being performed early in the pregnancy and presents a risk of fetal loss comparable to that of amniocentesis.[8]

Ultrasound is the most commonly used examination in prenatal diagnosis and has been utilized as an auxiliary method in the diagnosis of genodermatoses. In addition to the benefit of being non-invasive, it has the capacity to detect abnormalities in the absence of any family history. Some ultrasound findings during pregnancy may be suggestive of certain genodermatoses. For instance, the presence of pyloric atresia along with other features such as ureteral stenosis, arthrogryposis, and deformities of the nose or ear can raise suspicions of epidermolysis bullosa. In the case of harlequin ichthyosis, the hypothesis may arise from abnormal extremities, growth restriction, echogenic amniotic fluid, and facial dysmorphisms, including a flat face and a wide mouth with thick lips, which can also be visualized on three-dimensional ultrasound.[3,8]

OBJECTIVES

Revising, Identifying, and Describing the Imaging Characteristics of Fetal Genodermatoses.

METHODS

This is a narrative review with an emphasis on the collection of images. The databases used were MEDLINE via PubMed and Google Scholar. Studies were included (clinical trials, pictorial essays, literature reviews, case reports, among others) that address the topic, contain images from diagnostic methods, are in line with the research objective, and are available online in full text, published in the last five years, in English, Spanish, and Portuguese. The health descriptors (MeSH terms) in English are "Skin Diseases," "Ultrasonography," "Prenatal," and "Prenatal Diagnosis." The following search strategy was used in Google Scholar: ((Genodermatosis) AND (Ultrasound)). A total of 791 articles were found, which were initially selected by reading the titles, with 318 being excluded. Of the remaining 473 articles, 187 were chosen by reading the abstracts, and 33 were selected based on the presence of an ultrasonographic image, three of which specifically addressed ichthyoses and were used in this study. On the PubMed platform, the following search strategy was used: ((Skin Diseases) AND (Ultrasonography, Prenatal) OR (Prenatal Diagnosis)). A total of 4,087 articles were found, which were initially selected by reading the titles, with 3,254 being excluded. Of the remaining 833 articles, 196 were chosen by reading the abstracts, and six were selected based on the presence of an ultrasonographic image, two of which specifically addressed ichthyoses and were used in this study. The flowchart below illustrates the selection of the articles (figure 1).

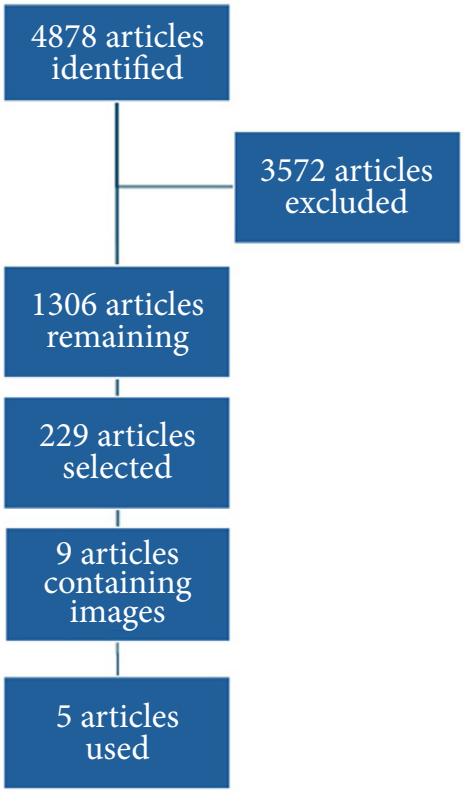

Figure 1. Flowchart illustrating the selection of articles.

RESULTS AND DISCUSSION

Table 1 illustrates the selected studies for the research, highlighting the criteria and images used.

Articles	Author	Images Used	Important Data Used
Prenatal diagnose of a fetus with Harlequin ichthyosis in a Chinese family.[9]	Jian W, Du Q, Lai Z, Li Y, Li S. (2018)	3	Ultrasonographic findings of fetal facial anomalies.
Harlequin ichthyosis – a disturbing disorder.[10]	Harish MR, Bhadbhade SP, Shashikumar BM, Deepadarshan K. (2018)	-	Various descriptions of possible alterations observed in obstetric ultrasound that contribute to diagnostic identification.
Recurrent case of a rare and devastating entity: Harlequin Ichthyosis.[11]	Alkiliç A (2019)	-	Use of 3D ultrasonography for the identification of late phenotypic expression.
Ichthyosis Prematurity Syndrome: a rare form but easily recognizable ichthyosis.[12]	Al-Khenaizan S, AlSwailem A, AlBalwi MA. (2021)	-	Identification of ichthyosis prematurity syndrome through the separation of the chorionic and amniotic membranes and polyhydramnios.
Prenatal diagnosis for restrictive dermopathy caused by novel mutations in ZMPSTE24 gene and review of clinical features and pathogenic mutations described in literatures.[13]	Wang Y, Liu C, Mai M, Ding H, Huang Y, Zhang Y, Zhao X, Du L, Xiong Y, Geng J, Yin A. (2020)	4	Ultrasonographic findings of alterations in limbs with fixed flexion and abdominal vascular alterations.

Table 1. Illustrates the main criteria used in the selected studies

Common clinical manifestations of harlequin ichthyosis include hardening of the skin's surface, which compromises the regulation of body temperature due to difficulty in water loss and increases the risk of infections. Additionally, respiratory alterations and dehydration are common.[9]

In obstetric ultrasonography, alterations such as changes in the morphology of the nasal bone or absent nose, ectropion, cleft lip, dysplastic ears, hypoplastic fingers of the hands and feet, curved toes, clenched fists, fetal growth restriction, polyhydramnios, and thick skin can be observed. Morphological ultrasonography confirms the changes found in the initial and routine obstetric ultrasound.[9,10]

In Figures 2 to 4, the following characteristics related to harlequin ichthyosis are observed: eyelid eversion, a large and open mouth, and abnormal facial features.

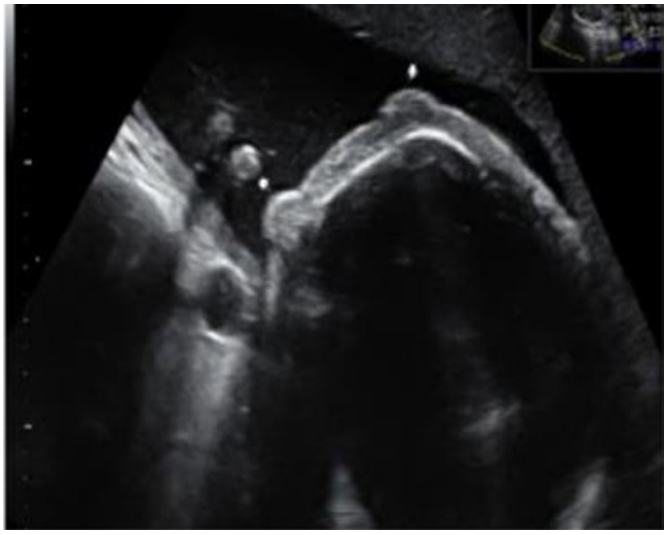

Figure 2. Two-dimensional ultrasonography – eyelid eversion of the fetus[9].

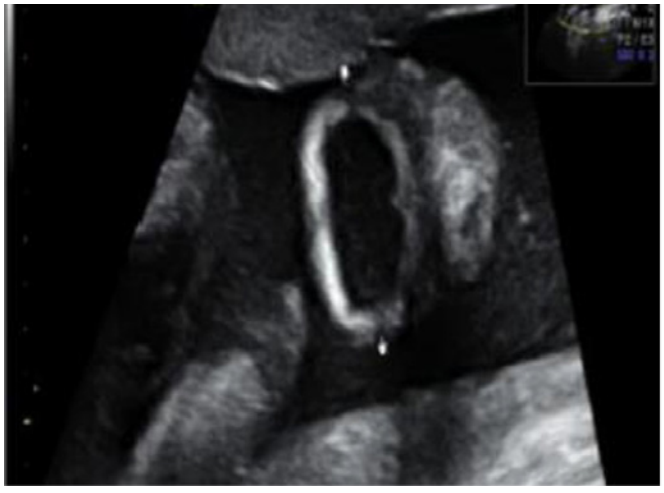

Figure 3. Two-dimensional ultrasonography – fetus with a large and open mouth[9].

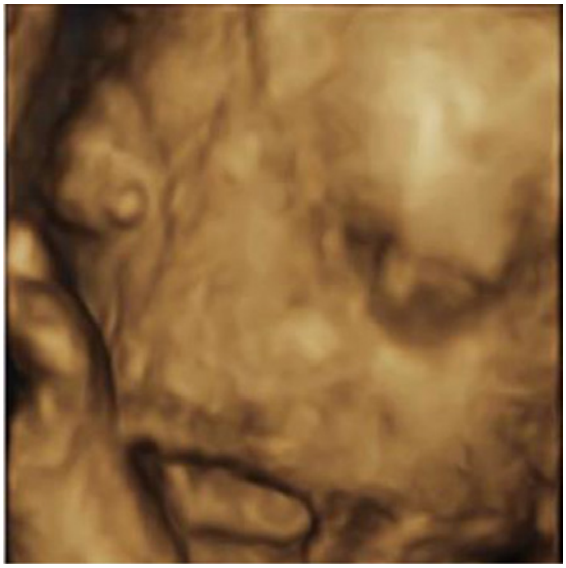

Figure 4. Three-dimensional ultrasonography – abnormal facial features [9].

Prenatal ultrasonography, especially 3D ultrasound, is a modality for prenatal diagnosis. However, despite having many distinct signs in the examination, such as short limbs, open mouth, joint contractures, edema of the hands and feet, and cloudy amniotic fluid, the late phenotypic expression of the disease poses a challenge for both timely detection and further treatment – Figure 4. [11]

In ichthyosis prematurity syndrome, another type of genodermatosis, prenatal ultrasonography may reveal separation of the chorionic and amniotic membranes and polyhydramnios with a starry sky appearance.[12]

Prenatal ultrasonography findings in restrictive dermopathy may include a fetus with asymmetric growth restriction, separation of the chorioamnionic membrane, polyhydramnios or oligohydramnios, a small continuously open round mouth, micrognathia, fixed flexion contractures of the upper limb, and varicosity of the fetal intra-abdominal umbilical vein. These findings are characterized in Figures [5-8.13]

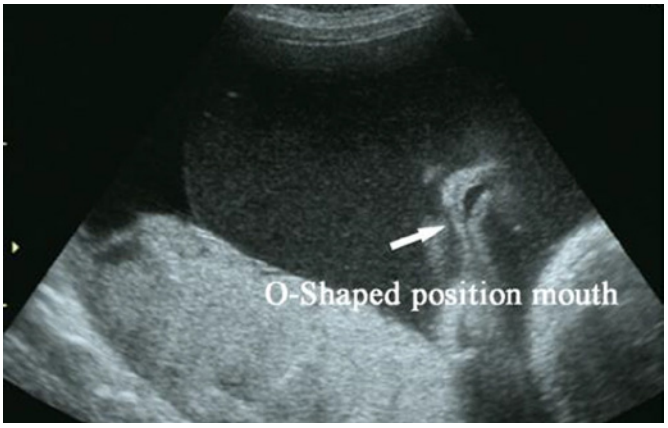

Figure 5. Ultrasound showing an open mouth in the shape of an "O". [13]

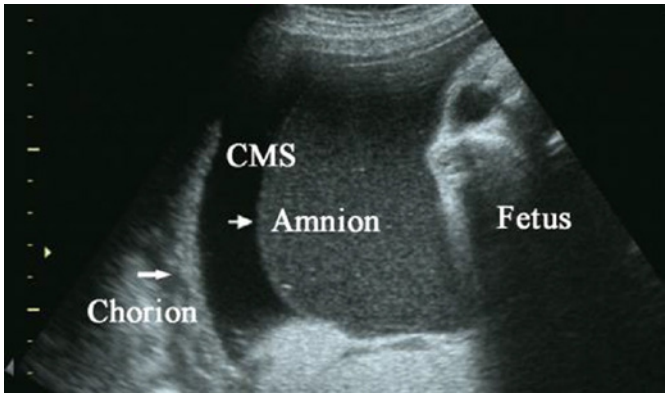

Figure 6. Ultrasound showing separation of the chorioamnionic membrane and polyhydramnios[13].

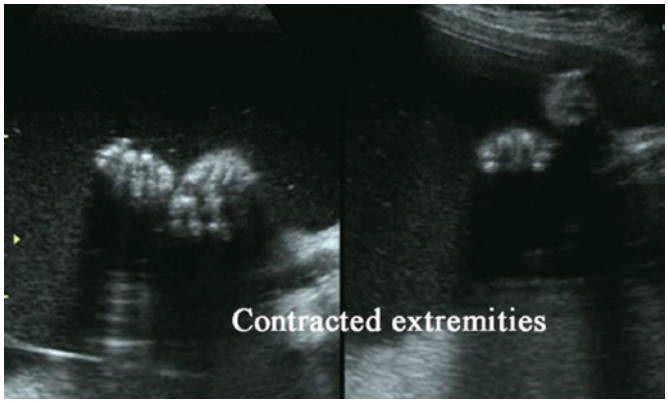

Figure 7. Ultrasound showing fixed flexion contractures of the upper limbs[13].

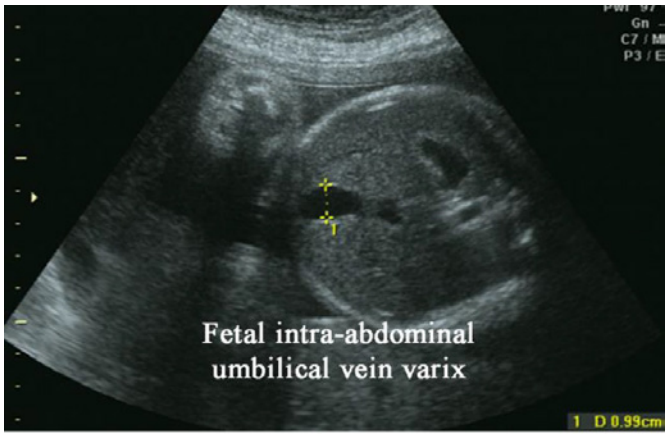

Figure 8. Ultrasound showing varicosity of the fetal intra-abdominal umbilical vein (dilation of 9.9 mm)[13].

CONCLUSION

Ichthyoses are rare genetic diseases that generally have a poor prognosis. Due to their intrauterine presentation, imaging diagnosis contributes significantly and continues to be the preferred method, offering the benefit of being non-inva-

sive and capable of detecting the disease without any family history. Therefore, it is essential for the imaging specialist to have knowledge about the pathology and, especially, about its characteristic findings identified through ultrasonography. Including the parameters of these dermatopathies in routine prenatal care is extremely important for effective screening. Consequently, due to the scarcity of studies on the subject, diagnosis often occurs late, worsening the prognosis for the fetus and increasing the family's suffering.

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CASE REPORT

DIAGNOSTIC AND PROGNOSTIC IMPLICATIONS OF AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE IN PRENATAL CARE: CASE STUDY AND CLINICAL CONSIDERATIONS

VINICIUS CAPELLARI GABANA[1], LUÍSA RIGON BORBA[1], YASMIN RICARTE HASS LOPES[1], ANDRÉ CAMPOS DA CUNHA[1], RAFAEL ROSA[1], JORGE ALBERTO BIANCHI TELLES[2]

ABSTRACT

INTRODUCTION: Autosomal recessive polycystic kidney disease (ARPKD) is the most frequently observed cystic kidney disease in the prenatal period. Our objective was to describe the prenatal findings of a fetus diagnosed with ARPKD, highlighting their importance for the diagnosis, management, and prognosis of patients.

CASE REPORT: The patient was a 16-year-old primigravida whose husband was consanguineous. She was referred for evaluation due to multicystic dysplastic kidneys in the fetus. The examination at 22 weeks revealed enlarged, hyperechoic dysplastic kidneys with cysts, associated with oligohydramnios. The ultrasound at 31 weeks showed reduced thoracic circumference and apparent pulmonary hypoplasia. Fetal magnetic resonance imaging (MRI) revealed similar findings, consistent with ARPKD. The child was born with Potter's facies and a severely distended abdomen, and passed away after birth due to respiratory dysfunction.

DISCUSSION: Prenatal identification through ultrasound of the renal characteristics associated with oligohydramnios was crucial for the diagnosis of ARPKD, especially in light of various differential diagnoses. Data from the clinical history and the results of the MRI evaluation were also important for confirming the diagnosis. Additionally, other findings, such as reduced thoracic circumference, assisted in the planning of the birth and determining the severity of the prognosis.

CONCLUSION: Our report highlights the importance of prenatal evaluation through ultrasound for the detection of findings that play a crucial role in both the diagnosis of ARPKD and its management and prognosis.

KEYWORDS: AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE; PRENATAL DIAGNOSIS; OLIGOHYDRAMNIOS; CLINICAL MANAGEMENT; PROGNOSIS.

INTRODUCTION

Polycystic kidney disease is a genetic condition that can follow either an autosomal dominant or autosomal recessive inheritance pattern. However, both forms are characterized by the presence of multiple renal cysts and are classified as ciliopathies due to the abnormal structure and function of cilia (organelles present on the apical surface of almost all epithelial cells and many endothelial cells), which contribute to cystic cell proliferation, fluid secretion, and changes in the extracellular matrix [1,2].

These conditions can be detected in the prenatal period through the identification of characteristic ultrasound findings. Additionally, these findings allow for the differentiation between adult disease, which follows a dominant pattern, and childhood disease, which has an autosomal recessive pattern. The latter is more commonly known as autosomal recessive polycystic kidney disease (ARPKD) and is the most frequently observed cystic kidney disease in the intrauterine period [3].

Thus, the aim of this report was to describe the prenatal findings of a fetus diagnosed with ARPKD, emphasizing their importance for determining not only the diagnosis but also the management and prognosis of patients.

CASE REPORT

The patient was a 16-year-old woman in her first pregnancy. She was referred to the fetal medicine service after an ultrasound showed a fetus with evidence of multicystic dysplastic kidneys. The husband was consanguineous, a first-degree cousin. In the second-trimester ultrasound at 22 weeks of gestation, dysplastic kidneys were observed, enlarged in

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size (the right kidney measured 6.1 x 3.2 x 3.2 cm, with a volume of 33.1 cm³, and the left kidney measured 5.7 x 3.5 x 3.3 cm, with a volume of 34.2 cm³), hyperechoic with multiple cysts inside, showing poor corticomedullary differentiation and associated with the presence of oligohydramnios (Fig. 1).

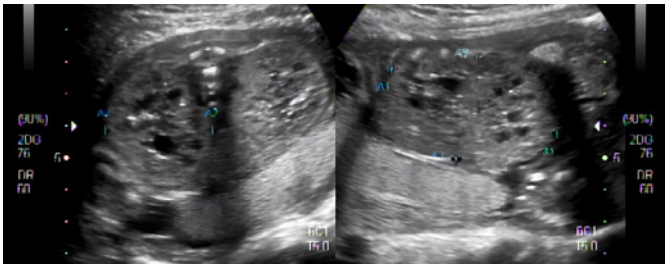

Figure 1. Two-dimensional ultrasound images taken at 22 weeks of gestation, showing the appearance of the kidneys, which are dysplastic and enlarged, as well as hyperechoic, with multiple cysts inside and poor corticomedullary differentiation.

Fetal echocardiography was normal. The fetal karyotype, obtained through cordocentesis, revealed a normal male chromosomal constitution (46,XY). The ultrasound performed at 31 weeks of gestation also showed reduced thoracic circumference associated with apparent pulmonary hypoplasia.

Fetal magnetic resonance imaging (MRI) revealed findings similar to those observed in the ultrasound evaluation, which were consistent with the diagnosis of ARPKD (Fig. 2).

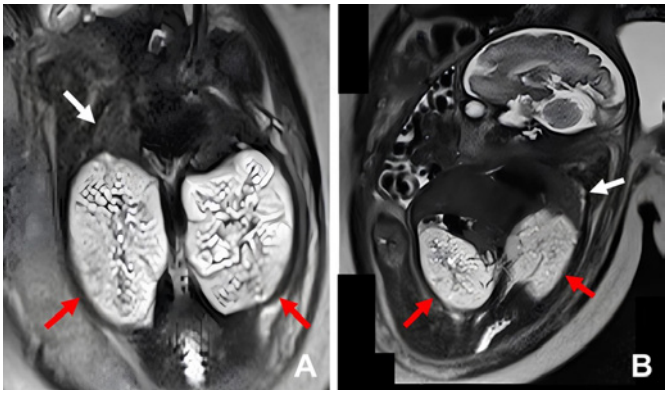

Figure 2. Appearance of the kidneys as seen through fetal magnetic resonance imaging. Note the similarity to the findings observed in the ultrasound examination. The red arrows indicate the kidneys, and the white arrows indicate the lungs, which appear hypoplastic based on their size (A and B).

The child was born via cesarean section, at term, weighing 3,130 g, with an Apgar score of 2 at both one and five minutes. Upon evaluation of the newborn, Potter's facies were observed (flattened face with prominent infraorbital grooves, micrognathia, and low-set ears), as well as a severely distended abdomen. The infant developed severe respiratory dysfunction and passed away a few hours after birth.

DISCUSSION

The assessment of fetal anatomy in the second trimester of pregnancy through ultrasound is an essential tool for diagnosing various congenital defects, with approximately 20% of these related to renal anomalies. One of the most suggestive findings of ARPKD is the presence of renal cysts, usually small (1-2 mm in diameter), detected between 21 and 24 weeks of gestation. The quantity and size of the cysts are important factors for diagnosis. Although hepatic involvement is characteristic of ARPKD, it is generally not detected before birth. Other relevant ultrasound findings include enlarged kidneys and reduced amniotic fluid volume, indicating renal dysfunction. The dilation of renal tubules also causes renal hyperechogenicity, and the fetal bladder may be small or not visualized due to low urine production [3-5].

In this case, fetal MRI complemented the ultrasound findings, confirming the diagnosis of ARPKD. MRI is particularly useful in situations of oligohydramnios, anhydramnios, maternal obesity, or poor fetal positioning, which can hinder the visualization of the kidneys and urinary tract [6].

The differential diagnosis of ARPKD includes various conditions involving renal cysts, such as Autosomal Dominant Polycystic Kidney Disease (ADPKD) and multicystic dysplastic kidneys. ARPKD may resemble Meckel-Gruber syndrome, but the latter presents additional characteristics, such as occipital encephalocele and postaxial polydactyly[4-6].

Fetal karyotyping was performed not to confirm ARPKD, as this is a genetic condition, but to exclude chromosomal abnormalities, such as those seen in trisomies of chromosomes 13 and 18, which can also be associated with cystic kidneys. Cordocentesis was chosen due to the presence of anhydramnios. Fetal echocardiography was conducted to rule out congenital heart defects, which are common in chromosomal syndromes [6].

ARPKD is a severe cystic kidney disease that can also affect the liver and biliary tract, with an estimated incidence of 1 in 20,000 births. It is caused by mutations in the PKHD1 gene, located on chromosome 6p12.3-p12.2. The mutations are generally unique to each family, complicating genotype-phenotype correlations and the implementation of direct diagnostic testing [3,7].

As an autosomal recessive condition, ARPKD can be associated with parental consanguinity and a history of affected siblings, although the absence of these factors does not exclude the diagnosis. Accurate diagnosis is essential for genetic counseling and determining the risk of recurrence, which is 25% for future children of the couple[4,8].

Furthermore, genetic counseling should address the prognosis and management of the pregnancy. In cases of Potter's sequence, such as in our patient, the prognosis is severe, with a high rate of extrauterine mortality. In less severe situations,

family counseling through birth planning and preparation for neonatal interventions, such as dialysis and mechanical ventilation, is essential [6,9].

In cases of ARPKD, the disease itself is not always present in the prenatal period; however, its early expression during this time is considered a factor for poor prognosis. The presence of oligohydramnios or anhydramnios is the most impactful finding in determining survival [4]. Additionally, reduced thoracic circumference is associated with pulmonary hypoplasia, which is common in these cases, usually secondary to the reduction or absence of amniotic fluid (oligohydramnios or anhydramnios). This is due to the absence of fetal urine production resulting from renal impairment, leading to fetal constriction and Potter's sequence, with findings such as facial flattening, prominent infraorbital grooves, and low-set ears (Potter's facies), as well as deformities with contractures or arthrogryposis of the limbs and pulmonary hypoplasia [1,2].

Pulmonary hypoplasia, secondary to oligohydramnios, is the leading cause of postnatal death, accounting for approximately 30% of deaths shortly after birth. However, neonatal survival has improved in cases with less severe renal impairment and absence of oligohydramnios [1,4,7].

Thus, the prenatal identification of these findings in suspected cases of ARPKD can be used as a tool for predicting perinatal risk and long-term prognosis [4].

CONCLUSION

This report highlights the importance of ultrasound in the prenatal diagnosis of ARPKD, allowing for the identification of renal and gestational findings that suggest the condition, even among various cystic kidney diseases. Clinical data and supplementary tests, such as MRI, also contribute to confirming the diagnosis. Additional examinations, such as karyotyping and fetal echocardiography, are useful in the differential diagnosis. Findings like oligohydramnios and reduced thoracic circumference are relevant for birth planning and prognosis determination.

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CASE REPORT

ALLANTOIC CYST ASSOCIATED WITH OBSTRUCTIVE UROPATHY: A CASE REPORT WITH SPONTANEOUS PRENATAL REGRESSION

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ABSTRACT

INTRODUCTION: The allantoic cyst is a dilation that occurs due to inadequate regression and closure of the urachus. Our objective was to describe the prenatal findings of a fetus presenting with an allantoic cyst and evidence of obstructive uropathy that progressed with spontaneous regression still in the second trimester.

CASE REPORT: The patient was a 17-year-old pregnant woman whose obstetric ultrasound at 16 weeks revealed a cord cyst measuring 2.3 cm in diameter, communicating with a dilated fetal bladder. The "keyhole sign" was observed, indicating possible urethral obstruction. One month later, dilation of both renal pelvises was also noted. At 24 weeks, the cyst was no longer visible, and the bladder dimensions were normal, which also occurred with the renal pelvises by 35 weeks. The child was born asymptomatic, with no persistence of the urachus.

DISCUSSION: There is a hypothesis that allantoic cysts may form due to increased pressure in the urinary tract caused by an obstruction, as seemingly observed in our case. It is noteworthy that both cases exhibited spontaneous and early involution compared to descriptions in the literature, possibly due to cyst rupture or resolution of the cause of the obstruction.

CONCLUSION: The diagnosis and description of the evolution of allantoic cysts during pregnancy are rare. They tend to exhibit spontaneous involution, but not as early as in our case, which may have occurred due to cyst rupture or natural resolution of fetal urinary obstruction.

KEYWORDS: CYSTS; UMBILICAL CORD; PRENATAL DIAGNOSIS; ULTRASOUND; SPONTANEOUS REMISSION.

INTRODUCTION

Umbilical cord cysts are relatively rare, with a prevalence ranging from 0.4% to 3.4% in the first trimester of pregnancy. These cysts can be classified into pseudocysts, which are more common and sometimes associated with chromosomal anomalies, and true cysts, which are less frequent and typically located near the fetal insertion of the umbilical cord [1].

The allantoic cyst is characterized by being a dilation caused by inadequate regression and closure of the urachus [2]. Some cases are associated with obstructive uropathy, leading to the hypothesis that the emergence of these cysts may occur due to increased pressure in the urinary tract caused by obstruction. However, its etiology is not yet fully understood [3].

Significant advances in the development of high-resolution ultrasound equipment have allowed for more accurate diagnoses of various types of fetal anomalies, including allantoic cysts present in the umbilical cord 1. Furthermore, this examination, being highly sensitive, has enabled the identification of detailed characteristics of these cysts, which can further assist in their diagnostic confirmation [4]. Although many allantoic cysts may spontaneously disappear during the prenatal period, possibly due to rupture, this resolution can result in the presence of a patent urachus after birth, often necessitating surgical intervention. However, the clinical significance and natural history of allantoic cysts are still underreported in the literature, as well as not fully understood [1].

In light of this, our objective was to describe the case of a fetus diagnosed with an allantoic cyst associated with obstructive uropathy, which exhibited spontaneous resolution. Additionally, we will discuss issues related to its diagnosis and origin, as well as its evolution.

CASE REPORT

The patient was a 17-year-old pregnant woman in her third pregnancy, with a prior history of two spontaneous miscarriages. She was referred at 16 weeks and 2 days of gestation due to a collection of fluid, with a thick wall, adhered to the fetal abdominal wall, of unclear etiology, associated with a possible posterior urethral stenosis.

The ultrasound performed at this stage of pregnancy in our service showed the presence of a cyst located in the umbilical cord, measuring 2.3 cm in diameter (Fig. 1A), along

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with bladder dilation, thickening of its wall, and evidence of the "keyhole sign," indicative of urethral obstruction (Fig. 2B). The renal pelvises were of normal size (the right measured 3.5 mm and the left 3.8 mm) (Fig. 2A). The examination performed at 18 weeks and 2 days showed similar findings.

The fetal karyotype, obtained through amniocentesis, was normal (46,XY). The ultrasound examination performed one month later showed an umbilical cord with three vessels and the presence of a cyst inside, measuring 2.7 cm in diameter (Fig. 1B). There was dilation of the renal pelvises (the right measured 6.8 mm and the left 6.6 mm) (Fig. 2C). Additionally, communication between the bladder and the allantoic cyst was visualized through the urachus (Fig. 2D). The amniotic fluid was found to be of normal volume.

In the ultrasound evaluation at 24 weeks and 2 days of gestation, the cyst in the umbilical cord was no longer visible. There was only a coiling of the umbilical cord near the abdominal wall (Fig. 1C). Additionally, the bladder had a normal shape and dimensions (Fig. 2F). The renal pelvises measured 6.0 mm on the right and 5.0 mm on the left (Fig. 2E).

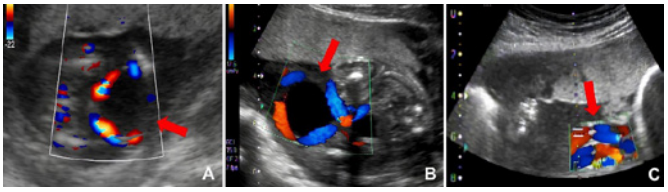

Figure 1. Two-dimensional ultrasound images using Doppler, showing the allantoic cyst (red arrows) at 16 weeks and 2 days (A), and at 21 weeks and 2 days (B). Note that at 24 weeks and 2 days, the cyst was no longer visible, and there was a coiling of the umbilical cord near the abdominal wall (red arrow) (C).

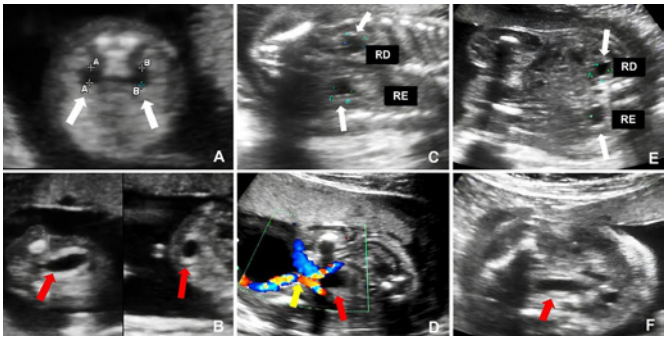

Figure 2. Images of the fetal urinary tract observed through two-dimensional ultrasound at different stages of gestation.

In the ultrasound examination at 26 weeks and 4 days, there was also a reduction in the size of both renal pelvises. The fetal echocardiogram with Doppler did not reveal any anomalies. At 35 weeks, the amniotic fluid index (AFI) was normal. The ultrasound performed near the end of the pregnancy, at 37 weeks, also showed no abnormalities.

The child was born via cesarean section at 37 weeks and 5 days of gestation, weighing 3,150 grams, with Apgar scores of 9 and 10 at one and five minutes, respectively. He was asymptomatic, with no signs of patent urachus or urethral obstruction. His renal function was normal.

DISCUSSION

Despite recent advances in imaging diagnosis, the prenatal description of allantoic cysts remains rare in the available literature [1,4,5]. Reports detailing their evolution, such as in the present case, are even less common [6].

From a diagnostic perspective, as observed in our report, two-dimensional ultrasound with Doppler is sufficient to identify the cyst. Important findings include the visualization of the cyst within the umbilical cord, among the vessels, and the identification of a communication with the fetal bladder [4]. Complementary examinations, such as fetal echocardiography, were crucial in excluding associated malformations.

Allantoic cysts tend to occur in isolation. However, the literature describes associations with other fetal anomalies, such as omphalocele, hypospadias, and Meckel's diverticulum [7], as well as chromosomal abnormalities like the microdeletion involving the 1q21.1q21.2 region [8]. Although the relationship with chromosomal alterations, such as trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome), is stronger in cases of umbilical cord pseudocysts 1, this finding reinforces the importance of laboratory tests, such as karyotyping and microarray (array-CGH), in cases of allantoic cysts [8,9].

In our case, ultrasound revealed findings suggestive of obstructive uropathy at the urethral level, which spontaneously resolved during gestation. The karyotypic analysis did not reveal any chromosomal abnormalities, but it does not exclude the possibility of microscopic alterations, such as microdeletions or microduplications, that may not be detected by this examination. These alterations can be identified using molecular cytogenetic techniques, such as FISH or array-CGH [10].

Allantoic cysts typically increase in size before resolving spontaneously, suggesting rupture before birth [1]. In the present case, we believe that the resolution occurred due to cyst rupture, as suggested in the literature [1], since the cyst slightly enlarged before disappearing. This may have resulted in the formation of a fistula, decompressing the urinary tract by allowing fetal urine to extravasate into the amniotic space.

Another hypothesis is that the resolution occurred due to decreased pressure in the urinary tract, resulting from the spontaneous resolution of the obstruction [4]. This assumption is supported by the absence of signs of obstructive uropathy after birth, such as the presence of a posterior urethral valve [4].

Allantoic cysts in the umbilical cord are often associated with patent urachus, a condition that typically requires surgical treatment [1]. The usual postnatal approach is surgical resection [5]. However, in our case, there was spontaneous resolution of the cyst during the second trimester, earlier than what is normally reported, which may explain the absence of patent urachus after birth. It is also noteworthy that, despite the signs of obstructive uropathy during gestation, the newborn's renal function

was preserved, avoiding complications such as the need for dialysis or kidney transplantation. This may be related to the early resolution of the signs of obstruction, as observed during pregnancy.

Infections are the primary complications associated with allantoic cysts [2]. Other possible consequences include prematurity, the formation of fistulas, abscesses [5], and, rarely, progression to malignancy [2].

CONCLUSIONS

The diagnosis and description of the evolution of allantoic cysts during pregnancy are rare. While they generally occur in isolation, some cases are associated with chromosomal anomalies or malformations, particularly urinary tract obstructions. These cysts tend to resolve spontaneously, but the early resolution observed in this case may have occurred due to cyst rupture, leading to fistula formation, or due to the spontaneous resolution of the urinary obstruction. This may have contributed to the absence of patent urachus after birth, as well as to the preservation of renal function.

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CASE REPORT

FETAL INTRAPERICARDIAL TERATOMA: A CASE REPORT

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ABSTRACT

INTRODUCTION: Primary cardiac tumors, including teratomas, are rare and usually diagnosed either intrauterine or postnatally. Intrapericardial teratoma is the second most common benign cardiac tumor in fetuses and can cause complications such as cardiac tamponade and fetal hydrops, leading to death. This report describes a rare case of fetal intrapericardial teratoma detected by ultrasound in a high-risk maternity unit.

CASE REPORT: A 32-year-old pregnant woman was diagnosed with a 32mm mediastinal mass, associated with pericardial effusion, mediastinal shift, and risk of hydrops. The patient was referred to another hospital for pericardiocentesis and tumor sclerosis procedures. Despite these attempts, the fetus developed hydrops and, after delivery by cesarean section, died due to pulmonary hypoplasia.

DISCUSSION: Early fetal diagnosis of cardiac tumors has become more accurate with advancements in imaging techniques. Intrapericardial teratomas are rare tumors that can lead to cardiac compression and fetal death. Early diagnosis is crucial for proper management, allowing interventions such as pericardiocentesis or surgical resection. Fetal surgery is a therapeutic option when available and performed before hydrops develops.

CONCLUSION: Early management and fetal surgery could have changed the prognosis in this case. Prompt referral to specialized centers is essential to improve perinatal outcomes.

KEYWORDS: INTRAPERICARDIAL TERATOMA, FETAL MEDICINE, FETAL CARDIAC TUMOR, PERICARDIOCENTESIS, HYDROPS, FETAL SURGERY.

INTRODUCTION

Primary cardiac tumors are rare diagnoses, typically made intrauterine or during the postnatal period. According to Tagliati et al.[1], these tumors are diagnosed in childhood or the fetal stage as multilocular intrapericardial lesions with cystic and solid components, typically located near the root of the pulmonary artery or aorta. According to Camargo et al.[2], they have an incidence of 0.009% in low- and high-risk ultrasound screenings. Approximately 90% of these tumors are benign and fall into five histological types: rhabdomyomas, teratomas, fibromas, hemangiomas, and hamartomas[2]. Rhabdomyoma is the most common among the benign histological types, accounting for 60-86% of cases, while teratoma is the second most frequent. Teratoma is a rare, histologically complex tumor of embryonic origin, composed of germ cell lineages from the endoderm, mesoderm, and ectoderm. Ultrasound and fetal echocardiography, according to Desmond et al.[3], frequently detect these pathologies. In the case of intrapericardial teratoma, this tumor mass, along with pericardial effusion, may cause cardiac tamponade, which, if relieved, can be life-saving for the fetus. The aim of this report is to describe a suspected case of this rare fetal pathology detected by obstetric ultrasound in a high-risk maternity hospital in Goiânia, Goiás, as well as to discuss the challenges and events related to the case.

CASE REPORT

The State Women's Hospital of Goiás (Hospital Estadual da Mulher de Goiás - HEMU) is a public hospital located in Goiânia (GO) that handles a significant number of fetal medicine cases from across the state of Goiás and is a national reference center in Brazil for surgery to correct imperfect twinning. In 20 years, this is the first suspected case of fetal intrapericardial teratoma.

The case involves a 32-year-old pregnant woman, in her second pregnancy, with a history of a first-trimester miscarriage 10 years prior, overweight, with no laboratory abnormalities or addictions. She was admitted at 23 weeks and 4 days to the High-Risk Obstetrics Department of HEMU with an external obstetric ultrasound describing a solid-cystic formation in close contact with the right side of the heart, measuring 28mm at its largest diameter, and an external echocardiogram reporting an extracardiac tumor associated with significant pericardial effusion.

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The institutional ultrasound evaluation revealed a well-defined, circular, and heterogeneous mass with cystic and solid areas inside, pulsatile, predominantly adjacent to the right atrium, measuring 32mm at its largest diameter. It was associated with moderate pericardial effusion and mediastinal shift to the left (Figure 1). Based on these ultrasound characteristics, the primary hypothesis of an intrapericardial teratoma was suggested.

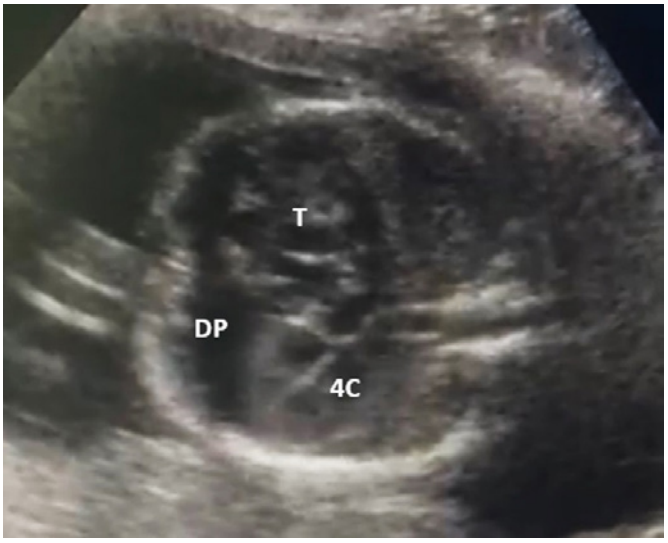
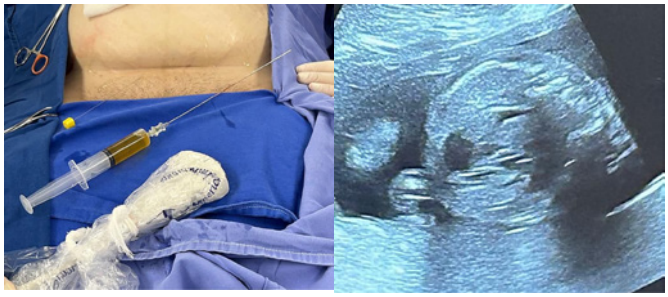


Figure 1: Transverse thoracic section demonstrating a large pericardial mass associated with significant pericardial effusion. 4C – four-chamber view; T – intrapericardial teratoma; DP – pericardial effusion.

Given the likely diagnosis, there was a need for surgical intervention to improve the fetal prognosis due to the possibility of progression in the dimensions of the mediastinal mass, leading to hydrops and fetal death. Due to the unavailability of physical resources at HEMU, the patient was referred to the Hospital de Clínicas of the Federal University of Goiás (HC-UFG) for evaluation.

During the admission examination in the Fetal Medicine department at HC-UFG, worsening of the pericardial effusion was noted, along with scalp edema. A pericardiocentesis procedure was proposed to relieve the fetal effusion and tumor sclerosis, aiming to delay the worsening of the condition and prevent fetal death before the patient could be transferred to a specialized center.

During hospitalization, the previously asymptomatic pregnant woman suddenly experienced severe abdominal pain and vomiting, leading to a diagnosis of intestinal intussusception, likely due to adhesions from a prior bariatric surgery. Consequently, an emergency laparotomy was indicated by the general surgery team, followed by pericardiocentesis to aspirate the pericardial effusion and a fine-needle aspiration of the mediastinal tumor, with sclerosis using hypertonic glucose, performed by the Fetal Medicine team at HC-UFG (Figures 2a and 2b).



Figures: 2a. Citrine fluid aspirated during pericardiocentesis; 2b. Ultrasound appearance after pericardiocentesis and tumor sclerosis.

A few days after the event, the patient was transferred to a Fetal Medicine Service in São Paulo for evaluation of mass resection. Due to the severity of the fetal condition and the immediate maternal postoperative state, the procedure was not indicated. Management continued with daily fetal echocardiograms and cardiotocography three times a day. Due to the recurrence of pericardial effusion in considerable volume, two additional pericardiocentesis were performed. However, during this time, the patient underwent a cesarean section on May 8, 2024, upon confirmation of fetal hydrops associated with cardiac arrhythmia. The neonate was born alive, weighing approximately 1500g, but progressed to death about three hours after birth, likely due to severe pulmonary hypoplasia developed as a result of the cardiac tumor and its complications. A histopathological examination of the tumor was not performed to confirm the ultrasound hypothesis.

DISCUSSION

Camargo et al.[2] reported that in the last decade, there has been a notable increase in the fetal diagnosis of primary cardiac tumors due to advancements in imaging techniques that can diagnose and classify the various histological types of the tumor with high accuracy. Rychik et al.[4] state that such tumors are primarily diagnosed in childhood or during fetal life.

In fetal life, it usually presents as pear-shaped images with a smooth and lobulated surface, heterogeneous echogenicity with cystic areas, with or without calcifications, and almost all are associated with pericardial effusion and located near the fetal right atrium, a description similar to the case in question. Increased vascularization can also be demonstrated using color Doppler. They are rarely diagnosed in adulthood, with few cases reported in the literature.

The presence of a cardiac tumor in the fetus can lead to significant hemodynamic complications that increase fetal and postnatal morbidity and mortality[2]. Garcia et al.[5] described that these tumors are associated with a severe clinical picture, where pericardial effusion combined with cardiac compression due to the mass effect can lead to progressive filling restriction, cardiac tamponade, hydrops, and fetal or neonatal death, reflecting the outcome of the case in question.

According to Garcia et al.[5], clinical management usually involves monitoring and measures for draining pericardial

fluid or delivery when the fetus reaches a viable gestational age for postnatal surgical resection. Prenatal resection, however, would be an ideal treatment option with good outcomes when performed before the onset of severe hemodynamic compromise. In the case in question, due to the non-viable gestational age and unavailability of fetal surgery, it was decided to monitor markers that anticipate intrauterine deterioration, along with pericardiocentesis and tumor sclerotherapy as a therapeutic strategy until access to definitive treatment.

According to Rychik et al.[4], in situations like this, where there is early detection of a tumor suspected to be an intrapericardial teratoma based on its appearance and location, careful and frequent monitoring is necessary to detect changes in tumor size and fetal cardiac output. The goal is to identify changes before the onset of hydrops, in order to avoid treatment in a state of severe hemodynamic instability. An increase in tumor size and abnormally low or declining cardiac output correspond to indications for treatment, thereby reinforcing the urgent nature of the presented case.

Desmond et al.[3] attributed surgical resection as the treatment of choice for cure. Rychik et al.[4] advocate for tumor resection as the most effective treatment since drainage of the cystic component and pericardiocentesis may not adequately relieve tamponade and may not inhibit the rapid growth of the tumor. Due to the progressive increase of these tumors, surgery for preterm infants at 28 weeks is acceptable using the EXIT (extrauterine intrapartum treatment) strategy or, when available, fetal surgery is possible with considerable chances of success if performed before the onset of fetal hydrops. However, given the availability of services, pericardiocentesis followed by fine needle aspiration and tumor sclerosis were the possible therapeutic alternatives to improve the fetal hemodynamic status.

Rychik et al.[4] described the first successful fetal surgery for the resection of an intrapericardial teratoma performed at 24 weeks of gestation and attributed the success of the intervention to early detection and intervention before fetal hydrops. Few studies evaluate the perinatal and long-term outcomes of fetuses with cardiac tumors. According to the cohort by Camargo et al.[2] conducted in 1991 and 2021 at two reference centers in fetal echocardiography, of the four cases of intrapericardial teratoma, three resulted in death, and one remains alive and asymptomatic after tumor excision.

CONCLUSION

Although the postnatal prognosis for newborns undergoing tumor resection is promising, prenatal follow-up presents a challenge. In the case at hand, the fetal intrapericardial teratoma could have been successfully treated with serial monitoring from its detection at an early gestational age and employing effective treatment as soon as signs of imminent fetal hydrops were identified. Therefore, it is crucial to refer patients to a multidisciplinary fetal therapy center at the moment of this diagnosis or upon the first findings predicting hemodynamic decompensation. If referred promptly, within the window of opportunity, it would have been possible to consider fetal surgery with good perinatal outcomes, thus altering the prognosis of this case that presented with a considerable degree of severity, hindering the use of therapeutic options with the best scientific evidence.

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CASE REPORT

ABSENCE OF THE CAVUM SEPTUM PELLUCIDUM: MULTIDISCIPLINARY APPROACH AND DIAGNOSTIC CHALLENGES IN FETAL MEDICINE

JULIANA PINTO COELHO[1], ARTHUR PETTERSEN[1], MARCOS FARIA[1], GABRIELA HISSA[1], HEVERTON PETTERSEN[1]

ABSTRACT

Introduction: The cavum septum pellucidum (CSP) is a cavity filled with cerebrospinal fluid, located between two thin sheets of the septum pellucidum. Its visualization is essential in the screening for anterior midline brain malformations, particularly due to its close relationship with the corpus callosum and the limbic system. The absence or alteration of the CSP is associated with various conditions, such as septo-optic dysplasia (SOD), agenesis of the corpus callosum, holoprosencephaly, and schizencephaly. Its persistence in adults, although often without implications, may be linked to neuropsychiatric disorders.

Case Report: A 22-year-old nulligravida patient presented with absence of CSP visualization and mild ventriculomegaly detected on ultrasound at 23 weeks. Complementary examinations included neurosonography and fetal echocardiography, which revealed no other anomalies. At birth, the newborn showed normal conditions and appropriate development up to 10 months of age, with no signs of neurological impairment. Neurological follow-up and magnetic resonance imaging are still pending.

Discussion: Although most cases of isolated CSP absence have a favorable outcome, it is important to consider that additional anomalies may be detected after birth, leading to unfavorable outcomes, such as alterations in neuropsychomotor development and hormonal deficiencies. Careful evaluation and postnatal follow-up are essential to identify potential complications and provide appropriate counseling to parents.

Conclusion: The prenatal diagnosis of isolated absence of the septum pellucidum may have a more favorable prognosis compared to cases associated with other anomalies. However, postnatal follow-up is crucial, as there may be associations not detected during fetal life, such as septo-optic dysplasia and other neurological deficiencies, which makes parental counseling a challenge.

KEYWORDS: CAVUM SEPTUM PELLUCIDUM, NEUROSONOGRAPHY, BRAIN MALFORMATIONS, AGENESIS OF THE SEPTUM PELLUCIDUM, SEPTO-OPTIC DYSPLASIA, PROGNOSIS.

INTRODUCTION

The cavum septum pellucidum (CSP) is a cavity filled with cerebrospinal fluid (CSF), situated between the two thin sheets of the septum pellucidum. It is bounded superiorly by the corpus callosum, inferiorly by the roof of the third ventricle and the anterior fornix, and laterally by the frontal horns of the lateral ventricles.

During embryonic development, the septum pellucidum forms between the 6th and 8th weeks of gestation and can be identified on obstetric ultrasound from the 17th week onwards. Its presence and morphology are important markers in the screening for brain malformations, as the CSP is visualized in axial views of the fetal brain as an anechoic, well-defined structure between the lateral ventricles. It is considered one of the main markers of the integrity of the anterior midline of the brain, essential for the proper development of the limbic system and the corpus callosum, with which it maintains a close embryological relationship. Although CSP agenesis is often associated with corpus callosum agenesis, it is not a pathognomonic sign[1-3].

The fusion of the septum pellucidum sheets typically occurs after birth, with the closure of the cavity around the first six months of life. However, persistence of the CSP can be observed in a significant percentage of the adult population, reaching up to 30%, and is often considered an anatomical variant without severe clinical implications in most cases. Nevertheless, an enlarged or persistently widened CSP has been associated with psychiatric disorders, such as schizophrenia and bipolar spectrum disorders, as well as other neuropsychiatric conditions[4,5].

Belhocine et al.[6], through a retrospective study using magnetic resonance imaging, diagnosed 34 out of 14,000 (0.02%) children with septum pellucidum agenesis[5]. However, isolated agenesis of the septum pellucidum is considered a rare condition, with an estimated prevalence of 2 to 3 per 100,000 live births.

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The absence of the CSP can be observed in association with complex anomalies, such as septo-optic dysplasia (SOD), a malformation characterized by the absence of the septum pellucidum, optic nerve hypoplasia, and hypothalamic/pituitary dysfunction[7,8]. Lepinard et al[8]. were the first to report a prenatal diagnosis of septo-optic dysplasia–Morsier syndrome. With the advancements in human genetics, a mutation in the HESX1 homeobox gene located on chromosome 3p14 has been associated with SOD[9]. These brain anomalies are generally associated with deficits in neuropsychomotor development and severe hormonal dysfunctions, which have significant prognostic implications[1,3,4,6-8]. Neuroimaging studies reveal that the absence or alterations of the CSP, particularly in the context of corpus callosum agenesis or septo-optic dysplasia, indicate brain developmental disorders that require more detailed investigation with fetal magnetic resonance imaging (MRI) to clarify the diagnosis and facilitate appropriate therapeutic planning[7,10].

DIAGNOSIS

The septum pellucidum is a structure composed of two thin sheets that delimit an anechoic space known as the cavum septum pellucidum (CSP) and is part of the anterior complex of the central nervous system (CNS). This structure can be visualized by ultrasound from the 17th week of gestation, progressively disappearing after the 37th week[1]. The CSP is identified in the transventricular, median sagittal, and transcaudate planes during the second-trimester morphology ultrasound, and its shape is predominantly square in axial views (in about 73% of cases) and triangular in 27% of cases–see figure 1.

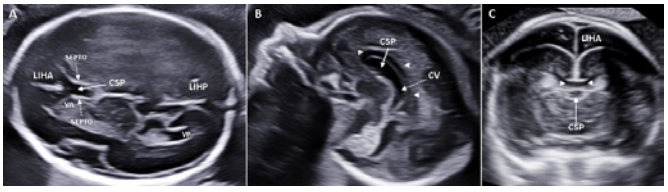

Figure 1. A - Transventricular view (LIHA: anterior interhemispheric line; CSP: cavum septum pellucidum; VA: anterior ventricle; VP: posterior ventricle; LIHP: posterior interhemispheric line). B - Median sagittal view (arrowhead: corpus callosum; CV: cavum vergae). C - Coronal transcaudate view.

The normal width of the CSP varies according to gestational age. Using a biparietal diameter (BPD) of 50 mm (20 weeks) and 80 mm (30 weeks), the CSP measures approximately 3.9 mm and 5.8 mm, respectively[11]. Measurements above the 95th percentile may be associated with aneuploidies, such as trisomy 18, 21, and chromosome 22 microdeletion[11,12]. The CSP should be present in 100% of fetuses between the 18th and 37th weeks, especially when the BPD ranges from 44 to 88 mm. It is essential to differentiate it from the anterior columns of the fornix, which are visualized as three echogenic lines and do not contain cerebrospinal fluid, and from the persistence of the cavum vergae (CV), which usually disappears after the 26th week of gestation. Proper differentiation between these structures is crucial for diagnosis and gestational follow-up. Figure 2 displays, in an inferior axial view, the hyperechogenic lines that belong to the anterior fornix (A) and, in a superior axial anechoic image, the cavum vergae (B).

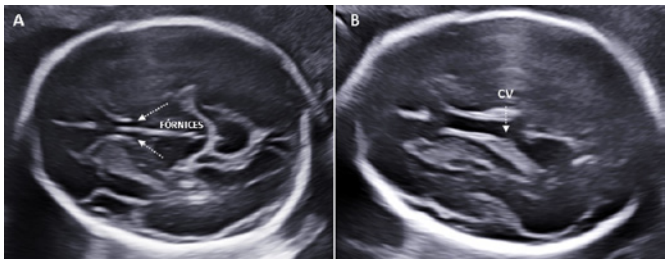

Figure 2. Axial sections of the cephalic pole. A - Inferior: fornices (three hyperechogenic lines). B - Superior: cavum vergae (CV), median and superior region.

The proper evaluation of the CSP is a crucial component of routine ultrasound examination, as its absence or alterations may indicate severe brain malformations, often associated with changes in the development of the corpus callosum and the midline of the brain.

The cavum septum pellucidum disappears in a defined sequence, with the cavum of the velum interpositum being the first to disappear, followed by the cavum vergae, both around the 26th week of gestation; this is followed by the CSP, which disappears after the 37th week. The absence of the CSP can occur in isolation, without associated brain or extracerebral anomalies, or it may be related to mild to moderate ventriculomegaly (measured as the posterior atrium being less than 15 mm). However, in some cases, its absence is associated with significant brain malformations, including holoprosencephaly, severe ventriculomegaly, agenesis or dysgenesis of the corpus callosum, schizencephaly, and septo-optic dysplasia[2,6,13].

Figure 3 illustrates the sagittal and anterior view of the cavum septum pellucidum (CSP), cavum velum interpositum (CVI), and cavum vergae (CV)[14].

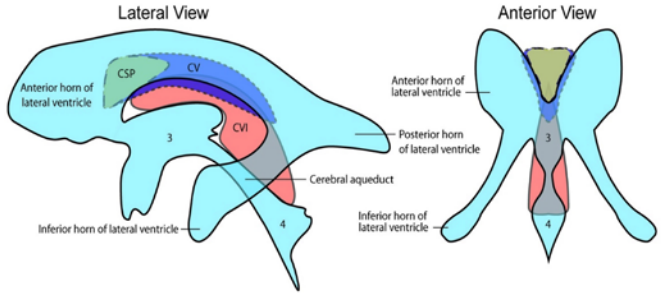

Figure 3 – The image illustrates the sagittal and anterior view of the types of cavum. (CSP = cavum septum pellucidum, CV = cavum vergae, and CVI = cavum velum interpositum)[14].

CASE REPORT

A 22-year-old nulliparous patient was referred by the SUS for follow-up in the postgraduate program of Fetal Medicine at Clínica Gennus, associated with the Faculdade de Ciências Médicas of Minas Gerais. Her personal and family history showed no diagnosed neurological diseases, with normal laboratory tests and previous ultrasounds within the normal range.

Ultrasound performed on 08/05/2023 at Clínica Gennus: Absence of visualization of the cavum septum pellucidum (CSP) in the axial, sagittal, and coronal sections, and identification of mild ventriculomegaly (Figures 4-6). No other associated structural anomalies were observed, particularly in the posterior fossa, posterior midline, and optic chiasm.

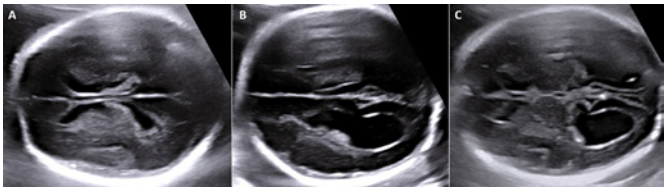

Figure 4. Axial image of the cephalic pole at three levels showing the absence of the cavum septum pellucidum and ventriculomegaly.

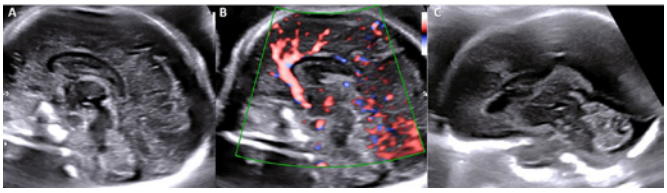

Figure 5. A. Median sagittal image of the cephalic pole showing the absence of the cavum septum pellucidum. B. Color Doppler showing the pericalosal artery.

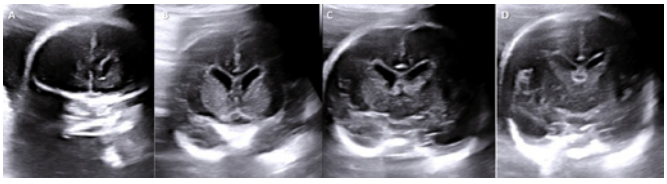

Figure 6. Coronal image of the cephalic pole at three levels showing the absence of the cavum septum pellucidum.

Complementary Evaluations:

To clarify the absence of the CSP and mild ventriculomegaly, the following were performed:

Endovaginal Neurosonography: Confirmed the findings of ventriculomegaly and absence of the cavum septum pellucidum. The optic chiasms, structures of the posterior midline, and posterior fossa were investigated, identified, and found to be normal (Figure 7).

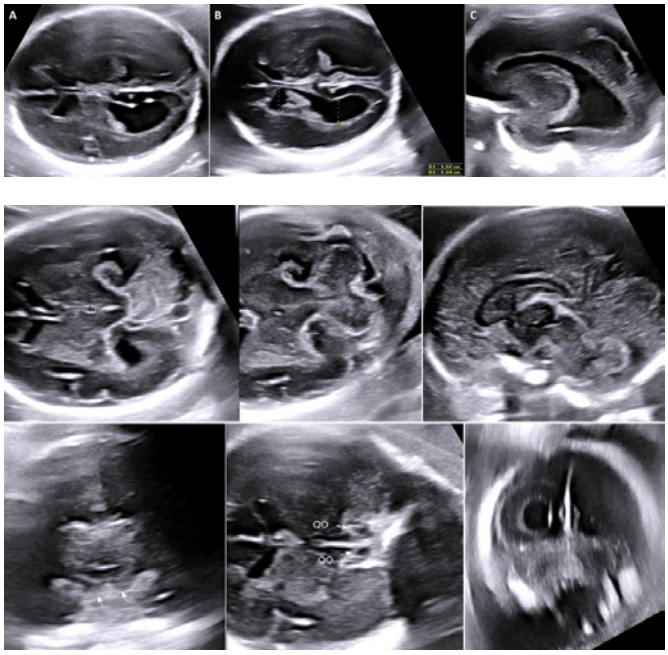

Figure 7. Fetal Neurosonography. A, B, C: Evaluation of ventriculomegaly. Images of the posterior midline and posterior fossa. Arrows indicate the optic chiasm.

Fetal Echocardiography: Normal, with no evidence of structural heart diseases.

Prenatal Management: During prenatal care, cytogenetic studies (karyotype) or fetal magnetic resonance imaging (MRI) were not performed, despite the findings of alterations in the central nervous system.

Delivery and Neonatal Evolution: Male newborn, delivered vaginally on 11/12/2023, at 40 weeks and 2 days of gestation. Birth weight: 3,220 g. Length: 49 cm.

Neonatal Conditions: Discharged on the second day of life, without apparent complications.

Postnatal Evolution: By 10 months of age, the infant showed adequate development in cognitive, sensory, visual, and motor aspects, with no signs of neurological impairment. However, neurological follow-up and magnetic resonance imaging (pending through the SUS) were recommended, especially due to the absence of the septum pellucidum and the mild ventriculomegaly detected during the prenatal period.

DISCUSSION

The isolated absence of the cavum septum pellucidum (CSP) is a condition that, in most cases, presents a favorable prognosis, with normal development and good outcomes. However, as highlighted in the literature, there is a risk of detecting additional cerebral anomalies after birth, which can negatively impact neurological development. Among the postnatal complications are alterations in neuropsychomotor development, visual impairments such as blindness, and hormonal dysfunctions [7].

Borkowski-Tillman et al.[3] highlight that, despite advance-

ments in imaging techniques, it is difficult to guarantee with absolute certainty the isolated absence of the CSP during the prenatal period, pointing to the possibility of other undetected malformations during gestation. The authors analyzed 47 fetuses, with 17/47 (15%) considered to have isolated CSP defects. Approximately 14 babies underwent neurological follow-up, and all were normal. On the other hand, at least 50% of fetuses with associated anomalies showed abnormal results[3].

Studies also show that even in cases where CSP agenesis appears to be isolated during the prenatal period, additional anomalies may be diagnosed later [4,6,7].

Damaj et al.[4] conducted a study with 17 cases of isolated CSP agenesis, where 14 out of 17 exhibited normal neurological development. However, in 3 out of 17 (18%) patients displayed behavioral problems, 2 out of 17 (28%) experienced language delays, and 3 out of 17 (18%) were diagnosed with septo-optic dysplasia.

Di Pasquo et al.[15] conducted a cohort followed by a meta-analysis, revealing that in 14% of cases (9 out of 70) of isolated CSP agenesis, an additional anomaly was detected after birth. Genetic testing was performed on 30 cases, resulting in two abnormal outcomes (9%) – microdeletion 1p14 and a variant of uncertain significance (VUS) at 10p13. Among the 79 fetuses monitored, 14 out of 79 (19%) presented with septo-optic dysplasia (SOD). Among the 46 infants who underwent neurological follow-up and did not have SOD, 3 out of 46 (6.5%) were diagnosed with severe neurological deficits. Furthermore, 60 fetuses were considered normal when the ophthalmological tract was analyzed by ultrasound and MRI; however, 6 out of 60 (9.1% - false negative) presented with SOD in the postpartum period. This evidence demonstrated that an apparently normal visualization of the optical pathways in prenatal imaging does not exclude the possibility of septo-optic dysplasia. Table 1 illustrates the findings of postnatal septo-optic dysplasia from this meta-analysis, reinforcing the importance of follow-up even when examinations appear normal in prenatal imaging.

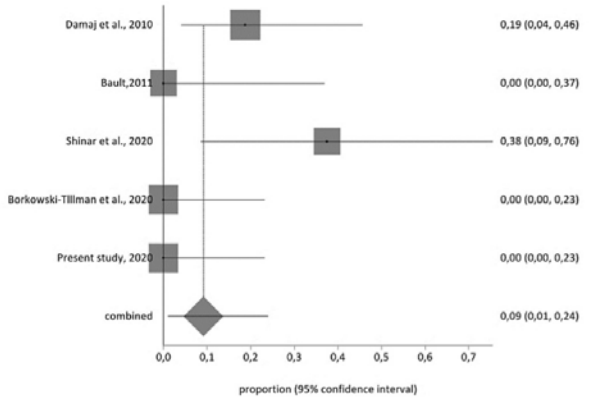

Table 1. Displays the proportion of cases of septo-optic dysplasia in fetuses that showed normal prenatal evaluation of the optic tracts, nerves, or chiasms.

Therefore, postnatal follow-up is crucial to monitor the development of these children, especially in cases of absent CSP, and should involve a multidisciplinary team, including neurologists, endocrinologists, and ophthalmologists.

CONCLUSION

The identification of the cavum septum pellucidum is essential in routine obstetric ultrasound starting from the 17th week of gestation, in axial cuts of the central nervous system. It is important not to confuse the CSP with the fornix or with the persistence of the cavum vergae.

Its absence is a significant marker of anterior cerebral midline defects. When the CSP is not visualized, it is essential to conduct a detailed evaluation of the CNS, including the optic pathways, through neurosongraphy, magnetic resonance imaging (MRI), and 3D/4D ultrasound. MRI between 28 and 32 weeks and after birth is highly recommended, as well as the performance of invasive tests, such as karyotyping or microarray, in cases with associated anomalies.

After analyzing these findings, we included in our fetal neurosonography examination the evaluation of the optic nerve, in addition to the investigation of the optic chiasm. Alonso et al.[16] described a method for identifying and measuring the chiasm, nerve, and optic tract using abdominal ultrasound. Through an axial image of the fetal head in the transventricular plane, the probe is moved caudally, and color Doppler is activated to identify the circle of Willis for orientation. Figure 8 illustrates how to identify the fetal optic chiasm, nerve, and tract.

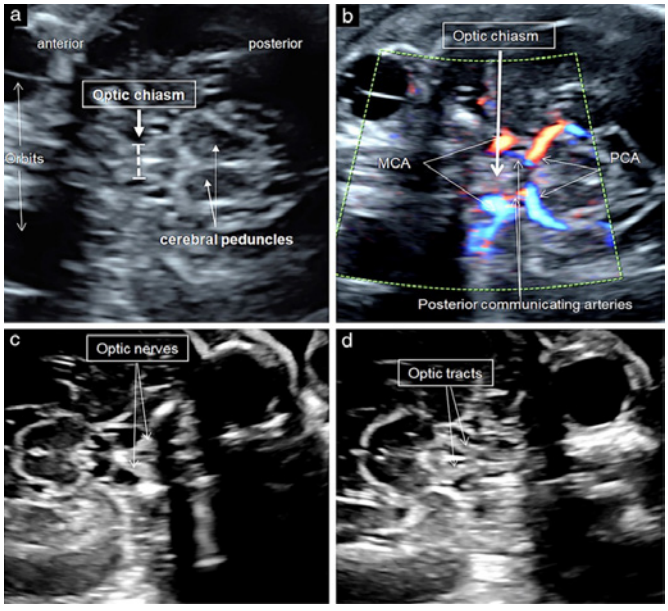

Figure 8. (a) Transabdominal ultrasound image of the fetal head at 26 weeks of gestation, demonstrating an adequate view to evaluate and measure the optic chiasm. At least the anterior orbit should be visible anteriorly and the cerebral peduncles posteriorly; laterally, the cerebrospinal fluid appears as an anechoic space around the echogenic X-shaped optic chiasm. Calipers

are placed at the center of the X-shaped structure, surrounded by an anechoic cerebrospinal fluid. (b) Transabdominal ultrasound image of the fetal head at 29 weeks of gestation at the level of the optic chiasm. Color Doppler is activated to show that the center of the optic chiasm corresponds to the origin of the middle cerebral artery (MCA), which arises from the internal carotids, and the relationship of the optic chiasm with the posterior cerebral arteries (PCA) and the posterior communicating arteries that form the circle of Willis. (c, d) Transabdominal ultrasound images of the fetal brain at 28 weeks of gestation, demonstrating normal optic nerves (c) and normal optic tracts (d) [16].

Although the type of delivery depends on specific obstetric indications, postnatal follow-up is necessary in all cases of isolated agenesis of the CSP, with an emphasis on neurological, endocrinological, and ophthalmological monitoring. Prenatal counseling in these cases poses a challenge, as additional malformations, such as septo-optic dysplasia and behavioral or hormonal changes, may arise after birth, compromising the initial prognosis.

Unlike other CNS anomalies, such as agenesis of the corpus callosum, which have more established diagnostic and prognostic criteria, the isolated absence of the septum pellucidum still lacks clear guidelines for accurate counseling. This necessitates rigorous follow-up and effective communication with the parents to prepare them for potential future complications.

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