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CASE REPORT

SEGMENTAL AGENESIS OF THE VAGINA AND FALLOPIAN TUBES: A CASE REPORT

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ABSTRACT

Müllerian anomalies are defined as the absence or underdevelopment of structures derived from the Müllerian duct, including the fallopian tubes, uterus, and the upper two-thirds of the vagina. It is considered a variant of Mayer-Rokitansky-Küster-Hauser Syndrome (MRKH) and the most common form of Müllerian dysgenesis. MRKH involves the agenesis or dysgenesis of the Müllerian portion of the vagina and uterus during embryogenesis, clinically presenting as primary amenorrhea, normal secondary sexual characteristics, a 46,XX karyotype, and a short vagina (depth of 1 to 2cm).

Diagnosis can be made through physical examination, hormonal profiling, and imaging studies. Studies suggest that the preferred first-line treatment should involve the use of vaginal prostheses for pressure dilation, with surgery reserved for cases where clinical treatment is unsuccessful. The objective of this study is to describe the case of a young patient who experienced severe pain in the hypogastric region, primary amenorrhea, and normal secondary sexual characteristics. During the diagnostic investigation, the occurrence of MRKH was confirmed.

KEYWORDS: MAYER-ROKITANSKY-KÜSTER-HAUSE SYNDROME, MÜLLERIAN AGENESIS, NORMAL SEXUAL CHARACTERISTICS, PRIMARY AMENORRHEA, HYPOGASTRIC PAIN

INTRODUCTION

Müllerian anomalies are defined as the absence or hypoplasia of structures derived from the Müllerian duct, including the fallopian tubes, uterus, and upper two-thirds of the vagina, and are considered a variant of Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS), which is the most common Müllerian dysgenesis. It is the second most common cause of primary amenorrhea, with an estimated incidence of approximately 1 in 4,500 female births[1,2].

MRKHS can be characterized by uterine muscular buds and normal fallopian tubes, either in its complete form or in its partial form, where uterine and fallopian remnants may be asymmetric. It was initially reported by Columbus in 1562. Later, Mayer in 1829 and Rokitansky in 1838 described the changes found during autopsies of what was then called "bipartite uterus." Kuster in 1910 suggested surgical therapy, and in 1962, Hauser described the syndrome, which consists of normal external genitalia, absent vagina, absent or rudimentary uterus, normal fallopian tubes and ovaries which may be associated with renal and skeletal abnormalities[4].

It is a rare condition in which patients have a 46,XX karyotype and normal secondary sexual characteristics, as the ovaries are present and functional, but menstruation does not occur. Its etiology is unknown, although there are hypotheses suggesting a genetic cause[2,11].

The syndrome is classified into three forms based on the involvement of structures beyond the reproductive system. The typical type, Type I, is characterized by changes restricted to the reproductive system. The second, Type II, is an atypical syndrome in which there is asymmetry in the uterus and anomalies of the uterine tubes. This form may be associated with ovarian disease, renal, bone, and congenital otological abnormalities. The third type, called MURCS, involves uterovaginal hypoplasia or aplasia, renal, bone, cardiac, and digital malformations. In the kidneys, there may be unilateral agenesis, horseshoe kidney, renal hypoplasia, ectopic kidneys, and hydronephrosis. In the bones, vertebral abnormalities are common, including vertebral fusion, particularly in the cervical region, Klippel-Feil syndrome, and scoliosis. Cardiac and digital abnormalities can also occur, such as syndactyly and polydactyly[2].

Surgical and non-surgical procedures allow the creation of a neovagina in patients, providing them with the opportunity to have a normal sexual life. Additionally, through assisted human reproduction techniques and uterine transplantation, women can have biological children[2,13].

In this present study, we present the case report of an 18-year-old adolescent with severe suprapubic pain, primary amenorrhea and normal secondary sexual characteristics, who underwent clinical and radiological investigation, leading to a diagnosis of MRKH syndrome, where surgical treatment was suggested and accepted in mutual agreement with the patient.

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N.E.O, 18 years old, female, white. She sought the gynecology service reporting intense pain in the hypogastric region and primary amenorrhea. She reported seeking healthcare services since the age of 14 due to amenorrhea complaints, without imaging investigation. At the age of 15, she began experiencing dysmenorrhea (pain scale: 10/10), associated with nausea and vomiting, pain in the lower limbs and lower back, with cyclic recurrence lasting one week per month. The patient sought the gynecology service again at the age of 18 with a significant worsening of pelvic pain, with no significant improvement with the use of analgesics, including a combination of non-steroidal anti-inflammatory drugs and strong opioids. The patient reported having her first sexual intercourse at the age of 18, denied dyspareunia or sinus bleeding.

Personal history with ongoing monitoring for keratoconus. Denies smoking and alcohol consumption, sedentary lifestyle. Regarding medications, she is taking continuous combined ethinylestradiol and cyproterone, as well as analgesics, including a strong opioid.

In the general physical examination, no alterations were observed, with no signs of chromosomal abnormalities. Pubertal development was classified as Tanner stage M5 P5. During the gynecological evaluation, vulvar inspection revealed the presence of small and large labia without a patent vaginal orifice (figure 1).

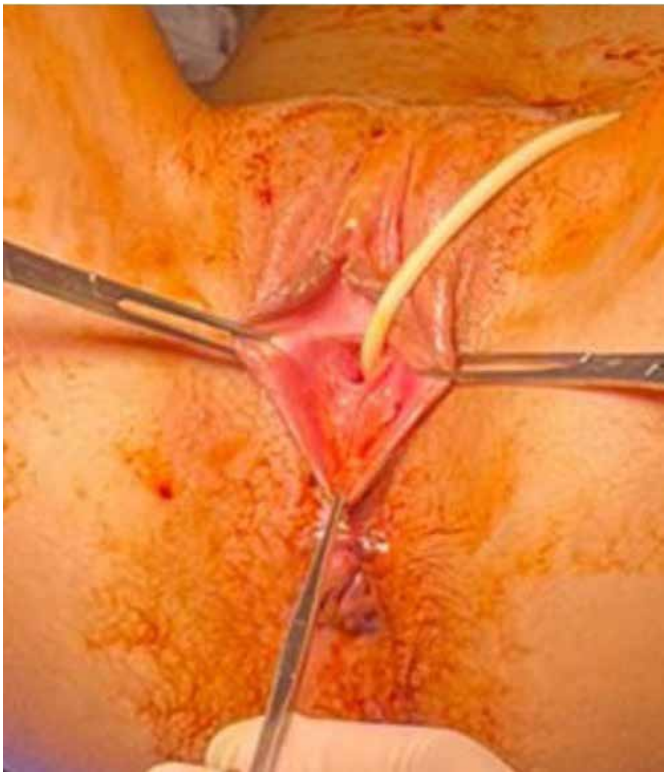

Figure 1: Image of external genitalia with the presence of labia minora and majora without changes. Absence of vaginal canal.

Complementary exams carried out

Endovaginal pelvic ultrasound, showing regular contours of the uterus and precise limits, measuring 11.00 x 5.70 x 6.90cm and a volume of 224.97cm³. Myometrium with heterogeneous texture. Endocervical canal closed. Bilateral ovaries without changes. Normal bilateral kidneys. Bladder visualized without abnormalities. (Figure 2)

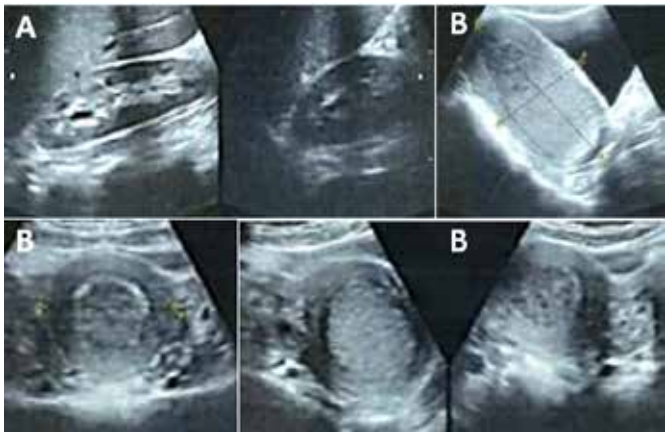

Figure 2: Images verified on abdominal ultrasound A: Normal kidneys. B: Large hematometra.

Pelvic magnetic resonance imaging: collapsed vagina, with the proximal and middle parts showing linear material (suspected fibrosis) with a distance of 5cm between the end of the vagina and the uterus, with a large amount of hematic material distending the endocervical canal, suggestive of hematocolpos.

After discussion with the patient, and aiming to improve incapacitating cyclic pain, the case was managed by performing a laparotomy to remove the rudimentary uterus. Follow-up appointments were scheduled for the creation of a neovagina.

Surgical procedure with a Pfannenstiel incision, no visualization of the fallopian tubes, confirmed the presence of bilateral ovaries with normal macroscopy. A single uterus distended by hematic content was observed, along with lesions compatible with endometriosis in pelvic organs, without communication with the vagina and without the presence of a uterine cervix. Clamping, sectioning, and ligature of the round ligaments, uterine vessels, cardinal ligaments, and uterosacral ligaments were performed. The complete release of the rudimentary uterus was achieved after releasing fibrosis linked to the proximal region of the vagina and the distal part of the uterus, with no access to the vagina. The opening of the surgical specimen, uterus, showed a volume of hematic content. (figures 3 and 4)

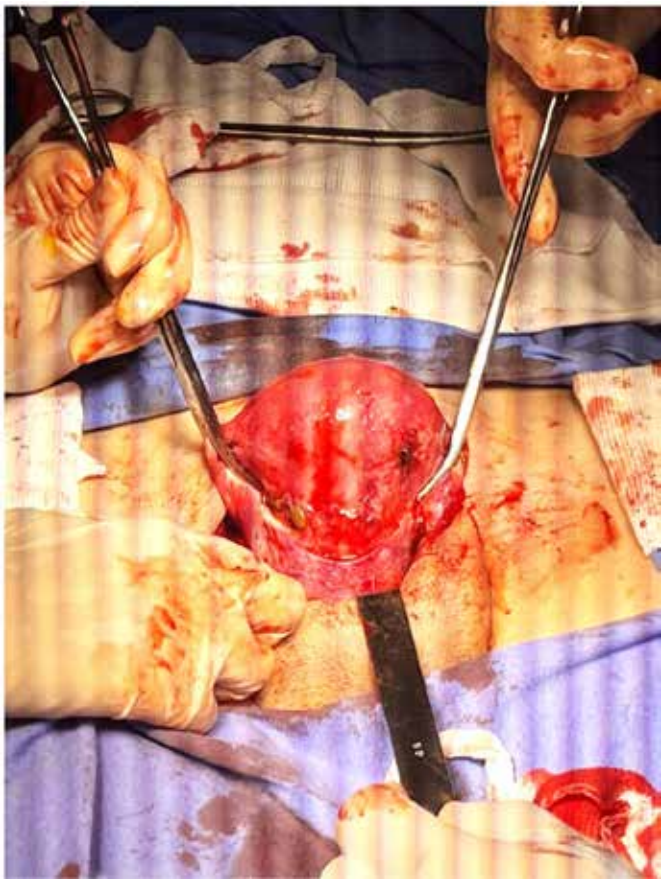

Figure 3: Intraoperative image of a rudimentary uterus with hematometra. No visualization of uterine tubes. Presence of hyperchromatic images suggestive of endometriosis lesions.

Figure 4: Images of a rudimentary uterus. In the left image, there is no presence of the uterine cervix. In the right image, there is a presence of abundant hematologic content.

DISCUSSION

MRKHS is a rare condition, with an incidence of 1 in 4,500 female births, making it the second most common cause of primary amenorrhea, after gonadal dysgenesis. It is defined as the absence or hypoplasia of structures derived from the Müllerian duct, including the fallopian tubes, uterus, and the upper two-thirds of the vagina, with MRKHS being the most common form of Müllerian dysgenesis[2,5].

The Müllerian and Wolffian ducts are the embryological precursors of the female and male internal reproductive systems, coexisting undifferentiated in the embryo until genetic determinants lead to their differentiation into ovaries or testes. In females, the Müllerian ducts differentiate into the Fallopian tubes, uterus, cervix, and the upper portion of the vagina[1,2], while the Wolffian ducts degenerate. When the formation and differentiation pathways of the Müllerian ducts are compromised during embryonic development, various Müllerian anomalies can occur, ranging from minor anatomical variations to complete aplasia of the structures that make up the female reproductive system. Within the spectrum of Müllerian anomalies, the most prevalent is vaginal agenesis, present in 90% of cases of malformations. It results from an inhibitory defect in the correct embryonic development of the paramesonephric ducts and can be associated with uterine anomalies, including agenesis, hypoplasia, duplication, or even a normal uterus, variability that characterizes MRKHS[7,12]. MRKHS occurs when both Müllerian ducts fail to develop, resulting in a rudimentary solid uterus and a non-patent vagina in patients with a 46 XX karyotype, normal Fallopian tubes, and ovaries[2,3].

Müllerian aplasia and incomplete Müllerian fusion are associated with the familial occurrence of the most common Müllerian differentiation disorders in girls. Its cause is not yet well defined but is related to some genes. It is evident that the HOX genes, a family of regulatory genes that encode transcription factors, are essential for the correct development of the Müllerian duct during embryonic development, and WNT4 may participate in uterine development, as a mutation of WNT4 has been reported in cases of MRKHS with hyperandrogenism[3,13].

While most cases are sporadic, the increasing number of familial cases, the pattern of congenital malformations involved in the syndrome, and the association with chromosomal rearrangements indicate that genetic factors may trigger the development of the syndrome. The most frequently suggested mode of transmission of SMRKH is autosomal dominant with incomplete penetrance and variable expressivity due to a single gene mutation. The association of Müllerian dysgenesis with various extragenital anomalies suggests that key genes involved in fetal development and sexual differentiation, such as HOX, WNT, and those encoding anti-Müllerian hormone and its receptor, may be involved in the development of the syndrome. For first-degree relatives, the risk of recurrence is 1-5%[2,3].

Generally asymptomatic during childhood, Müllerian malformations are mostly detected in adolescence, with the average age of diagnosis being between 15 and 18 years, reflecting the typical late diagnosis of these congenital anomalies[7].

The typical presentation is characterized by primary amenorrhea, with or without cyclic pain, such as complaints of hypogastric, lumbar, or pelvic pain, in patients who normally go through puberty, i.e., breast development and pubic hair

growth with normal stature, being, therefore, a pure female type but without menstruation, and without signs of virilization. In these patients, almost always, there is an outline of the vagina in the distal segment, which guides our treatment indication. The gynecological examination may detect the absence of the vaginal canal or vaginal shortening[2,5,7].

In cases where vaginal agenesis occurs with normal uterine development (6-10%), the diagnosis can be made early. The presence of a functioning uterus with obstruction of the menstrual outflow tract results in hematometra, characterized by intermittent pelvic and lower back pain occurring approximately every 3-4 weeks. This atypical and rare presentation of MRKHS is associated with normal pubertal development, endocrine status, and external genitalia. It begins with intense, intermittent, and monthly hypogastric and lower back pain, consistent with hematometra, at the age of [13]. Therefore, the age of diagnosis can be early[7,11].

In the presence of clinical suspicion, a meticulous physical examination is the first and essential step in establishing the diagnosis of the aforementioned syndrome. This examination reveals the development of secondary sexual characteristics at a normal stage for the patient's sex and age, a vulva with normal formation, and complete or partial absence of the vagina. Complementary tests show the 46XX karyotype, and pelvic imaging tests confirm the presence of normal ovaries and a rudimentary uterus. Ultrasound, even through the suprapubic abdominal route, can be sufficient in many cases. If there is doubt, magnetic resonance imaging (MRI) should be performed to define the diagnosis, as it has higher sensitivity and specificity in evaluating the syndrome. These tests will typically reveal the presence of symmetric or asymmetric uterine agenesis and complete absence or marked hypoplasia of the upper and middle portions of the vagina. Since it results from a different embryonic precursor, the lower third of the vagina is present, and this vaginal remnant may have varying depths (2-7 cm). Laparoscopy is indicated only when assessment by the two previous methods is unsatisfactory, and when it is possible to formulate a therapeutic plan through this procedure[2,5,7].

When diagnosing MRKHS, it is important to consider and exclude differential diagnoses in situations where the patient has primary amenorrhea and developed secondary sexual characteristics. This includes conditions like congenital absence of the uterus and vagina, isolated vaginal atresia with androgen insensitivity syndrome, and transverse vaginal septum with imperforate hymen[5,10].

In the investigation of the described case, in line with the literature, continued after the physical and gynecological examinations which raised suspicion of a possible genital tract malformation, the investigation proceeded with a transvaginal pelvic ultrasound, which suggested the diagnosis of segmental agenesis of the vagina and uterine tube (a Rokitansky variant) with a significant hematometra. In other words, there was the presence of vaginal agenesis with hematometra and intact adnexal regions (normal ovaries).

The diagnosis of these cases is not complete without investigating the possible presence of associated systemic malformations, which are evident in cases of the atypical form of the syndrome. In the investigation of this case, a renal and bladder ultrasound was performed, which, in the absence of findings, ruled out the association with ureterovesical malformations. With the absence of other malformations, the patient likely had a variant of MRKHS[6,7].

This is a syndrome with a significant psychological impact on young affected women, not only due to its clinical manifestations but also because of its interference with sexual life and the ability to conceive. It's important to highlight the psychological changes caused by the anatomical alterations that characterize it, leading to distress, anxiety, psychological consequences, and a decreased quality of life for patients after the diagnosis is confirmed. Infertility is the most challenging aspect to accept, which is why a multidisciplinary approach is necessary. The therapeutic approach for these cases will involve not only the repair of congenital anatomical defects but also a multidisciplinary assessment that includes psychological support as an integral part of treatment[5,7].

The recommended anatomical treatment is the creation of a neovagina, either through surgical or non-surgical means, which can allow these patients to have a normal sexual life. When the surgical approach is chosen, uterine remnants may be removed to prevent future endometriosis. For patients who wish to have children, adoption should be encouraged, and they should be presented with the possibility of having biological children through assisted reproductive techniques[5,8].

The Frank method and surgical neovaginoplasty (Vecchietti method) are the most commonly mentioned options in the literature for the treatment of Rokitansky syndrome. In the Division of Gynecological Clinic at the Department of Obstetrics and Gynecology of the Hospital das Clínicas at the University of São Paulo Medical School, the first choice for treating this syndrome is the Frank method, which involves progressive dilation of the vaginal canal with a rigid acrylic mold. When the patient adheres to the method and does it correctly, a functional vagina for sexual intercourse can be achieved in approximately six months, on average[2,15].

The choice of method still depends on the surgeon's preferences. Among the possible techniques is the Vecchietti procedure or traction neovaginoplasty, which does not require an external tissue graft and can be performed laparoscopically. However, this procedure carries potential complications related to the traction threads placed in the vesicorectal space and possible posterior vaginal prolapse. The Davydov three-stage technique involves abdominal mobilization of peritoneum, fixation of the peritoneum to the vaginal introitus, and closure that sutures the top of the new vagina. While the Davydov procedure is advantageous in terms of granulation and healing in the neovagina, the neovaginal tissue lacks lubrication, and the procedure carries the risk of intestinal and bladder injury. Intestinal neovaginoplasty typically uses the sigmoid colon and provides lubricated tissue with an excellent blood supply; however,

the procedure requires intestinal anastomosis and is associated with complications, including significant vaginal discharge, postoperative ileus, intestinal obstruction, intestinal ulceration, risk of malignancy, and colitis. The McIndoe procedure allows a vaginal approach to create the neovagina. Various types of graft materials have been used for the McIndoe technique, including autologous skin grafts, typically from the buttocks or thigh, amnion, peritoneum (Davydov procedure), autologous in vitro vaginal tissue, and labial or gracilis myocutaneous flaps. In this procedure, we modified the donor area to be the abdomen, allowing primary closure and a discreet scar. To prevent stenosis and achieve proper graft fixation in the recipient area and prevent shearing, we used a polyurethane foam. Various materials have been used to make these vaginal molds: a condom mold filled with cotton, a polyethylene bag filled with fiberglass wool, an inflatable vaginal stent, a vacuum-expandable condom mold, Surgi-Stuf, ORFIT "S" material, a polystyrene mold. With this surgical technique, we achieve an anatomically and functionally adequate neovagina[8,14].

There is a range of interventions available, including surgical and non-surgical options, that allow for the creation of a neovagina in patients. Regardless of the chosen modality, treatment should provide an anatomically and physiologically normal vagina with an appropriate length to ensure proper sexual function. However, treatment should only be initiated when the patient desires to start her sexual life. In this case, the most relevant need was to address the hematometra. Therefore, in the present case, therapeutic options were made based on three distinct points: treatment of the hematometra via laparotomy hysterectomy, a new intervention to provide functional sexual life, and addressing the inability to conceive[5,7,9].

CONCLUSION

The present case presented is a variant of MRKHS in which the uterus is preserved, the secondary sexual characteristics are within the normal range, and there are no associated systemic malformations. This condition has a significant impact on the patient's life.

The inherent difficulty in diagnosing the spectrum of Müllerian malformations is evident. Among which, it describes a condition that requires early diagnosis mainly at the clinic, where ultrasound may be sufficient in many cases to confirm the diagnosis. And if there is any doubt, MRI should be performed together. In this investigation, we can identify which type of Müllerian malformation the patient has, so that appropriate surgical planning or non-surgical interventions can be proposed, including multidisciplinary assessment, due to the great psychological impact of these patients.

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