Behind Amenorrhea

Joana Soares[1], Eulália Sousa[1], Bebiana Sousa[2], Carla Brandão[1], Cláudia Monteiro[1]

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Abstract

Mayer-Rokitansky-Kuster-Hauser syndrome is characterized by the presence of agenesis of the uterus and upper two-thirds of the vagina in girls with 46, XX karyotype and normal development of secondary sexual characters. It can occur as an isolated form (type I) or associated with renal, bone, heart, or hearing malformations (type II). We report a clinical case of an adolescent with primary amenorrhea and diagnosed with Mayer-Rokitansky-Kuster-Hauser syndrome type II. Monitoring patients with this syndrome is complex and requires a multidisciplinary approach centered on the patient and their family with a focus on gynecological, sexual, psychological, and infertility issues. In recent years, numerous efforts have been made to improve the knowledge about this disease. More recent studies have provided a better understanding of the etiology, diagnosis, treatment, and follow-up.

Keywords: Adolescent; Amenorrhea/etiology; Congenital Abnormalities; Uterus/abnormalities; Vagina/abnormalities; 46, XX Disorders of Sex Development/complications; 46, XX Disorders of Sex Development/diagnosis; 46, XX Disorders of Sex Development/diagnostic imaging

Introduction

Mayer-Rokitansky-Kuster-Hauser syndrome is a congenital Müllerian anomaly characterized by the aplasia of the uterus and upper two-thirds of the vagina.[1-8] It affects patients with adequate secondary sexual characteristics and a normal female karyotype.[1,2,4] It is a rare malformation that affects one in 4,500-5,000 female newborns. However, it is the second most common cause of primary amenorrhea after gonadal dysgenesis.[1,2,7,8] The etiology is unknown, but regulatory mechanisms (for example, epigenetic factors) and somatic genetic events during the fetal development could also be implicated.[6] The syndrome is categorized into two types, isolated uterovaginal agenesis (type I) or associated with renal, bone, heart, or hearing malformations (type II).[1,6]

In this article, we report a case of Mayer-Rokitansky-Kuster-Hauser syndrome type II to remember a rare cause of primary amenorrhea that requires a multidisciplinary diagnostic and therapeutic approach.

Case Report

A 15-year-old female patient was evaluated in general pediatrics due to primary amenorrhea without other associated symptoms. In the past medical history, cardiac surgery to correct interauricular and interventricular communication at the age of 4 years as well as hip epiphysiolysis and epilepsy since the age of 14 are noteworthy. There was no relevant family history. Physical examination showed secondary sexual characteristics compatible with the age (Tanner stage IV), normal external genitalia, but the vagina was absent. Initial investigation showed normal biochemical analyses (gonadotropins, estradiol, and androgen status) for the stage of Tanner and abdominopelvic ultrasound revealed uterine agenesis.

Posteriorly, for better anatomical characterization, an abdominal and pelvic magnetic resonance imaging was performed and showed agenesis of the uterus and the vagina as well as horseshoe pelvic kidney and hip osteonecrosis (Fig. 1). Chromosomal analysis revealed karyotype 46, XX. According to the imagiological findings, the final diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome type II was established. After diagnosis, she underwent the surgical correction of vaginal agenesis, maintaining multidisciplinary follow-up.

1. Pediatrics and Neonatology Department, Centro Hospitalar do Tâmega e Sousa, Penafiel, Portugal
2. Pediatrics Department, Centro Materno-Infantil do Norte Albino Arioso, Centro Hospitalar Universitário do Porto, Porto, Portugal
Corresponding Author
Joana Soares
https://orcid.org/0000-0002-0326-6547
73249@chts.min-saude.pt
Avenida do Hospital Padre Américo, Nº 210, 4560-136, Guilhufe, Penafiel, Porto, Portugal
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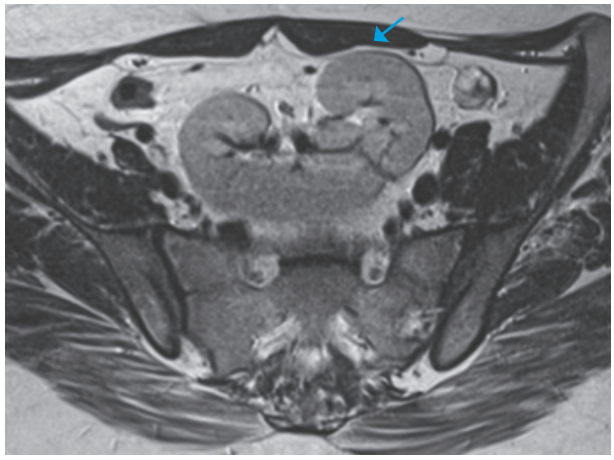

Figure 1. T2-weighted axial plane showing a horseshoe kidney.

Discussion

Mayer-Rokitansky-Kuster-Hauser syndrome typically presents with primary amenorrhea in adolescents following karyotype 46, XX, normal puberty and development of secondary sexual characteristics.[1,5,6] Vaginal agenesis with variable uterine development is observed.[1,5,6] A small percentage of adolescents with Mayer-Rokitansky-Kuster-Hauser syndrome (2%-7%) presents a rudimentary uterus with endometrium and may report cyclic pelvic pain at diagnosis.[1,2,5,6] In most cases, the ovaries are present bilaterally, but their location tends to be more cranial than the normal position and they are often found lateral to the external iliac arteries due to the absence of Fallopian tube.[1,5,6] Their physical examination is often normal with breast development, axillary and pubic hair distribution appropriate to the age, without virilization.[3,8] A pelvic exam reveals agenesia or hypoplastic vagina.[1,5,6]

In Mayer-Rokitansky-Kuster-Hauser syndrome type I, there is just the agenesis of the uterus and vagina in the presence of the remaining Müllerian structures and normal uterine tubes.[3,6] On the other hand, in type II or atypical Mayer-Rokitansky-Kuster-Hauser syndrome, other malformations are associated with congenital uterovaginal agenesis.[1-3,6] Approximately 25%-50% have renal malformations, such as renal agenesis, horseshoe kidney, hypoplasia, or renal ectopia.[3,6-8] About 10%-15% have concomitant bone malformations of the extremities, ribs, and spine (scoliosis, spinal fusion, and Klippel-Feil anomaly).[3,6] Cardiac and hearing malformations can also be present, although with lower incidence.[3,6]

The diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome requires a high degree of suspicion.[7] In childhood, the diagnosis often occurs most incidentally during the investigation of other diseases.[7] In adolescence, the etiological investigation of primary amenorrhea reveals this syndrome.[7] The main differential diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome are androgen insensitivity syndrome, 17β-hydroxylase deficit, isolated vaginal agenesis, imperforate hymen, and transverse vaginal septum.[1,5,7]

The etiological investigation of primary amenorrhea must include karyotype, imaging studies, and biochemical analysis with a gonadotropins, estradiol, and androgen status to establish the differential diagnosis between this syndrome and other causes of primary amenorrhea.[1,5,7] Hormonal, karyotype and imaging studies are also necessary to make the diagnosis of MRKH. [1,5,7] Abdominopelvic ultrasonography demonstrates the absence of the uterus and the presence of ovaries.[2,5-8] Pelvic magnetic resonance imaging, the gold-standard for the diagnosis of uterovaginal agenesis in Mayer-Rokitansky-Kuster-Hauser syndrome, presents great sensitivity and specificity.[3,6] It allows a better definition of pelvic structures, identifies an active endometrium, measures vagina dimensions and locates ectopic gonads.[3,6,8] The absence of a uterus between the bladder and the rectum can be confirmed.[3,6] Occasionally, a vestigial lamina in the uterus site can be confused with a normal uterus.[3,6] The investigation of renal, cardiac, and bone malformations is not routinely performed and should only be considered in the presence of specific symptoms or abnormalities on physical examination.[6] The karyotype is essential for the diagnosis.[6] However, a further genetic study is not necessary for the definitive diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome.[6]

In this clinical case, the abdominopelvic ultrasound showed uterine agenesis, confirmed by magnetic resonance imaging, along with normal hormonal measurements and normal female karyotype confirming the diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome type II. In this case, there was no prenatal history predisposing the patient to the disease, such as gestational diabetes or use of thalidomide. After the diagnosis, the adolescent and her family must be informed about the disease and its long-term consequences. Henceforth, maintaining a multidisciplinary follow-up becomes essential.[7] The diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome has a high psychosocial impact, leading to low self-esteem, depression, and anxiety, so that psychology monitoring is very important.[1,2,6,7]

The treatment of Mayer-Rokitansky-Kuster-Hauser syndrome remains controversial.[7] Creating a neovagina is the main therapeutic strategy available and should be programmed near the beginning of sexual activity

because emotional maturity and motivation are essential to fulfill long-term treatment.[1,7] The first line option for the creation of a neovagina is the non-surgical dilation of the vagina (Frank method), given the high success rate (around 90%) and low morbidity, but it is a long-lasting method.[1,5,7] Surgery is indicated for adolescents whose non-surgical treatment was ineffective and for those who choose this therapeutic modality as the first choice.[1,5,7] Many surgical techniques have been described for the creation of a neovagina, but there is no consensus on the most effective.[1,7] A neovagina will allow normal sexual activity, but infertility remains.[1,3,7] In this clinical case, it was decided to create a neovagina according to the adolescent option.

Infertility secondary to uterine agenesis is one of the most challenging consequences to accept, so family support becomes essential at this stage.[1] Uterine transplantation is the first treatment that will allow fertility and is a new hope for these young women.[6] Despite promising trials, further studies are required to prove the effectiveness of uterine transplantation.[6] Management and follow-up of patients with Mayer-Rokitansky-Kuster-Hauser syndrome are complex requiring a multidisciplinary approach centered on the patient and her family, addressing all the gynecological, sexual, psychological, and infertility issues.[6]

WHAT THIS CASE REPORT ADDS

- Mayer-Rokitansky-Kuster-Hauser syndrome is a malformation of the Müllerian ducts characterized by the congenital agenesis of the uterus and upper two-thirds of the vagina that can occur as an isolated form or associated with other malformations (renal, cardiac, skeletal).
- It should be suspected in adolescents with primary amenorrhea with the normal development of secondary sexual characters and 46, XX karyotype.
- Follow-up and management of patients with Mayer-Rokitansky-Kuster-Hauser syndrome is complex and requires a multidisciplinary approach centered on the patient and their family, addressing all the gynecological, sexual, psychological, and infertility issues.

Conflicts of Interest

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Confidentiality of data

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Por detrás de uma amenorreia

Resumo

A síndrome de Mayer-Rokitansky-Kuster-Hauser é caracterizada pela presença de agenesia do útero e dos dois terços superiores da vagina em raparigas com cariótipo 46, XX e desenvolvimento normal de caracteres sexuais secundários. Pode ocorrer de forma isolada (tipo I) ou associada a malformações renais, ósseas, cardíacas ou auditivas (tipo II). Neste artigo, descrevemos o caso clínico de uma adolescente com amenorreia primária com diagnóstico de síndrome de Mayer-Rokitansky-Kuster-Hauser tipo II. O acompanhamento de doentes com esta síndrome é complexo e requer uma abordagem multidisciplinar centrada na doente e na sua família, focada nas questões ginecológicas, sexuais, psicológicas e de infertilidade. Nos últimos anos, têm sido desenvolvidos inúmeros esforços para aumentar o conhecimento sobre esta doença. Estudos mais recentes permitiram compreender melhor a sua etiologia, diagnóstico, tratamento e seguimento.

Palavras-Chave: Adolescente; Alterações do Desenvolvimento Sexual/complicações; Alterações do Desenvolvimento Sexual/diagnóstico; Alterações do Desenvolvimento Sexual/diagnóstico por imagem; Amenorreia/etiologia; Anomalias Congénitas; Útero/anomalias; Vagina/anomalias