Mayer-Rokitansky-Küster-Hauser Syndrome: A Case of Primary Amenorrhoea and Diagnostic Approach

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Abstract

Background: Amenorrhoea, defined as the absence of menstruation, can be classified into primary and secondary types. Primary amenorrhoea is diagnosed when menstruation has not occurred by age 15 or within three years of breast development. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare cause of primary amenorrhoea characterized by uterovaginal aplasia in women with a normal 46, XX karyotype and secondary sexual characteristics. This case report discusses a 15-year-old girl diagnosed with MRKH syndrome after a thorough diagnostic workup. Methods: A detailed diagnostic evaluation was conducted, including physical examination, imaging (ultrasonography and MRI), hormonal testing, and chromosomal analysis. The patient presented with primary amenorrhoea and no family history of related conditions. Ultrasound and MRI confirmed the absence of a uterus and non-visualization of the ovaries. Hormonal tests were within normal ranges, and chromosomal analysis revealed a 46, XX karyotype. Results: The diagnostic workup confirmed an atrophic uterus with small bilateral ovaries and no functional endometrial tissue. Mayer-Rokitansky-Küster-Hauser syndrome was diagnosed. The patient was counseled regarding surgical options, including neovaginoplasty, to create a functional vaginal canal for sexual intercourse. Conclusion: MRKH syndrome, though rare, is an important consideration in cases of primary amenorrhoea. Timely diagnosis through imaging and chromosomal analysis is crucial for appropriate management. Psychological counseling and surgical options such as neovaginoplasty can significantly improve the quality of life for affected individuals, particularly regarding sexual health and reproductive possibilities. Addressing the psychological burden associated with infertility is also critical to patient care.

Keywords: Mayer-Rokitansky-Küster-Hauser Syndrome, primary amenorrhoea, uterovaginal aplasia, neovaginoplasty, Müllerian dysgenesis

Significance | This case highlights Mayer-Rokitansky-Küster-Hauser syndrome as a rare but important cause of primary amenorrhoea, requiring timely diagnosis.

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Introduction

Amenorrhoea, the absence of menstruation in women of reproductive age, is classified into two primary types: primary and secondary. Primary amenorrhoea is diagnosed when a woman has never menstruated by the age of 15 or within three years of thelarche, while secondary amenorrhoea is characterized by the cessation of menstruation for three months in women with previously regular cycles or six months in those with irregular cycles (Munro et al., 2022; Gaspari et al., 2023; Klein et al., 2019). Menarche, the onset of menstruation, typically occurs around the age of 12.5 years, though this can vary based on individual factors such as ethnicity, body weight, and nutritional status. Menarche generally follows the onset of thelarche, or breast development, which occurs between the ages of eight and ten. Medical evaluation is recommended for women meeting the criteria for primary or secondary amenorrhoea, as timely diagnosis and intervention are crucial (Sultan et al., 2018; Chumlea et al., 2019).

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In cases of primary amenorrhoea, it is essential to assess for delayed puberty if a 13-year-old girl shows no signs of breast development or other secondary sexual characteristics (e.g., pubic or axillary hair) (Golden and Carlson, 2008; Master and Heiman, 2006). The causes of primary amenorrhoea often involve dysfunctions in the hypothalamus, pituitary gland, or ovaries, or abnormalities in sexual development. Secondary amenorrhoea is more commonly associated with physiological conditions or medication use, although some medications can also contribute to primary amenorrhoea (Henkel, 2019).

One rare cause of primary amenorrhoea is Mayer-Rokitansky-Kuster-Hauser Syndrome (MRKHS), also known as Müllerian dysgenesis, which occurs in about one in every 5,000 female births. MRKHS is characterized by uterovaginal aplasia in individuals with a 46XX karyotype and normal secondary sexual characteristics. There are two main types of MRKHS: Type 1, which involves only uterovaginal agenesis, and Type 2, which includes additional anomalies affecting the fallopian tubes, kidneys, spine, and other organs (Nguyen et al., 2018). A third variation, Type 3, presents with a range of systemic abnormalities, including hearing loss, renal and skeletal malformations, and cardiac defects. The etiology of MRKH syndrome remains unclear, though it was previously thought to be associated with teratogenic exposure to substances like thalidomide and diethylstilbestrol (Bjørsum-Meyer et al., 2016). Treatment of MRKHS typically involves patient counseling and surgical creation of a neovagina to facilitate sexual intercourse. This case adheres to the SCARE 2020 guidelines (Agha et al., 2020). The diagnostic workup for amenorrhoea generally includes a thorough history, physical examination, hormonal evaluation, imaging, and chromosomal analysis. Treatment depends on the underlying cause and may involve lifestyle modifications, hormone therapy, medication, surgery, or mental health support. It is essential for healthcare providers to remain well-informed and proactive in managing amenorrhoea to ensure timely diagnosis and appropriate care, leading to better patient outcomes.

2. Case report

A 15-year-old girl presented with a history of primary amenorrhoea, though she reported no gastrointestinal or urinary symptoms. Her diagnostic workup for primary amenorrhoea revealed no family history of delayed menses, amenorrhoea, or endocrine disorders. She had no history of cyclical abdominal pain, smell perception issues, or prior abdominal or inguinal surgeries, chemotherapy, or radiotherapy. Physical examination showed she was 137 cm tall, weighed 26 kg, and had a chest circumference of 65 cm, with a BMI of 13.9 kg/m^2. Her vitals were normal, with a blood pressure of 110/70 mmHg and a pulse rate of 70 beats per minute. There was no evidence of breast development or axillary and pubic hair. Her external genitalia appeared underdeveloped, with shorter labia majora and labia minora and a smaller vaginal opening. There was no palpable abdominal mass, inguinal hernia, or detectable gonads in the inguinal region. An X-ray of her bone age was normal (Figure 1). Ultrasonography of the pelvis revealed an absent uterus and non-visualization of the bilateral ovaries, indicating an aplastic uterus. MRI confirmed the presence of normal kidneys, ureters, and a urinary bladder without abnormalities. The uterus appeared atrophic with a volume of 2.5 ml, and the uterine body to cervix ratio was 1:1, indicative of a prepubertal status. No functional endometrial tissue was present. The left ovary was small, containing fewer than two follicles, and the right ovary showed fibrotic tissue, suggesting an atrophic uterus with small bilateral ovaries. Hormonal tests, including FSH, LH, prolactin, and TSH, were within normal limits. Chromosomal analysis confirmed a 46, XX karyotype (Figure 2). Based on these findings, the patient was diagnosed with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome and was counseled on the option of neovaginoplasty surgery for vaginal correction.

3. Discussion

Müllerian agenesis, commonly referred to as Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, represents a spectrum of congenital malformations of the female reproductive system characterized by varying degrees of utero-vaginal agenesis in women with normal secondary sexual characteristics and a 46, XX karyotype. The condition has a reported prevalence of 1 in 5,000 females, making it the second most common cause of primary amenorrhoea after gonadal dysgenesis (CoAH, 2018). First described by Mayer in 1829 and later expanded upon by Rokitansky (1838), Küster (1910), and Hauser and Schreiner (1961), the syndrome results from disrupted development of the Müllerian duct system, which typically gives rise to the uterus, cervix, and the upper two-thirds of the vagina between the fifth and sixth weeks of gestation (Pizzo et al., 2013). MRKH syndrome is categorized into two types: Type I, which involves isolated utero-vaginal agenesis, and Type II, which includes extra-genital malformations such as renal agenesis, pelvic kidney, and skeletal, auditory, and cardiac anomalies. The MURCS association (Müllerian hypoplasia, renal agenesis, and cervicothoracic somite dysplasia) represents the most severe form of Type II MRKH syndrome (Ledig and Wieacker, 2018).

Ultrasonography is typically the first imaging modality used to assess MRKH syndrome, aiding in the identification of ovarian presence and uterine absence. However, the results can sometimes be inconclusive due to technological limitations (Londra et al., 2015). MRI is the preferred imaging technique for confirming the diagnosis and detecting any associated anomalies (Boruah et al., 2017; Fiaschetti et al., 2012). Preibsch et al. demonstrated a strong correlation between MRI findings and laparoscopy outcomes in

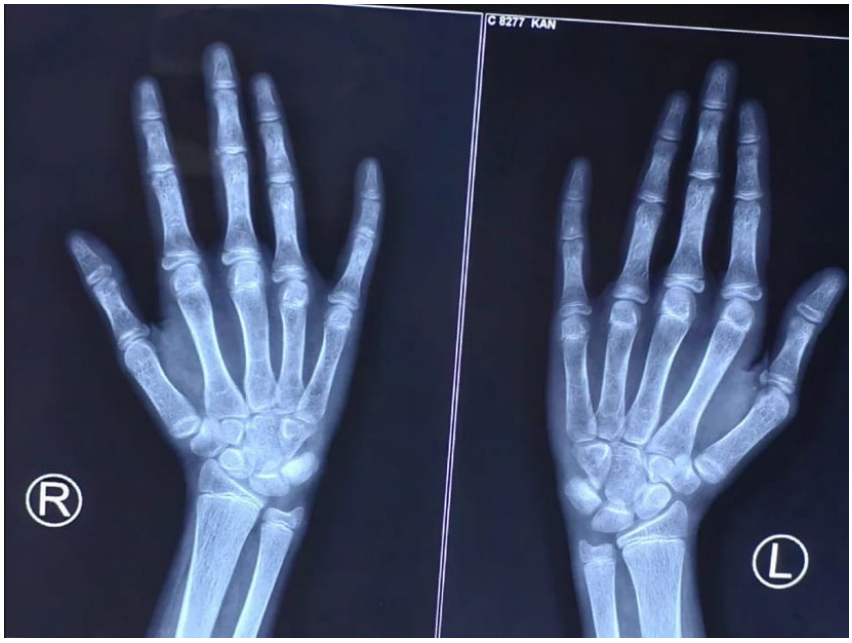
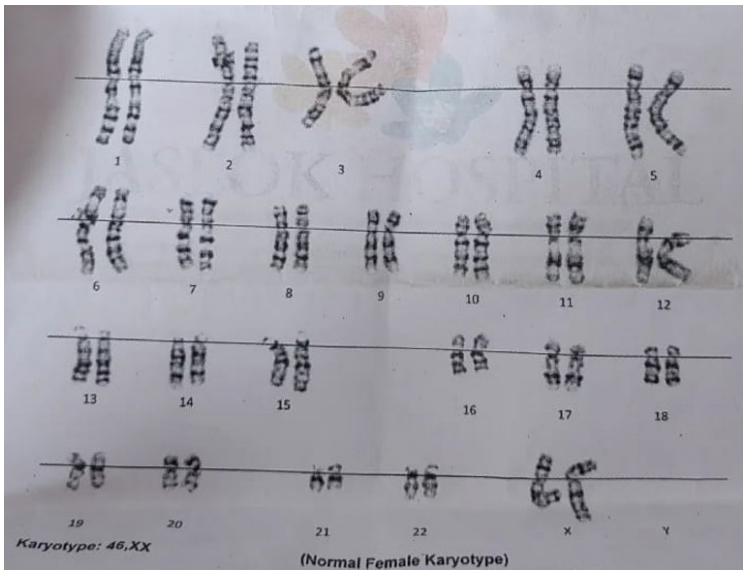


Figure 1. X-ray image showing normal bone age in a 15-year-old patient with primary amenorrhoea. No abnormalities are observed in bone development, confirming the absence of skeletal maturity delay.



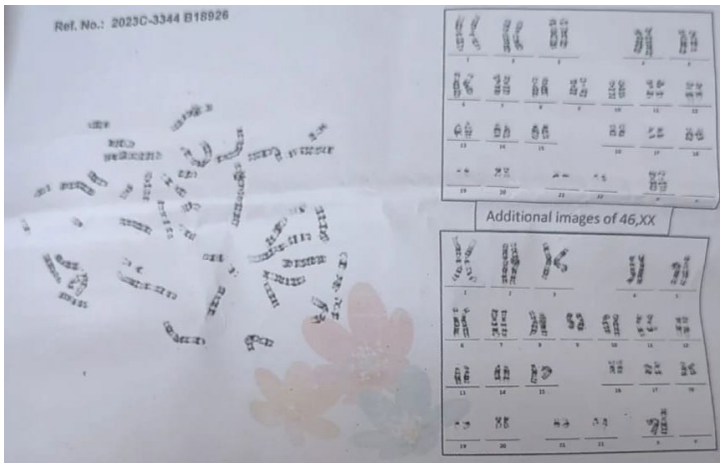


Figure 2. Karyotype analysis revealing a 46, XX chromosomal pattern in the patient, consistent with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome diagnosis.

MRKH syndrome patients, allowing for less reliance on invasive diagnostic procedures (Preibsch et al., 2014). Differential diagnoses for MRKH syndrome include androgen insensitivity syndrome, transverse vaginal septum, and imperforate hymen. Androgen insensitivity syndrome can be distinguished by the presence of a 46, XY karyotype, reduced pubic and axillary hair, elevated male hormone levels, and rudimentary testicles detected on MRI. The diagnosis of MRKH syndrome imposes a significant psychological burden due to its implications for fertility (Londra et al., 2015). Psychological counseling and support groups can help patients cope with emotional distress. Treatment options include neovaginal surgery or progressive vaginal dilators. For fertility, assisted reproductive technologies and surrogacy are potential options (Edmonds et al., 2012).

4. Conclusion

A lack of comprehensive evaluation, delayed diagnosis, and unclear etiology contribute to underestimating the prevalence of MRKH syndrome. Physicians must be well-equipped to educate patients about their diagnosis, treatment options, and reproductive possibilities. Addressing the psychological impact of MRKH syndrome is equally crucial, especially regarding feelings of inadequacy or isolation, which may arise during adolescence. While the condition is not life-threatening, timely diagnosis and proper management can significantly improve patients' quality of life, allowing them to engage in sexual activity and consider reproductive options such as surrogacy.

Author contributions

Z.S. contributed to the data collection and analysis. A.A.K. led the conceptualization, methodology design, and manuscript drafting. S.A.N. assisted with data interpretation and contributed to manuscript revisions. A.H.I. supported the statistical analysis and provided insights on research methodology.

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Competing financial interests

The authors have no conflict of interest.

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