Clinical and Radiological Findings in Mayer-Rokitansky-Küster-Hauser Syndrome type 2
A Case Report

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Abstract
Mayer-Rokitansky-Küster-Hauser syndrome (MRKHS) or (Müllerian Agenesis) represents uterovaginal aplasia or hypoplasia of unknown etiology in young women with usual 46, XX karyotype, and normal secondary sexual characteristics. We report a 15-year-old adolescent woman with primary amenorrhea, and normal pubertal secondary sexual characteristics, normal hormonal workup, and clinical examination. Abdominopelvic magnetic resonance imaging (MRI) revealed cervical and uterine agenesis, with the absence of the proximal thirds of the vagina. Both kidneys are fused in the right iliac fossa with oval lobulated appearance, picture of crossed fused ectopia. The ovaries are normal and located bilaterally. The diagnosis of MRKHS type 2 was confirmed based on clinical, biochemical, and radiological findings. The correct clinical and radiological diagnosis of MRKHS by MRI is crucial for the next steps in long-term management.

Keywords: Müllerian Agenesis, Uterovaginal malformations.
Introduction
The MRKHS represents uterovaginal aplasia or hypoplasia in young women with a usual karyotype. The documented incidence is 1/4000-5000 female birth. Primary amenorrhea is the presenting sign, despite the development of typical secondary sexual characteristics. The syndrome may be discovered accidentally during the first sexual experience by a failure to achieve normal vaginal intercourse. It is infrequently encountered that the teen girls with rudimentary uterine parts may experience recurrent abdominal pain at the time of presumed menstrual cycle (cryptomenorrhea). There are two distinct types of MRKHS: typical (type I) with uterovaginal aplasia and atypical (type II) that additionally associated with systemic congenital anomalies of different penetrance. MRKHS does not present with clearly identifiable genetic causes, although the familial clustering of the syndrome is shown. Genetic and environmental dynamics may add to the development of MRKH syndrome, although their specific contribution is often unknown.

The patient's history, clinical examination, ultrasound, MRI, and laparoscopy can assist in the initial diagnosis of MRKHS. The main focus of management is through several surgical and nonsurgical techniques to correct vaginal agenesis.

Case Report
In 2019, a 15-year-old adolescent presented to the clinic with primary amenorrhea. She had normal pubertal secondary sexual characteristics. Axillary and pubic hair started at the age of 13 to 14 years. She describes usual breast development for her age. She had no history of vaginal bleeding, discharge, or intermittent pelvic pain. She was indifferent to her complaint and satisfied with her body image. Her mother and two sisters had menarche at 13 and 14 years, respectively, with no history of amenorrhea in the first and second-degree relatives. Other parts of the history were noncontributory.

One month before the presentation, she consulted a gynecologist who ordered some hormonal and general investigations, with an ultrasonographic evaluation that failed to visualize the uterus. The diagnosis that urged the family to seek the second opinion. Investigations one month before presentation are listed in Table 1.
On examination: Lean adolescent with no apparent dysmorphic features, with normal vital signs. Weight 56.5 kg, height 1.64 m, and body mass index (BMI) 21 kg/m^2.

The cardiorespiratory examination was routine. Abdominal examination after the complete evacuation of the bladder was normal apart from fullness at the suprapubic area with a centrally located fixed mass of (9 x 9 cm), and failure to palpate both kidneys on examination.

Breast examination revealed Tanner stage 5 for both breasts, which is typical for her age. There were normal scalp and axillary hair density. No acne. She is Caucasian with fair skin with no abnormal discoloration. A fellow gynecologist examined the pubic area and revealed normal external genitalia, normal clitoris, and pubic hair distribution Tanner stage 3.

We ordered a new transabdominal ultrasound study, which revealed a centrally located pelvic kidney, normal both ovaries, with uterine agenesis. The radiologist advised for an MRI study for confirmation. Figures 1-3 demonstrate the representative radiographic findings. The diagnosis MRKHS type 2 was confirmed based on clinical, biochemical, and radiological findings. The patient and the family inquired more about the syndrome, progression, future management, and sexual activity.

Additional workup included cardiologist consultation who ruled out any possible associated hidden cardiac defects, an expert surgical opinion about possible surgical managements, and psychiatric evaluation. The chromosomal analysis was costly for the family, although it is important. In early 2020, the patient’s family requested an official full detailed report of her condition for a possible second expert surgical opinion.

Discussion

MRKHS carries complex clinical heterogeneity and genetic basis in most cases, given no family history of MRKHS in most cases.\textsuperscript{1,2}

Different studies described a wide range of MRKHS-associated malformations, like renal malformations 34-58%, skeletal 12-50%, and cardiac 1-3.6%.\textsuperscript{1,4,8,9} The difference in the incidence of malformation is affected by the number of cases chosen and being single-center
The incidence of renal malformations in MRKHS is higher than that of the general population, due to the association and interaction of the two ductal systems in utero. Normal androgen levels can usually be seen in women with the typical (type 1) MRKHS, with normal urinary excretion of steroid metabolites. Yet, women with MRKHS can have polycystic ovarian changes with associated hyperandrogenism, and even may develop ovarian malignancy, although this is rare. Patients with atypical (type 2) MRKHS may have gonadal dysgenesis or ectopic ovaries in the absence of other associated systemic malformations. Chromosomal aberrations may present in women with either type of MRKHS and may reach 1.4% in some series, contradicting the usual karyotype definition in the syndrome.

Figure 3 showed that the distal third of the vagina is present, with cervical and uterine agenesis. A large Chinese cohort study showed a highly variable phenotype of MRKHS that all the 594 patients showed complete vaginal atresia, cervical aplasia. However, one to three centimeters of the lower vagina may be present.

The diagnosis of MRKHS relies on non-invasive methods. Transabdominal ultrasonography is a useful first investigation in suspected patients. Abdominopelvic MRI provides a more precise diagnosis when ultrasonographic findings are unclear. The addition of laparoscopy aids the final diagnosis of MRKHS, especially in cases of the rudimentary uterus, although the American College of Obstetricians and Gynecologists recommends against. The differential diagnosis of MRKHS includes vaginal structural anomalies like congenital vaginal agenesis, low transverse vaginal septum, and imperforate hymen. The 46 XY chromosomal aberration syndromes may be considered in the differential diagnosis.

The main focus in the management of MRKHS through surgical and nonsurgical techniques is to improve sexual activity through the creation of a neovagina and vaginal elongation, that alleviates some of the psychological burden and inferiority feeling that they were devoid of the vagina.

Patients with MRKHS may require a sophisticated custom-made multidisciplinary approach through gynecological, endocrinologic, and surgical care. Psychomental and sexual
healthcare should be offered through counseling, peer support groups, with specialized sex and relationship therapy to promote high levels of sexual well-being.13,14

**Conclusion**
The correct diagnosis of MRKHS and its associated malformations is the most crucial step in active management. MRI can provide a precise diagnosis in most cases of MRKHS, whether type 1 or 2.

**Conflict of Interest**
The authors declare no conflicts of interest.

**Funding**
No funding was received for this study.

**References**


Table 1: Different investigations result that were performed one month before presentation.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Results</th>
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<tbody>
<tr>
<td>Abdominopelvic ultrasound study</td>
<td>Malrotated kidney, non-visualized uterus, normal ovaries.</td>
</tr>
<tr>
<td>Follicular Stimulating Hormone (FSH)</td>
<td>2.8 mIU/mL (2.8 IU/L)</td>
</tr>
<tr>
<td>Luteinizing Hormone (LH)</td>
<td>1 mIU/mL (1 IU/L)</td>
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<tr>
<td>Prolactin</td>
<td>15 µg/L (652.17 pmol/L)</td>
</tr>
<tr>
<td>Dehydroepiandrosterone Sulphate (DHEA-S)</td>
<td>193 µg/dL (5.21µmol/L)</td>
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<tr>
<td>Cortisol</td>
<td>13 µg/dL (358.64 nmol/L)</td>
</tr>
<tr>
<td>Adrenocorticotrophic Hormone (ACTH)</td>
<td>25 pg/mL (5.5 pmol/L)</td>
</tr>
<tr>
<td>Estradiol (E2)</td>
<td>22 pg/mL (80.76 pmol/L)</td>
</tr>
<tr>
<td>17-hydroxyprogesterone (17-OHP)</td>
<td>105 ng/dL</td>
</tr>
<tr>
<td>Thyroid Stimulating Hormone (TSH)</td>
<td>0.9 ng/ml (0.9 uIU/L)</td>
</tr>
<tr>
<td>Total Testosterone (TT)</td>
<td>17 ng/dL (0.59 nmol/L)</td>
</tr>
<tr>
<td>Anti-Müllerian hormone (AMH)</td>
<td>13.1 pmol/L</td>
</tr>
<tr>
<td>Complete blood picture and film</td>
<td>Normal</td>
</tr>
<tr>
<td>Anti-tissue Transglutaminase IgA subtype</td>
<td>1.2 U/mL</td>
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**Figure 1:** Coronal T2 weighted magnetic resonance image shows the presence of bilateral normal sized-ovaries. Both kidneys are fused in the right iliac fossa with oval lobulated appearance, picture of crossed fused ectopia of the kidneys.

**Figure 2:** Axial T2 weighted magnetic resonance image demonstrates the crossed fused ectopia that appears as a midline mass. The ovaries are normal and located bilaterally.

**Figure 3:** Complete uterine body and cervical agenesis, with the absence of the proximal third of the vagina leaving short vagina (22 millimeters only), in the sagittal T2 image.