

Mayer Rokitansky Küster Hauser (MRKH) Syndrome: A Case Report

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Abstract: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare disorder of congenital uterine malformation characterized by aplasia of the uterus and the upper two-thirds of the vagina. This disease may cause a significant decrease in quality of life. This article reviews the case report of a 21-year-old woman came with primary amenorrhoea and underdeveloped breasts. External physical examination showed female sexual maturity consistent with Tanner stage 1. Ultrasound examination and abdominal CT scan showed uterine hypoplasia and no ovaries. There were no abnormalities of other organs in the abdomen. The laboratory test showed testosterone levels <2.5ng/dL, FSH 0.16 mIU/ml, LH <0.5 mIU/ml, and 46 XX karyotypes. The patient was given estrogen hormone replacement therapy to improve the patient's quality of life by enlarging breasts, preventing osteoporosis, and reducing the risk of heart and vascular disease. Our patient had MRKH syndrome type B/atypical-M4 characterized by uterine hypoplasia and agenesis of bilateral ovaries.

Keywords: Amenorrhoea, mayer-rokitansky-küster-hauser syndrome, ovarian ggenesis, uterine hypoplasia

1. Introduction

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare congenital disorder of female genital organs. This syndrome is characterized by aplasia of the uterus and upper two-thirds of the vagina with normal development of secondary sexual characteristics and a normal 46 XX karyotypes. MRKH syndrome is also known as CAUV (Congenital Absence of the Uterus and Vagina), MA (Müllerian Aplasia), or GRES (Genital Renal Ear Syndrome). The latter synonym is due to the phenotype variant of MRKH syndrome which is manifested not only in the reproductive organs but also in the kidneys, spine, ear, and also heart.¹

The incidence of MRKH syndrome has been estimated at 1 in 4,500 female births. The cause of this syndrome is still unclear. For a long time, this syndrome was considered a sporadic disorder, but an increasing number of familial cases support the hypothesis of genetic causes. In familial cases, this syndrome appears to be inherited as an autosomal dominant pattern. This indicates the involvement of developmental gene mutations or an imbalance of multiple chromosomes.¹

A long-term retrospective study in Denmark found an MRKH syndrome incidence of 1 in 4,500 to 5,000 live female births. According to the Danish national birth register, it was found that renal malformations were the most common extragenital malformations in patients with MRKH syndrome. However, in 33.9% of patients with renal malformations, no urinary tract imaging was performed. Only three cases of MRKH syndrome were found with a familial pattern, suggesting that the incidence of familial MRKH syndrome is still controversial.² MRKH syndrome is a rare disorder but may reduce the quality of life significantly. Therefore, this syndrome becomes an interesting case and it is important to understand.

2. Case Report

A 21-year-old Balinese female patient came with the complaint that she had never had menstruation and her breast did not growth like her peers. She went to a Gynaecologist first time at the age of 16 years. The patient stated that the result of the ultrasound examination at that time showed a delayed uterine growth. Then, the patient was given therapy for the development of her breasts and uterus, but the patient did not remember the medicine's name that was received from the obstetrician at that time. At the age of 21, the patient came to the hospital with the same complaints. She never had menstruation and her breasts was underdeveloped. The abdominal ultrasound examinations showed no visible uterus so the patient was referred to our hospital for further examinations.

The patient weighs 47 kg and height 160 cm. Based on the physical examination, it was found that the patient's vital signs and general condition were within normal limits. On the gynaecological examination, there were no glandular tissue found in the breast and the pubic hair did not grow (see Figure 1). Thus, the external female genitalia in this patient was consistent with Tanner stage 1. The vaginal examination using a speculum and vaginal sondage was also performed in this patient. There was an impression of a rudimentary cervical canal (Figure 2) and a vaginal length of 6 cm. On vaginal toucher examination, it was found that the uterus and right and left adnexa were not palpable.

Further radiological and laboratory examinations were done on this patient. The ultrasound examination showed no visible uterus and adnexa (Figure 3). The hormone levels in this patient were as follows: testosterone levels <2.5ng/dL, FSH 0.16 mIU/ml, LH <0.5 mIU/ml, and a karyotype of 46 XX. The patient also underwent a computed tomography scan (CT scan) with contrast. The CT scan results showed a uterine-like structure with a size of 1.2x0.9 cm. Thus, a hypoplastic uterus was suspected in this patient. There were no abnormalities found in the liver, gallbladder, pancreas, spleen, right and left kidneys, and bladder.

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Therefore, the patient was diagnosed with MRKH syndrome and given estrogen hormone therapy with a dose of 0.3 mg/day orally which can be increased gradually to a dose of 1-1.25 mg/day. The patient was also educated regarding their risk of infertility.



Figure 1: The patient's external genitalia was consistent with Tanner stage I. There were underdeveloped breasts and no pubic hair



Figure 2: Vaginal inspection showed an impression of a rudimentary cervical canal

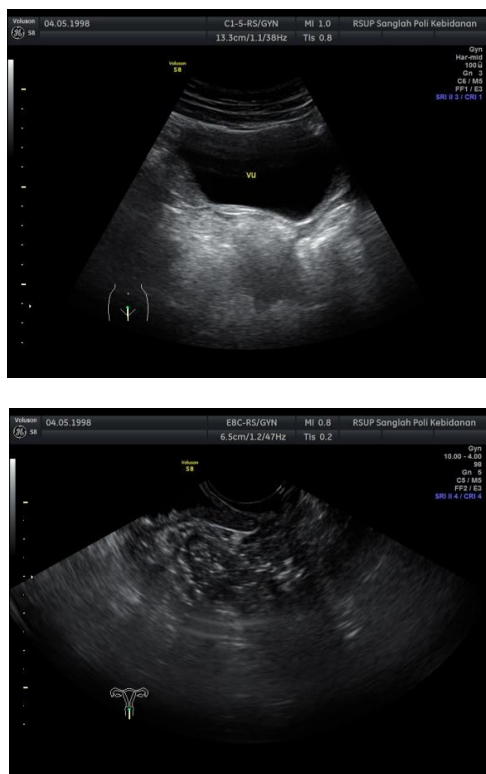


Figure 3: There was no uterus and adnexa found based on the ultrasound examination

3. Discussion

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is characterized by congenital aplasia or severe hypoplasia of structures originating from the Mullerian ducts, including the upper vagina, uterus, and fallopian tubes.³ This syndrome is very rare, where the estimated incidence is 1 in every 4500 women.^{1,2} Women with this syndrome are characterized by primary amenorrhoea but have normal secondary sexual signs, 46 XX chromosomes, normal ovarian function in most cases, and a deformed uterus and proximal (upper 2/3 portion) of the vagina.⁴

The first clinical manifestation of MRKH syndrome is primary amenorrhoea. The external physical examination may show complete puberty with secondary sexual characteristics of a normal woman (pubic hair and breast development consistent with Tanner stage 5) and normal external genitalia. Through the vaginal inspection, the clinician may find the reduced form of vaginal invagination (2-7 cm).¹

The diagnosis of MRKH syndrome is usually based on radiological examination. The main options for radiological examination in MRKH syndrome are ultrasound and magnetic resonance imaging (MRI). The ultrasound examination has the advantage of being more accessible and more widely available, but it is not always effective in identifying underdeveloped Mullerian duct structures and ovaries, which are located high in the pelvis and often at the periphery of the pelvis. The presence of extra-pelvic ovaries has been reported in 16-19% of cases. Most ultrasound examinations in this syndrome show no visible uterus and cervix. MRI examination of the pelvis is used to find abnormalities of other organs in the abdomen.⁵ If the MRI

examination is not possible, ultrasound examination has almost equal ability in making the initial diagnosis of this syndrome. The thing to keep in mind is that ureteral anomalies and skeletal anomalies may not be adequately diagnosed by ultrasound examination alone. An examination using a CT scan is usually avoided because it rarely offers an advantage over MRI for diagnosis of MRKH syndrome and has a greater radiation exposure.⁶ Laparoscopy may be indicated when pelvic symptoms are present due to uterine horns and remnants of Mullerian duct structures with functional endometrium. However, it is not preferred as a diagnostic tool because it is invasive and requires general anesthesia.⁶ The algorithm for the diagnosis of MRKH syndrome can be seen in Figure 4.

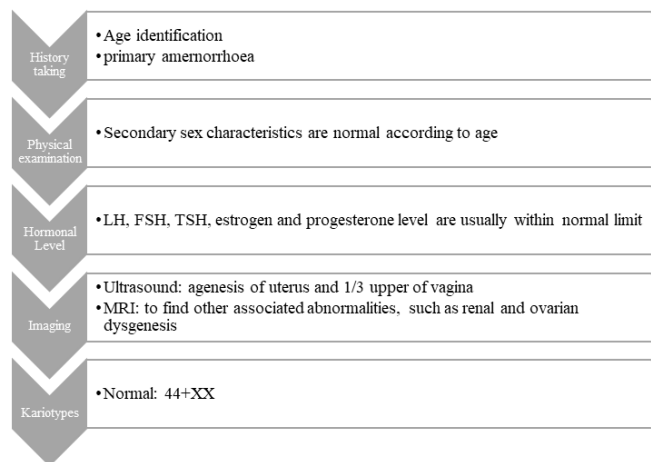


Figure 4: MRKH Syndrome Diagnosis Algorithm

There are two main types of MRKH syndrome, type A and type B. MRKH syndrome type A has an isolated variant of Mullerian duct malformation where there is agenesis of uterus, cervix, and proximal two-thirds of vagina, but has a normal bilateral ovarian function. MRKH Syndrome type B is associated with similar Mullerian agenesis as type A, but also has abnormalities in other organs, such as kidney, bone, and heart. Besides, type B MRKH syndrome may not have bilateral ovaries. Duckett classified Mullerian ducts disorders based on physical examination, ultrasound, and findings on laparoscopy. The Duckett classification system has five grades based on the abnormality in the Mullerian ducts system as explained in Table 1.⁷

Table 1: Classification of Abnormalities in the Mullerian Ducts (M) System

Grade	Abnormalities
M0	a unilateral system normally formed but unfused/retained septum
M1	vaginal agenesis alone. Uterus normal.
M2	vaginal and uterine agenesis.
M3	total Mullerian agenesis
M4	Mullerian and ovarian agenesis

Our 21-year-old female patient presented with complaints of never having menstruation (primary amenorrhoea) whereas normal menarche usually occurred at the age of 10-15 years. On physical examination, it was found that there was no glandular tissue in the breast and no pubic hair that was consistent with Tanner stage 1. The ultrasound, abdominal

CT scan, and karyotype examination result showed a possible diagnosis of MRKH type M4 syndrome where there is total agenesis of the Mullerian ducts system and the ovaries. The hormonal level in this patient was low in FSH and LH levels, while in MRKH syndrome the levels of hormones such as LH, FSH, estrogen, testosterone, TSH, and prolactin level is tended to be normal.⁷

A hypogonadotropic hypogonadism state may occur in MRKH syndrome accompanied by ovarian agenesis (the M4 grade). The laboratory test results may show a low level of testosterone or estrogen (hypogonadism) due to complete or partial absence of gonadotropin-releasing hormone (GnRH)-mediated release of LH and FSH (hypogonadotropic hypogonadism) with normal anatomy and anterior pituitary function. In our patient, there was an isolated GnRH condition so the breasts were underdeveloped and primary amenorrhoea was present. Our patient also had low FSH and LH levels. There are two major concerns of the MRKH syndrome which are sexual activity and the potency to be pregnant. The sexual activity may be achieved by surgical vaginoplasty or non-surgical vaginal dilation procedures to form the vaginal organs. Meanwhile, the potential for future pregnancies can be achieved by in-vitro fertilization techniques followed by embryo transfer to surrogate mothers in women with normal ovarian function.⁷ However, in the case of total agenesis of uterus and ovarium, as in our patient, tend to have a poor prognosis regarding the fertility problems.

This patient is given pharmacological therapy in the form of oral estrogen preparations at a dose of 0.3 mg/day which can be increased gradually to a dose of 1-1.25 mg/day. The aim of this hormonal therapy was to enlarging breasts, preventing osteoporosis, and reducing the risk of vascular and heart disease. Hormonal therapy is not routine management of MRKH syndrome. However, there are cases where MRKH syndrome may occur together with dysgenesis or disorders of ovarian formation which are classified as Mullerian duct formation disorders (M4). Therefore, this estrogen preparation therapy is required for optimal breast development in patients with this syndrome.⁸ Recommended dosages of hormonal replacement therapy in MRKH syndrome are listed in Table 2.

Table 2: Recommendation for Hormone Replacement Therapy

Estrogen	Progesterone	
	Continuous	Sequential
Micronized 17 β -estradiol 1-2 mg per day (oral)	Medroxyprogesterone acetate 2.5-5 mg per day (oral)	Medroxyprogesterone acetate 10 mg per day (oral) for 12 days per month
Micronized 17 β -estradiol 100 μ g per day (transdermal)	Micronized progesterone 100 mg per day (oral)	Micronized progesterone 200 mg per day (oral) for 12 days per month
Conjugated estrogen 0.625-1.25 mg per day (oral)		

4. Conclusion

In cases of MRKH syndrome, it is necessary to carry out a thorough assessment starting from the history taking, physical examination, imaging (ultrasound, abdominal CT scan), hormonal examinations (testosterone, FSH, LH), and karyotyping to determine the patient's genotype. Our patient had type B/atypical-M4 MRKH syndrome which is characterized by uterine hypoplasia and agenesis of bilateral ovaries. These patients are given estrogen hormone replacement therapy to improve the patient's quality of life.

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