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Mayer Rokitansky Kuster Hauser Syndrome: A Case Study of Mullerian Agenesis in a Patient

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Abstract
Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is an uncommon congenital malformation characterised by agenesis or hypoplasia of the vagina and uterus. It occurs due to failure of development of the Mullerian duct. Its incidence is 1 per 4500 female births. Mostly, girls present with primary amenorrhoea. The diagnosis of MRKH has a significant impact on the lives of women especially in the way they perceive themselves as healthy and functioning women. We present a case of Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome. A 23year old single nullipara presented with failure to initiate menstruation since puberty. She has normal secondary sexual characteristics however she had a completely sealed portio-vaginalis and absent vagina. Abdominopelvic ultrasound showed a hypoplastic uterus and her karyotype is XX. A diagnostic laparoscopy revealed rudimentary fallopian tubes, hypoplastic uterus, absent cervix, a single ovary in the midline, with a grossly normal urinary bladder. The experience of failure to initiate menstruation in individuals with MRKH syndrome negatively affects their quality of life. Treatment includes psychological counselling and vaginoplasty.

Keywords: Amenorrhoea, Mayer-Rokitansky-Kuster-Hauser syndrome, Mullerian duct.

INTRODUCTION
Developmental anomalies of the Mullerian duct are among congenital disorders of interest to which Mayer Rokitansky Kuster Hauser syndrome (MRKH) is one of the wide variety of malformations (Anu *et al*, 2021). Mayer Rokitansky Kuster Hauser syndrome (MRKH) is a congenital malformation characterised by aplasia of the uterus and upper two-third of the vagina, with normal female secondary sexual characteristics and a normal karyotype (46 XX) (Amadou *et al*, 2020). The estimated prevalence is 1 in 4500 live births (American College of Obstetricians and Gynaecologists, 2018). There are two types of MRKH syndrome that have been described- MRKH syndrome Type I (typical) which is entirely a pelvic abnormality affecting the development of proximal vagina and uterus, and Type II (atypical). The atypical type is also associated with renal, vertebral, auditory, or cardiac defects (Anu *et al*, 2021; Rall *et al,* 2015) and occasionally coexisting with imperforate anus (El-Agwany, 2016). Primary amenorrhoea forms the most typical presenting feature worldwide (Ajiboye *et al*, 2017; Anu *et al*, 2021; El-Agwany, 2016). Other common features include coital difficulty and infertility (Omotayo *et al*, 2016). Mayer Rokitansky Kuster Hauser syndrome poses a serious challenge to the attending gynaecologist because it is not amenable to conventional forms of assisted reproductive techniques. It is also psychologically distressing to the patient/family discovering that some of her organs are absent, the difficulty in penetrative sexual intercourse

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and her inability to conceive (Ajiboye *et al*, 2017). Treatment options for Mullerian agenesis include surgical creation of a neovagina and vaginal dilation. Surrogacy, adoption and uterine transplantation provide motherhood options for women with MRKH syndrome (Herlin *et al,* 2020).

CASE PRESENTATION

A 23year old single, nullipara, not sexually active, presented with failure to initiate menstruation since puberty. She had no cyclical lower abdominal pain or swelling, no voiding difficulties, urinary incontinence or other lower urinary tract symptoms. The patient has normal secondary sexual characteristics when compared to her peers. She had no hearing loss and no history suggestive of cardiac defects. There was no similar history in her siblings and no history suggestive of exposure to teratogenic drugs in utero with no other co-morbid condition.

Examination revealed a young lady whose general condition was satisfactory with a body mass index of 21.04kg/m^2. Her breast is Tanner stage 5. She had no skeletal deformity. Her abdomen was unremarkable. Pelvic examination revealed normal female external genitalia, normal female pattern of hair distribution, normal urethral orifice but with a completely sealed portio-vaginalis and absent vagina.

Abdominopelvic ultrasound showed uterus of 1.32cm in maximum AP diameter, the kidneys were normal in position and size with a conclusion of hypoplastic uterus. Karyotyping revealed XX, hormonal profile was normal, routine packed cell volume was 33%, electrolyte, urea and creatinine were normal.

She had examination under anaesthesia and diagnostic laparoscopy which further confirmed sealed portio-vaginalis with absent vagina, rudimentary fallopian tubes and hypoplastic uterus, absent cervix, a single ovary in the midline, with a grossly normal urinary bladder.
A diagnosis of primary amenorrhoea due to Mullerian agenesis was made and the patient and her family were counselled on the findings and prognosis.

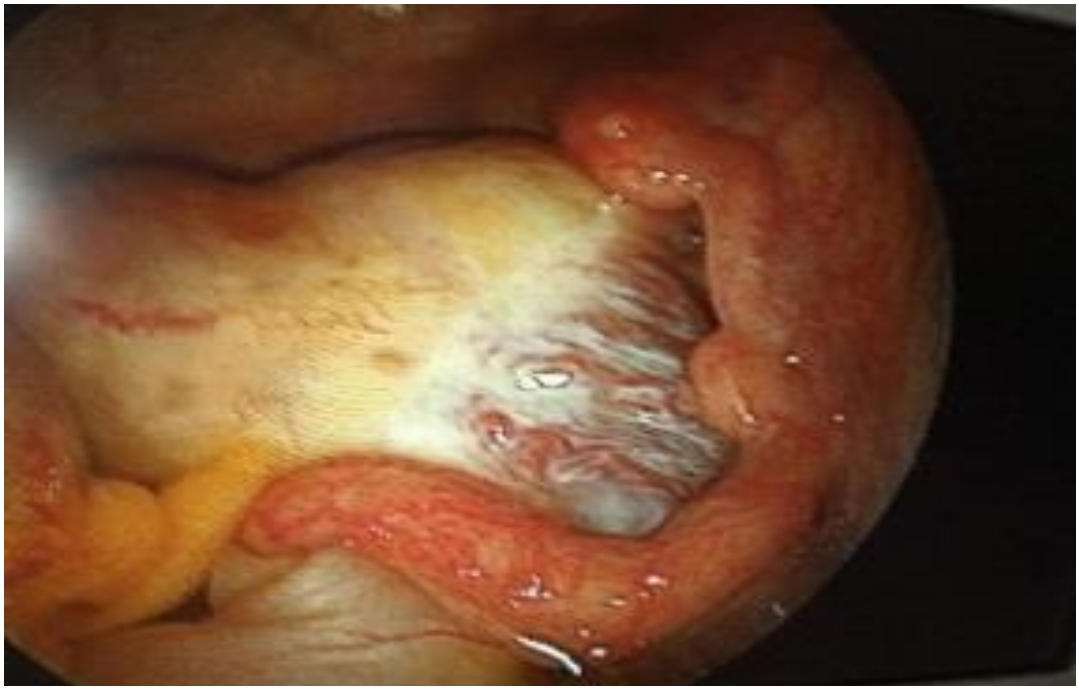

Fig 1: Rudimentary fallopian tubes and hypoplastic uterus (laparoscopic image)

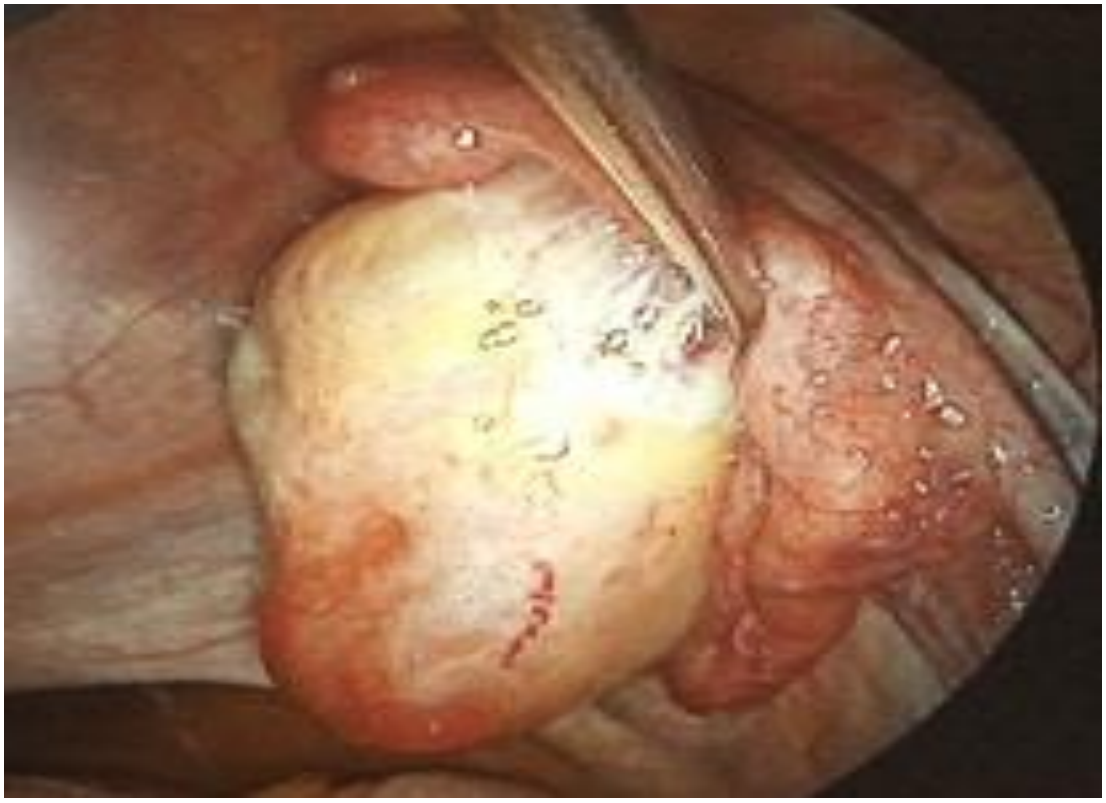

Fig 2: Single ovary in the midline (laparoscopic image)

DISCUSSION

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome occurs as a result of malformation of the Mullerian ducts which starts developing around the 5th - 6th week of intrauterine life. The uterus, fallopian tubes, cervix, and upper two-thirds of the vagina originate from the Mullerian duct or the paramesonephric duct, and the lower part of the vagina originates from the urogenital sinus. The upper part of the Mullerian duct forms the two fallopian tubes whereas the lower part of the two ducts fuse to form the uterus, cervix, and upper two- thirds of the vagina (Cunha *et al,* 2018; Herlin *et al,* 2020). The ovaries are of a different embryologic origin and they are normal in structure and function, as such, patients with this syndrome usually appear normal on physical examination, with normal height and secondary sexual characteristics. The labia majora, labia minora, clitoris, hymen and distal part of the vagina are usually present because they have a different embryonic origin (Ajiboye *et al*, 2017).

The aetiopathogenesis of MRKH syndrome is unclear. However, recently, it has been suggested that epigenetics may be implicated and this assumption is based on reports of one of two monozygotic twins developing MRKH syndrome, while the second twin was spared (Milsom *et al,* 2015). Others have also demonstrated an autosomal dominant pattern of inheritance of this condition (Nidhi *et al,* 2018). MRKH syndrome occurs as a purely genital malformation (type I), but also with associated malformations (type II and MURCS association; Mullerian, renal, cervicothoracic somite abnormalities). The type II MRKH was found in 35.2% of patients while 1.7% fulfilled the criteria for MURCS syndrome (Pietzsch *et al,* 2024).

The most common presenting symptom is primary amenorrhoea and the mean age at presentation is 16.7±2.4 years, which is the appropriate time for consultation for primary amenorrhoea (Ng *et al,* 2020). Our patient has normal secondary sexual characteristics and

didn't perceive absence of menstruation as an immediate problem which accounted for her presentation at the age of 23 years. Other symptoms of MRKH syndrome are inability to engage in sexual intercourse, dyspareunia and occasionally, cyclical lower abdominal pain (Choussein et al, 2017; Dabi *et al,* 2020; Matemanosak *et al*, 2024; Pietzsch *et al,* 2024).
Physical examination in patients with MRKH syndrome include normal female phenotype, with normal secondary sexual characteristics and a blind ending short vagina. The labia majora and minora, clitoris, hymen and distal portion of the vagina are usually present (Anu *et al,* 2021).

After history and examination, diagnosis of MRKH syndrome is made by laboratory investigation, radiological evaluation and karyotyping. Laboratory investigation includes hormonal profile i.e. Luteinizing hormone (LH), Follicle stimulating hormone (FSH), Oestrogen, Testosterone, Thyroid stimulating hormone (TSH) and prolactin. Usually, in MRKH syndrome, hormonal profile is normal (Nidhi *et al,* 2018). On radiological evaluation, ultrasound reveals absent uterus and cervix with mostly normal bilateral ovaries. For the confirmation of diagnosis and surgical planning, Magnetic resonance imaging (MRI) of the abdomen and pelvis is the investigation of choice. In addition to the findings of absent uterus and cervix with absence of upper two-thirds of the vagina, MRI helps to detect other associated anomalies (Fiaschetti *et al,* 2012; Nidhi *et al,* 2018). Skeletal survey can be done to rule out skeletal anomalies (Nidhi *et al,* 2018). On karyotyping, normal 46 XX karyotype is found in patients with MRKH (Matemanosak *et al,* 2024). This current patient had 46 XX Karyotype with a normal hormonal profile, MRI was however not done due to its unavailability at the time of her evaluation.

If these findings are inconclusive, laparoscopy is indicated in confirming the absence of the uterus and the presence of the ovaries (Okhionkpamwonyi *et al,* 2020). This diagnostic modality was offered to this patient and it revealed rudimentary fallopian tubes and hypoplastic uterus, absent cervix, a single ovary in the midline, with a grossly normal urinary bladder. Abnormally located ovaries have been reported in patients with MRKH syndrome (Matemanosak *et al,* 2024; Wang et al, 2018).

Following the diagnosis of MRKH syndrome, these patients suffer extreme anxiety with very high psychological distress when told they have no uterus and vagina and cannot bear children (Yakasai *et al,* 2015). In fact, this anomaly, compromises sexual intercourse and fertility and results in intense psychological suffering in these patients who feel diminished in their femininity (Callens *et al,* 2014). Therefore, it is recommended that the patients and caregivers should be offered guidance and psychological support (Anu *et al,* 2021; Wagner *et al*, 2016). The patient and her family were duly counselled on her condition.

The immediate differential diagnosis of MRKH syndrome is androgen insensitivity syndrome (AIS). AIS results from inactivating mutation of androgen receptor leading to absence of development of male characters. In AIS, young girls present with primary amenorrhoea with scarce pubic and axillary hair growth. On further investigation, no uterus, cervix and ovaries are seen, rather intraabdominal testicles are found. On karyotyping, genotype 46 XY is found. In AIS, surgery needs to be done to remove gonads due to risk of gonadal malignancy (Aminu *et al*, 2018; Nidhi *et al,* 2018).

The management of MRKH syndrome is multidisciplinary involving the general surgeon, gynaecologist, urologist, plastic surgeon, and the psychologist (Choussein *et al*, 2017; Kinyina *et al,* 2022). Both non-surgical and surgical management options have been proposed for MRKH syndrome (Choussein *et al,* 2017), but these two options offer only palliative therapy

(*Aminu et al,* 2018). Vaginoplasty and vaginal dilation can be performed to allow for satisfactory sexual intercourse. A neovagina can be created using non-surgical methods (dilators) if a vaginal dimple is present and in case of its absence, several surgical measures are available (Nidhi *et al,* 2018). Surgical options involve the creation of a neovagina between the bladder and the rectum with the Wharton, McIndoe, Davydov techniques (Callens *et al,* 2014; Omotayo *et al,* 2016). Vaginoplasty can be done using intestinal segments such as the sigmoid colon (Amadou *et al,* 2020; Kinyina *et al,* 2022). Surgical traction of the vaginal dimple using the Vecchietti technique has also been described (Callens *et al,* 2014). This patient was counselled on all these options of management.

The timing of the surgical or nonsurgical creation of the neovagina should be planned for when the woman is emotionally mature and expresses the desire for correction (Aminu *et al,* 2018). Adoption and surrogacy are recommended for those wishing to have children. As ovulation usually occurs among women with Mullerian agenesis, *in vitro* fertilization and surrogacy can be opted by those who desire their genetic offspring. Uterine transplant has now emerged as a fertility treatment modality for women with MRKH syndrome (Okhionkpamwonyi *et al*, 2020).

CONCLUSION

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is a rare congenital disorder characterised by uterine and vaginal agenesis. Typically, the presentation is primary amenorrhoea, inability to achieve penetration during sexual intercourse with normal secondary sexual characters. Ultrasonography reveals absence of uterus and cervix. They have a normal 46 XX karyotype. The patient and family need urgent psychological counselling. Neovagina is firstly created by serial vaginal dilators and vaginoplasty can be done to allow for sexual intercourse. Pregnancy can be achieved by using latest *in vitro* fertilization techniques and surrogacy.

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