Abstract

Mullerian agenesis is one of the causes of developmental defect of genital tract and is also known as Mayer Rokitansky-Kuster-Hauser syndrome. The chief complaint is primary amenorrhoea. The incidence is 1: 4,000-10,000 females. A female unmarried girl aged about 15 years was brought by her parents to Gynaecological Outpatient Department (OPD), National Institute of Unani Medicine (NIUM), Bangalore in 2014 with the complaint of lower abdominal pain every month since the age of 12 years and not having attained menarche. On the basis of signs, symptoms and ultrasonography (USG) the case was diagnosed as Mullerian agenesis or Mayer Rokitansky-Kuster-Hauser syndrome (MRKHS) type II.

Keywords: Mullerian agenesis, MRKHS Type II, Absent uterus, vagina and kidney, USG diagnosis.

Introduction

Mullerian agenesis is also referred to as mullerian aplasia, Mayer Rokitansky-Kuster-Hauser syndrome or vaginal agenesis. The incidence is 1 per 4,000-10,000 females. Ninety percent affected women have reproductive tract abnormalities. After gonadal dysgenesis, mullerian agenesis is the second most common cause of primary amenorrhoea. Upper part of mullerian duct forms uterus, cervix, fallopian tubes and upper part of vagina, whereas caudal part of mullerian duct forms lower part of vagina. Failure of embryologic growth of the mullerian duct causes agenesis or underdevelopment of vagina, uterus or both. The vaginal canal is absent or markedly shortened, but the ovaries are normal in structure and function. Examination reveals an absence or severe hypoplasia of the upper vagina as well as frequent uterine agenesis. Most Mullerian Duct Anomalies (MDAs) are associated with functioning ovaries and normal external genitalia. These abnormalities are often recognized after the onset of puberty. The young women often represent with absence of menstruation.

There are two types of MRKHS. Type I or Typical and Type II or Atypical. In Type I, lower part of mullerian duct is affected leading to absence of upper vagina and uterus, whereas in Type II, both upper and lower part of the mullerian duct is affected and is often associated with other anomalies like renal, skeletal and hearing defects. Affected women usually have absence of menstruation by the age of 15 years i.e. primary amenorrhoea due to absence of uterus and cervix. Women with MRKH syndrome have normal chromosome pattern i.e. 46 XX with normal female external genitalia, breast, pubic hairs and functioning of ovaries. The cause of MRKH syndrome is unknown, although it probably results from a combination of genetic and environmental factors. It is believed that MRKH syndrome is caused by exposure of the foetus to some medical illness or drugs during pregnancy. However, studies have not yet identified an association with maternal drug use, illness or other factors. Most cases of MRKH syndrome occur in people with no history of the disorder in their family. Less often, MRKH syndrome passes through generations in families.

On physical examination patients with mullerian agenesis have normal height, secondary sexual characteristics, body hair and external genitalia. Furthermore, a vagina is either absent or present as a short blind ended structure without a cervix at the vaginal apex. Patients with mullerian agenesis have a normal 46 XX karyotype and a normal hormonal profile.

Conventional three-dimensional ultrasonography and magnetic resonance imaging can be used to evaluate the mullerian structures. Management of patients with mullerian agenesis includes psychosocial counseling to address the functional and emotional effects of genital anomalies as well as correction of the anatomical defect. After the diagnosis of mullerian agenesis, the adolescent should be offered counseling to emphasize that healthy sexual relationships are possible. Future fertility options should be addressed with adolescents and their parents or guardians. In type I mullerian agenesis, nonsurgical creation of the vagina is the appropriate approach in most patients. Nonsurgical creation of the vagina is self-dilatation by placing successive dilators on the vaginal dimple for 30 minutes to 2 hours per day. It will take several months to achieve their goal and are likely to be successful with this technique. Surgical creation of vagina is elective and it requires ongoing postoperative dilation to maintain adequate vaginal length and diameter. In type II, assisted reproductive techniques and use of a gestational carrier (surrogate) is appropriate.
Case presentation
An unmarried female patient aged 15 years attended Gynaecology OPD of NIUM with the complaint of lower abdominal pain every month since the age of 12 years. She was admitted and on interrogation she revealed that she never had menses. There was no history of thyroid dysfunction, family history of delayed menarche, surgical intervention and other relevant medical diseases. Her mother denied any medical treatment during her pregnancy except routine supplements. There was no radiological exposure during pregnancy or consanguinity among parents.

Patient was studying in XI standard, had mixed diet with good appetite, sleep and normal bowel habits. On physical examination, she was of average built, her height was 152 cm and weight was 42 kgs. Pallor, cyanosis or puffiness was not seen on face. Webbing of neck was seen. Secondary sexual characters were normally developed with the tanner stage IV, axillary and pubic hair distribution was found to be normal. Breasts were normally developed. On systemic examination, chest was bilaterally symmetrical, no added sounds were present. Heart sounds were normal. On abdominal examination, abdomen was flat, no scar, tenderness or organomegaly was present. On genital examination, external genitalia were normal, but vaginal orifice was absent.

Vitals were normal. Blood pressure was 110/70 mm of Hg, pulse 82/min, afebrile and respiratory rate was 22/min. Since patient never had menses she consulted gynecologist for the complaints of amenorrhoea and was investigated accordingly. She came to NIUM Gynaecology OPD with previous reports of different investigations. She had USG abdomen on 31/10/2013 which showed an absent uterus, but both ovaries were normal. The right ovary was 31.9 X 12.6 mm and left ovary was 29.9X 10 mm size. Right kidney was absent but left kidney was of normal size with regular smooth outline. Absence of any adnexal or intra-abdominal mass were reported. Another abdominopelvic scan on 07/06/2014 showed an absent uterus and right kidney with normal ovaries. These findings were suggestive of a radiological diagnosis of agenesis of uterus and right kidney. A final diagnosis was rudimentary uterus with absent right kidney.

Hormonal and cytogenetic profile were not done but was advised. On the basis of signs and symptoms and radiological findings the case was diagnosed as Mullerian agenesis or MRKH syndrome Type II.

Management of patient with MRKH type II
Patients with MRKH syndrome suffer from severe distortions of body image, anxiety, depression, inter personal sensitivity and face a lot of psychological distress at diagnosis. Hence in this case, patient was counseled regarding the advancement of surgeries for malformations coping with vaginoplasty. Surgical correction of the vaginal anomaly permits normal sexual function and, possibly, reproduction with assisted techniques, so that a woman without a uterus can have her own genetic children. Patient was also informed about surrogacy. As these facilities were not available in our Institute, the patient was referred to a higher centre for further management.

Discussion
The syndrome of congenital absence of the uterus and kidneys in association with short or absent vagina was first described by Mayer, Rokitansky, Kuster Hauser and Schreiner. In this syndrome the first sign is absence of menstruation. Primary amenorrhoea is defined as failure to reach menarche. Evaluation should begin if menarche is not achieved by the age of 15 years or if menarche has not occurred within five years of thelarche. Differential diagnosis of primary amenorrhoea encompasses all hormonal and genetic disorders.

In hypogonadotropic hypogonadism breast development is poor and external genitalia are undeveloped. In pure gonadal dysgenesis the individuals are phenotypically female, average height, external and internal genitalia are normal with bilateral streak gonads and delayed development of secondary sexual characters. In adrenogenital syndrome, phenotypically female, average stature, labial fusion and enlarged clitoris, internal genitalia are normal. In cretinism, the stature is average with external genitalia and breasts are under developed, pubic and axillary hair are scanty. In hypothalamic-pituitary dysfunction, short stature, internal and external genitalia are underdeveloped. In primary ovarian failure, tall physical appearance, external and internal genitalia are under developed. In Turner syndrome, short stature, webbed neck, mentally retarded, secondary sexual characters are poor, cubitus valgus, broad shield chest, short fourth metatarsal, congenital malformations of cardiac, renal or great vessel (coarctation of aorta), underdeveloped external genitalia, uterus, fallopian tubes and vagina are present, but gonads are streak.

In Mullerian agenesis or in Mayer Rokitansky-Kurzer-Houser Syndrome type I, secondary sexual characters are normal. Primary amenorrhoea is present. Uterus and Vagina are absent, clitoris, ovaries are normal, breast development is normal, testosterone level is normal, Mullerian system is absent or rudimentary, wollfian system is absent, normal karyotype 46XX, where as in MRKH syndrome type II urological anomalies are associated i.e. unilateral or bilateral kidneys are absent in 40% of cases, skeletal malformation are seen in 12% of cases. Uterine anomalies are often associated with vaginal underdevelopment. Absence of both Mullerian ducts lead to absence of uterus and vagina. In cryptomenorrhoea, developmental defect of genital tract like imperforate hymen, transverse vaginal septum are seen. Periodic lower abdominal pain, urinary symptoms like frequency, dysuria, retention of urine due to elongation of urethra and suprapubic swelling.
may be seen. In vulva a tense bulging membrane of bluish colour is seen, because of accumulation of blood behind vagina.

In androgen insensitivity syndrome, sexual hair is absent or sparse, primary amenorrhea is present, uterus is absent vagina is short and blind, clitoris enlarged, gonads (testes) placed in labia or inguinal region or intraabdominal, breast development is normal. Serum testosterone level slightly elevated, both mullerian and wolffian systems are absent, karyotype is 46XY and associated anomalies are rare. Gonads secrete Anti-Mullerian hormone (AMH) and androgen receptors are defective. The present case was presented with primary amenorrhea and normal secondary sexual characters with absent uterus, vagina and kidney with normal ovaries. Based on signs/symptoms and investigation, patient was diagnosed as a case of Mullerian agenesis or Mayer Rokitansky-Kurser-Houser Syndrome Type II.

Conclusion

Mullerian agenesis or MRKH syndrome is rare and it affects 1:4,000-10,000 women. These patients typically present with primary amenorrhea in adolescence with normal growth and development. The most important steps in this case are proper diagnosis and effective management of the underlying condition. Due to wide variation in clinical presentations, mullerian duct anomalies may be difficult to diagnose. Evaluation for associated congenital anomalies and psychosocial counseling before any treatment or interventions are essential, because of the implication for reproduction, these patients require psychological support, which should be offered as part of therapy. In type I nonsurgical creation of the vagina is self-dilatation by placing successive dilators on the vaginal dimple for 30 minutes to 2 hours per day. Surgical creation of vagina is elective and it requires ongoing postoperative dilation to maintain adequate vaginal length and diameter. In type II variety assisted reproductive techniques and surrogate is appropriate.

Editor’s comment

Early and correct identification of underlying anatomic disorders such as Mullerian agenesis, will allow provision of proper care, according to the patient’s needs and the existing abnormalities. Vaginal dilatation has been recommended as a first-line treatment, because of its less invasive character and high success rate. In cases in which surgical intervention is required, referrals to higher centers with expertise in this area should be considered because few surgeons have extensive experience in construction of the neovagina.

References


