Case Series

ANNALS OF MEDICINE & SURGERY

OPEN

Mayer–Rokitansky–Küster–Hauser syndrome managed with McIndoe's vaginoplasty: a case series and literature review

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Introduction: Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is a congenital anomaly characterized by the absence of the uterus and the upper two-thirds of the vagina. It is a rare congenital anomaly with an incidence of 1 in 5000 female live births.
Case series: The authors describe three cases of females presenting with primary amenorrhoea who were diagnosed with MRKH syndrome. The patients were managed with McIndoe's vaginoplasty with neovagina creation with an amnion graft.
Discussion: Management of MRKH syndrome involves vaginoplasty with neovagina creation. The approach to neovagina creation can be done surgically or non-surgically. Non-surgical creation of the vaginal cavity involves serial use of vaginal dilators, while there are several ways for surgical creation of neovagina. The modified Abbe-McIndoe procedure using amnion to create neovagina is a minimally invasive, rapid, and simple procedure with no risk of immune rejection because the amnion membrane lacks histocompatibility antigens. In addition, the graft is also readily available, storable, and inexpensive.
Conclusion: Diagnosis of MRKH syndrome can be made when a young female with primary amenorrhoea and normal secondary sexual characteristics has agenesis of the uterus, and upper two-thirds of the vagina revealed on ultrasonography or magnetic resonance imaging. The patient can be offered treatment with vaginoplasty with neovagina creation.

Keywords: Congenital anamoly, McIndoe vaginoplasty, MRKH syndrome, Primary amenorrhoea

Introduction

Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome, also known as Mullerian aplasia (MA) or congenital absence of the uterus and vagina (CAUV) syndrome, is a condition characterized by congenital aplasia of the Mullerian duct and underdeveloped female genital organs with normal secondary sexual characteristics and normal female karyotype (46, XX)[1]. The Mullerian duct or paramesonephric duct (PMD), which forms the upper two-thirds of the vagina, uterus, cervix, and fallopian tubes, fails to form or develop, which results in underdeveloped organs[2].

It is a rare congenital anomaly with an incidence of 1 in 5000 female live births[3] and is often undiagnosed till puberty when the female fails to attain menarche and presents with primary amenorrhoea[1]. In this case series, we present three cases of females in the time frame of three years who presented with complaints of primary amenorrhoea. We hereby discuss the role of appropriate surgical procedures for a better outcome for the patients presenting with this rare anomaly. This report has been written in line with CARE guidelines[4].

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:3206–3210

Received 29 December 2023; Accepted 20 February 2024

Published online 18 March 2024

http://dx.doi.org/10.1097/MS9.0000000000001877

Case series

Case number 1

A 19-year-old female presented to our tertiary care centre with complaints of primary amenorrhoea. She failed to attain menarche but had lower abdominal heaviness and discomfort every month. On examination of her external genitalia, her labia majora, labia minora, and external urethral meatus were normal with normal pubic hair distribution and development. However, a short blind-ending vagina of length 1 cm with dimpling at the apex was seen. She had normal secondary sexual characteristics. There was no history of amenorrhoea in her first or second-degree relatives.

Her thyroid function tests and other relevant investigations were normal. On transabdominal ultrasonography, the uterus and vaginal canal were absent (Fig. 1). On magnetic resonance imaging (MRI) of her pelvis, agenesis of the uterus, cervix, and proximal two-thirds of the vagina was present (Fig. 2). She was diagnosed with MRKH and surgery was planned. She underwent McIndoe's vaginoplasty with neovagina creation.

With the patient in the lithotomy position, two medium Allis tissue forceps were placed at the lateral margin of the labia minora on either side of the dimple. About 30 ml of normal saline was injected, a transverse incision was given at the area of the dimple (Fig. 3) and blunt hydro-dissection was carried out directed proximally to create neovagina. Care was taken not to

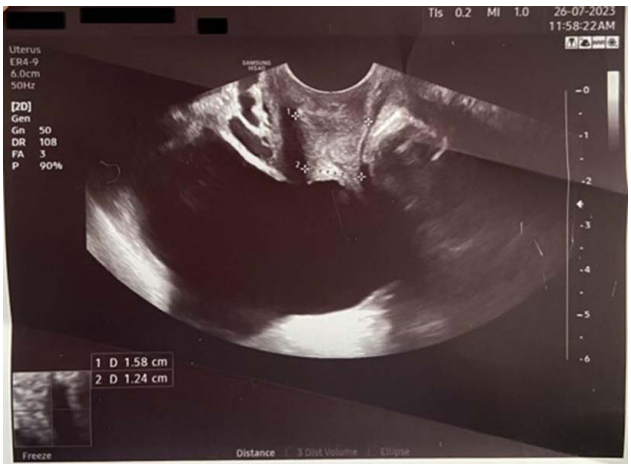

Figure 1. Ultrasonography showing the distance between rectum and urethra at different points in absence of vagina and uterus (as shown by red lines).

damage the rectal wall with a finger placed per anal at the rectal lumen. Foley's catheter was kept in situ to separate the bladder and urethra. Amnion graft was mounted to the newly created vaginal wall and the pre-formed vaginal mould of the appropriate size. The mould with the amnion graft was placed over the neo-vaginal canal and fixed in situ with four stitches (Fig. 4). Mould was kept attached to the newly created vagina by stitching its pedicle to the perineal skin which was kept intact for 5 days. Then, the stitch was removed before the patient was discharged. She was advised to keep mould by changing the condom every day for 2 weeks, then for the next 2 weeks, and she was asked to keep the mould with the condom only at night, followed by alternate nights for 1 month. She was called for follow-up at 2, 6 weeks, and 3 months. On her latest follow-up in the third month, her newly formed vaginal canal was intact with a length of 7 cm without any postoperative complications (Fig. 5).

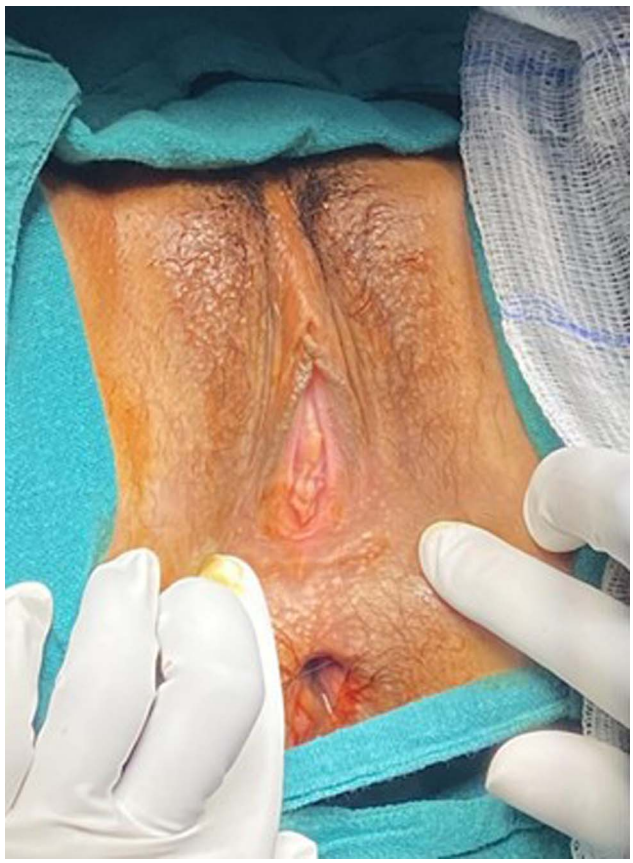

Figure 3. Blind vagina with dimpling preoperatively.

Case number 2

A 42-year-old female presented to our tertiary care centre with complaints of primary amenorrhoea. She had no history of cyclical abdominal pain or discomfort. On general examination, she had short stature, a webbed neck, and polydactyly with normal secondary sexual characteristics. On local examination,

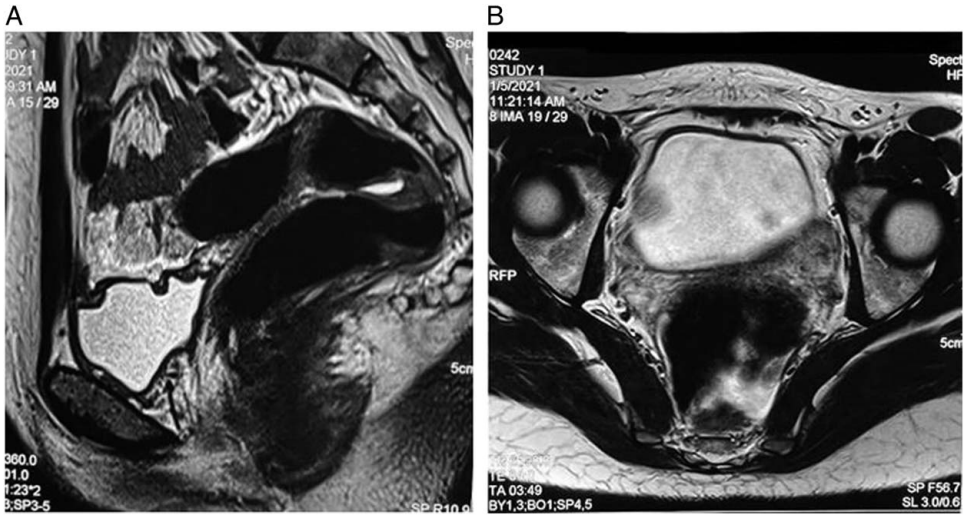

Figure 2. MRI showing absence of uterus with the presence of ovary. (A) Longitudinal section. (B) Transverse section.

Figure 4. McIndoe vaginoplasty with neovagina creation after mould application.

labia majora, labia minora, and external urethral meatus were well developed with normal public hair development. She also had a blind-ending vagina of length 3 cm with an absent cervix at the apex. Diagnosis of MRKH was made based on ultrasonography. She also underwent a similar procedure with a similar follow-up.

Case number 3

A 21-year-old female presented to our centre with primary amenorrhoea with normal development of secondary sexual characteristics; she also had no history of cyclical abdominal pain or discomfort; on local examination, pubic hair was present with normal labia majora, labia minora, clitoris, and urethral orifice. On per speculum examination, a blind vagina with dimpling was noted. On per vaginal examination, the uterus was not appreciated, and agenesis was suspected. On MRI, the uterus and upper two third of the vagina were absent, with normal appearances of the lower third of the vagina suggestive of complete mullerian agenesis [(MRKH) syndrome-type A). She also underwent a similar procedure, and a similar follow-up was performed.

Discussion

The aetiology of MRKH syndrome is not yet known. There are multiple theories with multiple genes implicated regarding the etiopathogenesis of the condition. Most cases of MRKH syndrome are sporadic, with only a few reports of familial condition[5]. The most commonly reported chromosomal regions and genes linked with MRKH syndrome are 1p31-1p35 (*WNT4* gene), 1q21.1 (*RBM8A* gene), 16p11 (*TBX6* gene), 7p15.3 (*HOXA* gene), 22q11.21, 17q12 (*LHX1* and *HNF1B* genes), and Xp22[5]. The establishment of the aetiology of this condition could help develop gene therapy, which can aid in the prevention or treatment of MRKH syndrome.

There are two types of MRKH syndromes: Type I MRKH syndrome (isolated uterovaginal aplasia) is characterized by agenesis of the uterus, and upper part of the vagina with normal fallopian tubes with no extragenital abnormalities and Type II

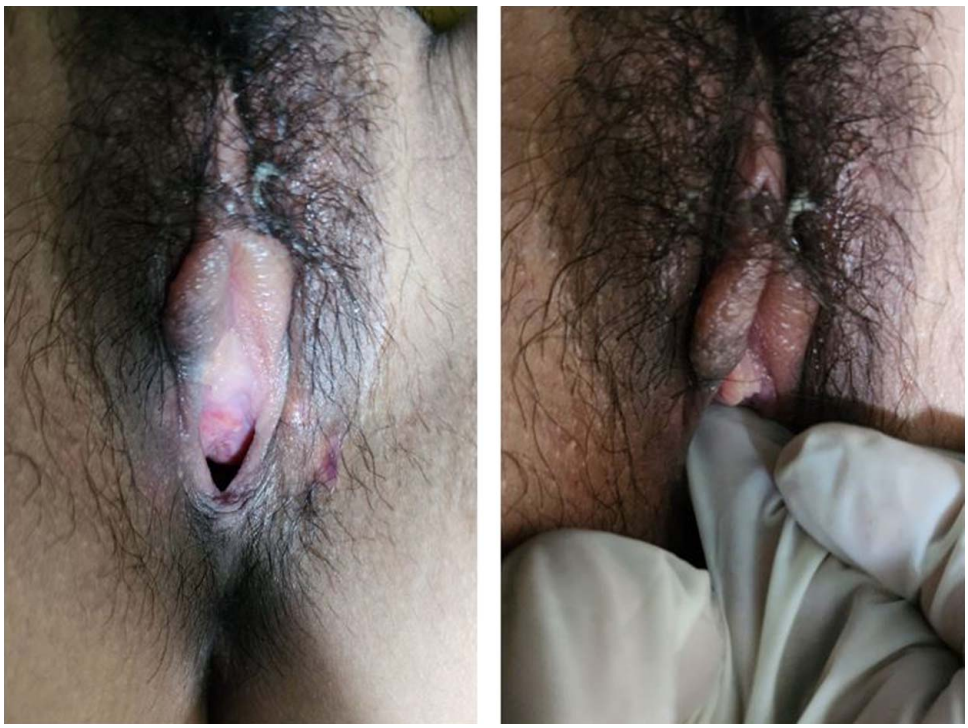

Figure 5. Patent neovagina of 7 cm on follow-up at third month.

MRKH syndrome refers to those cases of Mullerian agenesis associated with extragenital abnormalities such as musculoskeletal defects or renal anomalies such as renal ectopia, renal agenesis, renal hypoplasia and horseshoe kidney or ear abnormalities[1].

Females with MRKH syndrome can present with primary amenorrhoea with normal secondary sexual characteristics, usually during adolescence. Patients can also present with cyclical abdominal pain and dyspareunia/apareunia[6]. The first case in our case series also had abdominal discomfort every month. In the evaluation of a patient with primary amenorrhoea and normal secondary sexual characteristics, after ruling out pregnancy with confirmation of the absence of uterus and upper 2/3rd of the vagina and the presence of ovary based on transabdominal ultrasonography, diagnosis of MRKH syndrome can be made[6]. When there are no internal genitalia linked to primary amenorrhoea but normal external genitalia, cases of imperforate hymen are included in the differential diagnosis for the current patients. A primary amenorrhoea complaint linked to sporadic stomach pain and swelling may be present in the case of an imperforate hymen. This syndrome can also be mimicked by cases of testicular feminization in genetically XY individuals. When it comes to genetic screening, cases of testicular feminization can be ruled out, but rectal examination and imaging techniques like ultrasound and MRI can rule out cases of imperforate hymen[7].

On ultrasonography, the vestigial lamina underneath the peritoneal fold may be wrongly interpreted as a juvenile uterus; however, the hyperechogenic line corresponding to the uterine mucus membrane is absent in the vestigial lamina[2]. Renal malformations should also be evaluated during ultrasonography[6]. MRI should be performed when available as it can help evaluate any Mullerian abnormalities (aplasia or any uterine remnants), ovaries, and extragenital involvement[6]. For verification of a normal female karyotype (46, XX), G/Q-banding chromosomal analysis is commonly done[6]. Patients with androgen insensitivity syndrome (AIS) can have a similar presentation of primary amenorrhoea with normal breast development and absent uterus and upper vagina. However, patients of AIS have testes with the absence of pubic hair and male karyotype (46, XY)[2].

Treatment of MRKH syndrome is done with neovagina creation. Neovagina creation can be non-surgically or surgically. Nonsurgical creation of a new cavity can be done through the serial self-application of a number of vaginal dilators progressively increasing in size and length on the vaginal dimple for 20–30 min per day[8]. This process can take several weeks to months and can only be done if the vaginal dimple is long enough (2–4 cm)[2,8].

There are several surgical procedures for the creation of neovagina. McIndoe's operation involves the creation of the vaginal cavity by dissection of space between the rectum and bladder and insertion of a vaginal mould covered with split skin grafts[9]. Modifications of this procedure include relying on spontaneous epithelization, vulvar tissue, labia majora flaps, labia minora grafts, or synthesized biomaterial[2,6]. Laparoscopic Vecchietti vaginoplasty involves attaching subperitoneal threads to a mould in the vagina and placing a surgical traction device on the anterior abdominal wall[10]. Laparoscopic Davydov procedure uses the patient's own peritoneum for epithelization of the neovagina. This procedure is considered simple and safe, and the epithelium of the neovagina can react to hormonal changes and sexual excitation like normal vagina tissue making better lubrication. However, in the postoperative period, patients have to use the dilator for a long period until they can perform sexual intercourse[11].

One of the proposed new methods to create a neovagina is using the small intestine or part of the colon. The advantages of this method are that it does not require continuous and long-term dilatation, there is less chance of stenosis and obstruction, and there is less risk of fungal diseases. However, this method requires abdominal surgery[11]. Full-thickness skin graft (FTSG) can also be used to create neovagina in MRKHS as there is less incidence of vaginal contraction or foreshortening. However, there is a high risk of developing granulation in the donor graft and chances of development of ischaemia and necrosis in the donor area[12].

The modified Abbe-McIndoe procedure using amnion to create neovagina is a minimally invasive, rapid, and simple procedure with no risk of immune rejection because the amnion membrane lacks histocompatibility antigens. In addition, the graft is also readily available, storable, and inexpensive[13,14]. Due to these advantages, this procedure can be suitable for low and middle-income countries (LMIC).

In comparison with non-surgical methods, surgical neovagina creation is an invasive procedure that requires anaesthesia, surgical expertise, and adequate post-surgical dilatation to avoid the formation of strictures[15]. The disadvantage to non-surgical dilatation involves the risk of low compliance, long duration of treatment, and complications such as urethritis, cystitis, vesicovaginal or retro-vaginal fistula, and secondary prolapse[2,15]. Due to the long duration of treatment and the need for good compliance with self-dilatation, patients may prefer surgical correction rather than the self-dilatation technique; however, surgery still requires post-surgical dilatation to avoid stricture formation[2,15].

Conclusion

Diagnosis of MRKH syndrome can be made when a young female with primary amenorrhoea and normal secondary sexual characteristics has agenesis of the uterus, and upper two-thirds of the vagina revealed on ultrasonography. An MRI of the pelvis can confirm the diagnosis and provide more information on anatomy. Once a diagnosis has been made, the patient can be offered treatment with vaginoplasty with neovagina creation which can restore the anatomical integrity of the vagina and enables the patient to achieve sexual functionality and an improved quality of life.

Ethical approval

Patient anonymity is maintained throughout this manuscript. Ethical approval and consent was obtained for publication from the patient.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

Not applicable.

Author contribution

A.C.: drafting the work, manuscript writing and editing. S.A.: drafting the work, manuscript writing and editing. A.D.: drafting the work, manuscript writing and editing. R.B.: manuscript editing. A.B.: manuscript editing. A.C.: manuscript editing. R.S. B.: surgical procedure, patient care. A.D.: surgical procedure, patient care, manuscript editing.

Conflicts of interest disclosure

All authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Dr Anjana Dongol.

Data availability statement

Research data associated with case report are available.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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