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Original Article

Mayer-Rokitansky-Küster-Hauser syndrome: Evaluating how and to what extend management is essential

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Abstract

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, also referred to as Müllerian agenesis, is the second most common cause of primary amenorrhea. It is characterized by congenital aplasia or absence of the uterus, cervix, and the upper 2/3 of the vagina in phenotypically normal 46,XX females. Embryological evidence shows that MRKH syndrome occurs due to the failure of Müllerian ducts development, which in turn leads to a poorly developed vagina, cervix, uterus or even an absence of either organ. Usually patients present at puberty due to primary amenorrhea. So, mostly they visit to gynecological department but management is multi-model and multi-disciplinary. In this study, we have presented our experience of management of MRKH syndrome.

Materials and methods

A prospective observational study was being carried out in BSMMU from Oct. 2018 to Oct. 2021. A total 27 patients were diagnosed with MRKH syndrome.A total 27 patients were diagnosed with MRKH syndrome and evaluated for classification by X-ray, ultrasonography, hormonal evaluation and MRI for selected cases.

Results:

A total 27 patients were evaluated among them 9 patients were operated under paediatric surgery department. Patients age ranged from 13-18 years, mean age was 15.1 years.Type I MRKH syndrome patients were 11 and Type II MRKH syndrome were 16. We had treated 4 cases of Type-I and 5 cases of Type-II MRKH syndrome.

Conclusion:

Management of MRKHS is challenge in Bangladesh perspective. Surgery is not only the treatment but main focus should be in counselling for next conjugal and social life.

Keywords: MRKHS, BSMMU

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Introduction:

An umbrella term “disorders/differences of sex development (DSD)” widely used to refer all kinds of sexual disorders was proposed in the Chicago Consensus held in 2005 [1]. There are different variety of DSD in which non-hormonal DSD is one. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is one of the non-hormonal multiple malformation syndromes in DSD. MRKH syndrome is a rare congenital disorder that affect female. It is characterized by congenital absenceor rudimentary uterus and vagina in an individual with an XX karyotype. It is observed in one in 4,000 to 5,000 births [2]. It occurs due to mutation in Anti-mullerian hormone or Anti-mullerian hormone receptor. We mostly face such patients in our institute. Usually patients present at puberty due to primary amenorrhea. So, mostly they visit to gynecological department but management is multi-model and multi-disciplinary. In

this study, we have presented our experience regarding evaluation and management of MRKH syndrome.

Methods:

A prospective observational study was being carried out in BSMMU from Oct. 2018 to Oct. 2021. A total 27 patients were diagnosed with MRKH syndrome and evaluated for classification by physical examination (over all body status, perineum and secondary sexual characteristics) X-ray (for skeletal evaluation), ultrasonography of whole abdomen (kidney, adrenal gland, ovary, uterus, cervix and vagina), hormonal evaluation and MRI (condition of the mullerian duct structure and distance between vestibule to lower most position ofmullerian duct structure) for selected cases. Age, type of MRKHS, management planand operativeprocedure, follow-up and social life were recorded.

Results:

A total 27 patients were evaluated among them 9 patients were operated under paediatric surgery department. Patients age ranged from 13-18 years, mean age was 15.1 years. Mostly patients visited direct to gynaecological department with complain of primary amenorrhea or cyclical pain, after evaluation they referred to paediatric surgeons. Karyotyping of all patients was 46 XX. Type I MRKH syndrome patients were 11 and Type II MRKH syndrome were 16. Wehad treated 4 cases of Type-I and 5 cases of Type-II MRKH syndrome. Others patients are waiting for their management according to schedule. 60 % patients had renal abnormality and 10 % had skeletal abnormality in type II MRKHS. 80% patients visited with primary amenorrhea and 20 % with absent of vaginal opening. Out of 27 patients, 3 patients had small (1-2cm) and 1 patient has 4cm vaginal length were treated by vaginal dilatation. 2 patients had distal vaginal atresia and managed by pull-through vaginoplasty. Other hand, 7 patients had absent vagina and treated with replacement vaginoplasty by large gut. 3 cases after treatment got married. All patients are in follow-up.

Discussion:

Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is the most common form of vaginal agenesis, characterized bycongenital aplasia or hypoplasia or absence or malformationof fallopian tubes, uterus, cervix, and upper part of the vagina, that are derived from Mullerian structure. The structure and function of the ovaries are usually normal, although gonadal dysgenesis and ovarian agenesis have been reported in some cases. It is also known as Müllerian agenesis, CAUV (congenital absence of the uterus and vagina), MA (Müllerian aplasia) as well as Mayer–von Rokitansky–Küster malformation complex [2-4].

Exact etiology of MRKH syndrome has been unclear but consider to be environmental, non-genetic (maternal diabetes) or genetic in origin [5-7]. During embryonic development, Müllerian ducts (paramesonephric) usually differentiate into upper two-thirds of the vagina, uterus, cervix and fallopian tubes. MRKH syndrome could result from either a genetic defect in the Müllerian duct formation process or a pathogenic activation of anti-Müllerian hormone (AMH) signaling pathway. The mode of inheritance believed to be autosomal disorder with variable phenotypic expression from single mutant gene [10,11]. It occurs due to association of mutation of genes like HOXA, WNT4, WT1, PAX2, AMH, AMHR2 and others genes [2,9].

MRKH syndrome can be classified as — type I (isolated) or Rokitansky sequence (OMIM 277000), and type II (associated) or MURCS association (Müllerian duct aplasia, renal dysplasia and cervicothoracicsomite anomalies; OMIM 601076). Type II being the more frequent one [12]. while other study shows, frequency of type I and type II MRKH syndrome is 56–72% and 28–44%, respectively [13,14]. In our study type II MRKHS was more. Type I MRKH syndrome is usually characterized by a blockage or a defect in the upper vagina, cervix and uterus, along with normal fallopian tubes and ovary [7,15] also called Isolated utero-vaginal aplasia. while type II MRKH syndromemore frequently associated with musculoskeletal defects, several renal defects (such as renal unilateral agenesis, renal ectopia and horseshoed kidney) and, to a lesser extent, auditory and cardiac defects [3,16]. Renal malformations are the most frequent extragenital abnormalities in MRKH syndrome occurring in 30–40% in European cohorts. Unilateral renal agenesis (URA) is the most frequent anomaly accounting for around half of all renal malformations associated with MRKH syndrome[9].

MRKH syndrome patients havenormal external genitalia (clitoris, vulva, labia minora and labia majora). Andthe patients typically have a normal reproductive endocrine function and reach puberty showing normal signs of thelarche and pubarche. Clinically, patients will have an imperforate hymen and a proximally obstructed vagina canal, which in turn leads to primary amenorrhea and cyclic pelvic pain at puberty. Patients are

usually diagnosed at adolescence when they fail to onset their menstrual cycle (menarche).Other symptoms include dyspareunia or apareunia [3,9].

Diagnosis by clinical features, imaging by ultrasonography of vagina and pelvis and MRI of pelvis or by laparoscopic examination and ovarian biopsy [15,17-19]. These will provide complexity of the anatomical defect in the MRKH syndrome patients [3]. Other related laboratory tests include Karyotyping/chromosome analysis, LH, FSH, androgens and oestrogen, which are generally considered to be normal in MRKH syndrome. Ovary anomalies are rare and only found in 5–10% [9]. Different anomalies previously reported include unilateral agenesis, ectopic ovaries, polycystic ovaries, streak ovaries, and rarely tumors [20].

Treatments usually range from non-surgical (e.g., dilation procedures) to surgical approach (e.g., vaginoplasty surgery) [3]. The most commonly used non-invasive method is self-dilation by dilator (also referred to as Frank's method).However, non-surgical procedure can be applied only when the vaginal dimple is deep enough (2–4 cm) [7]. Disadvantages in dilation therapy include the risk of low compliance (especially in younger patients), time consume needed for a satisfactory result, the discomfort that some patients experience, and a low risk of urethral dilation [21].

Surgical procedures include vaginoplasties using various autografts such as McIndoe vaginoplasty (split-skin graft covering a mold placed in the dissected pouch between the rectum and bladder), Baldwin vaginoplasty (bowel graft), Davydov vaginoplasty (peritoneal graft) and Williams vulvavaginoplasty (labia majora flaps) [22-24]. An alternative traction based surgical method is the laparoscopic or traditional Vecchietti vaginoplasty. The only drawback of the abovementioned surgical procedures (except Vecchietti's) is the requirement of long term post-operative dilations (i.e. patient has to perform regular dilation to prevent collapse or shrinkage of the vagina) [3.9]. More recently the use of bioengineered tissue havebeen described for the creation of a neovagina. An intestinal vaginoplasty can be performed using a segment of sigmoid colon, ileum, or jejunum. With this approach, there is a low risk of tissue shrinkage and little need for long-term vaginal dilation. The tissue produces "lubrication"; however, the discharge at times can be excessive [2].

Discussing different treatment options with the patient, it is important to emphasize that there is no quick solution to obtain a functional vagina and surgical options still require continued postoperative dilation, by regular intercourse or vaginal dilators, to ensure satisfactory long-term outcome [9].Since 2002, The American College of Obstetricians and Gynecologists (ACOG) has recommended dilation therapy as first line treatment based on the high overall success rate (90–96%), being non-invasive with a low complication rate, and low costs [25]. surgery should be reserved for patients experiencing failure with dilation therapy and emphasizes that surgery still requires post-surgical dilation to avoid strictures. Dilation therapy as first choice is also supported by Callens et al. [21], which further suggest laparoscopic Vecchietti vaginoplasty as preferred second-line therapy [9].

Treatment in childhood or early adolescence is not recommended, because of unacceptable complication rate and because full understanding and engagement from the patient is required for optimal results.Treatment consisting of creating a neovagina must be offered to patients only when they are ready to start sexual activity and also when they are emotionally mature.-Continued surveillance of psychological well-being of these patients should be considered [2,7].

Although 27 patients of MRKH syndrome visited to outdoor, only 9 patients have got treatmentbecause of hospital management scarcity. 5 patients had married after treatment, but 2 of them got divorced because husband's family wants child and other is leading normal married life. 1 patient had normal sexual life while 4 had painful intercourse. There is slight vaginal secretion daily in vaginal replacement case.After counselling to parents and patients, most of often refuse to go over surgical procedure except those whose has cyclical pain and hematometra. Surgery is not the main treatment in our context but counselling about complication,maintenance, consequences and effect in marital life.

Reference:

1. Hughes IA, Houk C, Ahmed SF, Lee PA, Society LW. Consensus statement on management of intersex disorders. Journal of pediatric urology. 2006 Jun 1;2(3):148-62.
2. Londra L, Chuong FS, Kolp L. Mayer-Rokitansky-Kuster-Hauser syndrome: a review. International journal of women's health. 2015 Nov 2:865-70.
3. Patnaik SS, Brazile B, Dandolu V, Ryan PL, Liao J. Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome: a historical perspective. Gene. 2015 Jan 15;555(1):33-40.

4. Fontana L, Gentilin B, Fedele L, Gervasini C, Miozzo M. Genetics of mayer–rokitansky–küster–hauser (MRKH) syndrome. Clinical genetics. 2017 Feb;91(2):233-46.

5. Simpson JL. Genetics of the female reproductive ducts. American journal of medical genetics. 1999 Dec 29;89(4):224-39.

6. Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E, Prieto L, Frias JL. Epidemiological analysis of outcomes of pregnancy in gestational diabetic mothers. American Journal of Medical Genetics. 1998 Jun 30;78(2):140-5.

7. Morcel K, Camborieux L, Programme de Recherches sur les Aplasies Müllériennes (PRAM) pram-network. coordination@ univ-rennes1. fr, Guerrier D. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. Orphanet journal of rare diseases. 2007 Mar 14;2(1):13.

8. Pizzo A, Laganà AS, Sturlese E, Retto G, Retto A, De Dominici R, Puzzolo D. Mayer-rokitansky-kuster-hauser syndrome: embryology, genetics and clinical and surgical treatment. International Scholarly Research Notices. 2013;2013.

9. Herlin MK, Petersen MB, Brännström M. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: a comprehensive update. Orphanet Journal of Rare Diseases. 2020 Dec;15(1):1-6.

10. Opitz JM. Vaginal atresia (von Mayer-Rokitansky--Küster or MRK anomaly) in hereditary renal adysplasia (HRA). American journal of medical genetics. 1987 Apr;26(4):873-6.

11. Pavanello Rde C, Eigier A, Otto PA: Relationship between Mayer-Rokitansky-Kuster (MRK) anomaly and hereditary renal adysplasia (HRA). Am J Med Genet 1988, 29:845-849.

12. Guerrier D, Mouchel T, Pasquier L, Pellerin I. The Mayer-Rokitansky-Küster-Hauser syndrome (congenital absence of uterus and vagina)–phenotypic manifestations and genetic approaches. Journal of negative results in biomedicine. 2006 Dec;5:1-8.

13. Lalatta F, Motta F, Restelli E, Bellini M, Miozzo M, Gervasini C, Dallapiccola B, Gentilin B, Fedele L. Dysmorphologic assessment in 115 Mayer–Rokitansky–Küster–Hauser patients. Clinical Dysmorphology. 2015 Jul 1;24(3):95-101.

14. Deng S, He Y, Chen N, Zhu L. Spectrum of type I and type II syndromes and associated malformations in Chinese patients with Mayer-Rokitansky-Küster-Hauser syndrome: A retrospective analysis of 274 cases. Journal of pediatric and adolescent gynecology. 2019 Jun 1;32(3):284-7.

15. Valappil S, Chetan U, Wood N, Garden A. Mayer–Rokitansky–Küster–Hauser syndrome: diagnosis and management. The Obstetrician & Gynaecologist. 2012 Apr;14(2):93-8.

16. Morcel K, Guerrier D, Watrin T, Pellerin I, Levêque J. The Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: clinical description and genetics. Journal de gynecologie, obstetrique et biologie de la reproduction. 2008 Aug 23;37(6):539-46.

17. Berger A, Batzer F, Lev-Toaff A, Berry-Roberts C. Diagnostic imaging modalities for Müllerian anomalies: the case for a new gold standard. Journal of Minimally Invasive Gynecology. 2014 May 1;21(3):335-45.

18. Bermejo C, Martínez Ten P, Cantarero R, Diaz D, Pérez Pedregosa J, Barrón E, Labrador E, Ruiz López L. Three-dimensional ultrasound in the diagnosis of Müllerian duct anomalies and concordance with magnetic resonance imaging. Ultrasound in Obstetrics and Gynecology. 2010 May;35(5):593-601.

19. Rousset P, Raudrant D, Peyron N, Buy JN, Valette PJ, Hoeffel C. Ultrasonography and MRI features of the Mayer–Rokitansky–Küster–Hauser syndrome. Clinical radiology. 2013 Sep 1;68(9): 945-52.

20. Miao Y, Wen J, Huang L, Wu J, Zhao Z. Diagnosis and management of ovarian tumor in Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. BioMed research international. 2018 Mar 12;2018.

21. Callens N, De Cuypere G, De Sutter P, Monstrey S, Weyers S, Hoebeke P, Cools M. An update on surgical and non-surgical treatments for vaginal hypoplasia. Human reproduction update. 2014 Sep 1;20(5):775-801

22. Banister JB, McIndoe AH. Congenital absence of the vagina, treated by means of an indwelling skin-graft. Proc R Soc Med. 1938;31:1055–6. 129.

23. Baldwin J. Formation of an artificial vagina by intestinal transplantation. Ann Surg. 1904;40:398–403. 130.

24. Davydov S. Colpopoiesis from the peritoneum of the ueterorectal space. Obstet Gynecol. 1969;12:255–7.

25. ACOG Committee Opinion No. 728: Mullerian Agenesis: Diagnosis, Management, And Treatment. Obstet Gynecol. 2018;131:e35–42.