



How to diagnose and treat mullerian malformations? A concise systematic review

Gabriela Pedroso Domingues^{1*}, Giovanna Pedroso Domingues¹, Hérya Maciel Gonçalves¹, Tamara Veiga Faria¹

¹ FACERES - Medical School of Sao Jose do Rio Preto, Sao Paulo, Brazil.

*Corresponding author: Gabriela Pedroso Domingues,
FACERES - Medical School of Sao Jose do Rio Preto,
Sao Paulo, Brazil.

Email: gapedroso08@gmail.com

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Introduction

Mullerian malformations comprise failures in the fusion of the paramesonephric duct to the midline urogenital sinus during the embryological process [1]. In normal development, due to non-opposition of the anti-Mullerian hormone, produced by the SRY gene, the bilateral Mullerian ducts fuse at their caudal end in the midline, evolving to the formation of the uterus in its central portion and, in the lower portion, the upper 2/3 and of the vagina; the cranial portion, in turn, will give rise to the fallopian tubes in the future [1,2].

Moreover, the defects present in clinical abnormalities such as kidney and obstetric: agenesis uterus-vaginal-tubal, septate uterus, uterus bicornuate rudimentary and didelf as well syndromes, the most frequent Mayer-Rokitansky-Kuster-Hauser (MRKH) [1]. Among the various anomalies present in the clinic, MRKH usually courses with primary amenorrhea, as its first manifestation, being characterized by uterovaginal agenesis, with karyotype 46, XX. It can be isolated (type I) or associated with extragenital malformations (type II), and may manifest renal and skeletal anomalies and, more rarely, auditory and cardiac defects [3,4].

This review aimed to understand which are the most common presentations of Mullerian malformations, diagnosis and the treatment of the same, since there are few studies and much of the content available in its entirety is presented in the form of case isolated reports.

Methods

This systematic literature review was based on the following question: What is the clinical picture, the diagnosis and what is the best approach for treatment?

The selected articles needed to meet the following specifications to be eligible: free full-text clinical trial type, controlled and randomized trial, analysis and systematic review published in the last 5 years (2016 to 2021), with no language specificity. The bibliographic search was performed based on electronic data: PubMed, Scielo and BVS/LILACS in August 2021. The terms used for research were "Mullerian Malformations" and "Mullerian Malformations".

A priori, in the selection of studies, articles that did not meet the objectives of the review based on titles, abstracts, introduction and objectives were excluded. In the background, unselected articles were submitted to exclusion justifications. To be selected, was assigned to answer the following topics: the country and the year of publication, the purpose, the type and methodology (study design) and the scientific question posed by this study. In cases of disagreement between evaluators, they were analyzed by the supervisor of this work.

Results and Discussion

The total of n=53 articles were found, with n =44 from the PubMed platform, n =4 from Scielo and n=5 from Lilacs. Of the articles that met the inclusion criteria, n=12 were found in total, of these only n =4 were from Lilacs and n =8 from PubMed. From these articles, n =12 were used in this review. Other 41 articles were not used because they had nothing to do with the scientific question of the study or were related to other issues (Table 1).

Table 1. The presentation of the clinical conditions, diagnosis and treatments found during the research.

Articles	Symptoms	Diagnosis	Treatment
<i>Paz Montañez. 2020 [7]</i>	Chronic pelvic pain, dysmenorrhea, didelphic uterus, urinary infections and ipsilateral renal agenesis.	Confirmation by laparoscopy.	-
<i>Huneus A.2017 [8]</i>	Dysmenorrhea, chronic pelvic pain after menarche, renal agenesis ipsilateral I nometrorragia.	Physical examination, transabdominal gynecological echotomography and magnetic resonance imaging.	Reese surgical ction vaginal septum. Operative protocol: diagnostic laparoscopy, diagnostic vaginoscopy, hysteroscopy and surgical vaginoscopy.
<i>Fernández JA.2019 [9]</i>	Case1: anorectal malformation with rectobuccal fistula, narrow vagina. Case 2: agenesis and anorectal fistula, hemi-uterine rudimentary, ovary and are querdo rudimentary communication with no womb. Case 3: agenesis of uterus and ovary, right renal agenesis, single perineal orifice, underdeveloped gluteal muscles without anal fovea.	In general: Physical examination, ultrasound, laparoscopy.	In general: colostomy and anorectoplasty.
<i>Passos IMPE.2020 [1]</i>	Primary amenorrhea, dysmenorrhea, pelvic pain, endometriosis, sexual difficulties and low self-esteem.	Two-dimensional or three-dimensional ultrasound, MRI, histerossalpingo -contrast-sonography, hystero ssalpingograsia of x-ray, hysteroscopy and laparoscopy.	Surgical treatment in cases of vaginal obstruction and dilatation in cases of vaginal agenesis.
<i>Herlin MK.2020 [4]</i>	Amenorrhea after puberty, dyspareunia and cyclic abdominal pain.	Two-dimensional and three-dimensional ultrasound, magnetic resonance, hysterosalpingo - contrast-sonography, X -ray hysterosalpingography, video-hysteroscopy and videolaparoscopy.	Targeted treatments for each patient and uterine transplantation in case of infertility.
<i>Josso N, 2020 [6]</i>	Virilization of the NB.	Sorologia and measurement of AMH serum testosterone.	-
<i>Ledig S, 2018 [3]</i>	Primary amenorrhea, absence of uterus and upper vagina.	UGS transabdominal, RM, laparoscopy.	-
<i>Ación P, 2016 [10]</i>	Agenesis or hypoplasia of an urogenital crest, unilateral renal genesis, ipsilateral blind hemivagina syndrome, diverse Mullerian presentations.	Imaging: MRI, HSGs, ultrasound transrretal or transvaginal and 3D pyelography iv, CT.	Laparotomy with atretic cervical resection and uterine body reimplantation in the neovagina
<i>Zafarani F, 2017 [11]</i>	Infertility, abnormal uterine bleeding, and symptoms related to uterine fibroids.	Hysterosalpingography.	-
<i>Yang QM, 2019 [12]</i>	Hemicavi of the blind, hematometry, hematosalpinx, unilateral endometriosis, dysmenorrhea, abdominal pain.	Three-dimensional (3D) ultrasound.	Hysteroscopy and laparoscopy combined with guided ultrasound.
<i>Baral Ross JH, 2018 [5]</i>	Uterus agenesis, menorrhea, dyspareunia, apaneuria.	Clinical diagnosis based on primary amenorrhea and inability to penetrate the vagina	-
<i>Kaur P.2021 [2]</i>	Menorrhagia or dysmenorrhea, undressrinia, obstetric complications.	By imaging: hysterosalpingography, USG and magnetic resonance	Aggressive prenatal care in the case of a pregnant patient with a bicornuate uterus and laparoscopy in cases of recurrent miscarriages and a history of premature birth

Conclusion

Although Mullerian malformations are not as recurrent in the female population worldwide, the most prevalent in the research was the Mayer-Rokitansky-

Küster-Hauser Syndrome (MRKH), coursing with the clinic of genital anomalies such as agenesis of the uterus and vagina, primary amenorrhea, it may also present extragenital anomalies (renal and vertebral). Second, OHVIRA Syndrome which presents with didelphic uterus

and ipsilateral renal agenesis. In general, all alterations present primary amenorrhea, dyspareunia, dysmenorrhea and uterovaginal agenesis. For diagnosis, the most used methods were laparoscopy, ultrasonography, hysterosalpingography and magnetic resonance. The conduct for the treatment varies and is directed to each patient, however, surgical methods such as hysteroscopy, laparoscopy and laparotomy are those that proved to be more applicable during the research. Furthermore, the greatest diagnostic difficulties were shown with the few available studies in the area of gynecology and obstetrics. One of the main reasons is the lack of knowledge about OHVIRA Syndrome, lack of knowledge between vaginal atresia and anorectal malformations, differential diagnosis in patients with primary amenorrhea with renal, genital and/or spine malformations, as well as the similarity of Rokitansky Syndrome to the Syndrome of Androgen Insensitivity due to the shortening of the vaginal canal.

Keywords: Congenital malformation. Paramesonephric ducts. Mullerian ducts. Diagnosis. Treatment.

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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References

1. Steps IMPE, Britto RL. Diagnosis and treatment of mullerian malformations. *Taiwan J Obstet Gynecol.* 2020 Mar;59(2):183-188. doi: 10.1016/j.tjog.2020.01.003. PMID: 32127135.
2. Kaur P, Panneerselvam D. Bicornuate Uterus. [Updated 2021 Jul 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK560859>
3. Ledig S, Wieacker P. Clinical and genetic aspects of Mayer-Rokitansky-Küster-Hauser syndrome. *Med Genet.* 2018;30(1):3-11. doi: 10.1007/s11825-018-0173-7. Epub 2018 Feb 21. PMID: 29527097; PMCID: PMC5838123.
4. Herlin, MK, Petersen, MB & Brännström, M. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: a comprehensive update. *Orphanet J Rare Dis* 15, 214 (2020). <https://doi.org/10.1186/s13023-020-01491-9>
5. Baral Ross Juana Himilce, Orozco Hechavarría Nélide, Prades Hung Eliecer. Mayer- Rokitansky syndrome - Küster-Hauser or agenesis of the uterus and vagina in a young patient. *MEDISAN* [Internet]. August 2018 [cited on September 6, 2021]; 22 (7): 552-558. Available at: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192018000700552&lng=es .
6. Josso N, Rey RA. What Does AMH Tell Us in Pediatric Disorders of Sex Development? *Front Endocrinol (Lausanne).* 2020 Sep 8;11:619. doi: 10.3389/fendo.2020.0619. PMID: 33013698; PMCID: PMC7506080
7. Paz- Montañe z, Jamer J, Guzmán G, Fernanda L, Acosta-Aragón, Amparo M. OHVIRA syndrome, about a case / A case of OHVIRA syndrome. (2020). *Univ. health ;* 22(3): 288-291, Sept.-Dec. 2020. Article in Spanish | LILACS, COLNAL | ID: biblio-1139850
8. Huneus Andrea, Sanz Acuña Antonia, Pino Poblete Víctor Manuel, Cunill Eduardo. Syndrome hemivagina obstructed, Uterus didelphic y ipsilateral renal agenesis (OVHIRA) Drained Partially-uterine fistula Uterus Espontánea . *Rev. Chile obstetrics gynecol.* [Internet]. 2017 Dic [cited 2021 Sep 06] ; 82(6): 595-602. Available at: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262017000600595&lng=es. <http://dx.doi.org/10.4067/S0717-75262017000600595>.
9. Fernández Fernández, J. Ángel, & Marín Rincón, GM (2019). Mayer- Rokitansky - Küster-Hauser syndrome associated with anorectal malformation . *Repertorio De Medicina Y Cirugía Magazine,* 28(3), 191–195. <https://doi.org/10.31260/RepertMedCir.v28.n3.2019.962>
10. Acién P, Acién M. Diagnostic imaging and cataloging of female genital malformations. *Insights Imaging.* 2016 Oct;7(5):713-26. doi: 10.1007/s13244-016-0515-4. Epub 2016 Aug 9. PMID: 27507534; PMCID: PMC5028344.
11. Zafarani F, Ahmadi F, Shahrzad G. Hysterosalpingography in The Assessment of Congenital Cervical Anomalies. *Int J Fertil Steril.*

2017 Jul-Sep;11(2):71-78. doi:
10.22074/ijfs.2017.4716. Epub 2017 Feb 16.
PMID: 28670423; PMCID: PMC5347453.

- 12.** Yang QM, Li H, He SH, Chen D, Chen L. Pregnancy in a blind hemi-cavity of Robert's uterus with ipsilateral renal agenesis: a case report and literature review. J Int Med Res. 2019 Jul;47(7):3427-3434. doi:
10.1177/0300060519850422. Epub 2019 May 27.
PMID: 31130027; PMCID: PMC6683884.