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DIAGNOSTIC LAPAROSCOPY IN MAYER-ROKITANSKY-KÜSTER-HAUSER SYNDROME : A CASE REPORT

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Abstract

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital condition resulting from Müllerian agenesis, characterized by the absence or underdevelopment of the uterus and upper two-thirds of the vagina, while maintaining a normal female phenotype and karyotype (46,XX). This case report details the presentation, diagnosis, and management of a 24-year-old female patient with primary amenorrhea due to MRKH syndrome. The patient presented with typical secondary sexual characteristics and an absence of menstruation. Diagnostic imaging, including ultrasonography and laparoscopy, confirmed the absence of the uterus and the presence of normal ovaries and fallopian tubes, consistent with Type I MRKH syndrome. Management options, including reproductive counseling and vaginal reconstruction techniques, were discussed to address the patient's physical and psychological well-being. Surgical exploration ruled out other associated anomalies. This case highlights the importance of early diagnosis, multidisciplinary management, and patient counseling to improve quality of life and provide clarity regarding reproductive possibilities for MRKH patients.

Keywords: ***MRKH syndrome, primary amenorrhea, Müllerian agenesis, reproductive counseling, vaginal reconstruction***

INTRODUCTION

Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome is a form of Müllerian agenesis characterized by aplasia or hypoplasia of the uterus and the proximal two-thirds of the vagina, while the phenotype and karyotype remain normal (46,XX). Patients with MRKH typically present with normal female external genitalia, normal breast development, and pubic hair growth (Jain et al. 2018).

The incidence of MRKH is approximately 1 in 4,500 live female births. MRKH syndrome is categorized into three types: Type I (typical MRKH), Type II (atypical MRKH), and Type III (MURCS syndrome - Müllerian agenesis, renal agenesis, and cervicothoracic somite dysplasia). A meta-analysis of 521 MRKH cases revealed that 64% of patients had typical MRKH, 24% had atypical MRKH, and 12% presented with MURCS syndrome. Surgical intervention to create a neovagina can restore normal sexual function. Although women with this condition are unable to conceive naturally, they may have children through assisted reproductive techniques, such as gestational surrogacy (Jain et al. 2018; Nakum et al. 2015).

MRKH syndrome is a notable cause of primary amenorrhea in women. Amenorrhea is defined as the absence of menstruation for at least three consecutive months. It is classified into physiological amenorrhea (e.g., prepuberty, pregnancy, lactation, menopause) and pathological amenorrhea, which includes primary and secondary amenorrhea. Primary amenorrhea is defined as the absence of menstruation by the age of 14 years with no development of secondary sexual characteristics, or by the age of 16 years with normal development of secondary sexual characteristics (Pizzo et al. 2013). The etiology of MRKH syndrome remains unclear, but it is hypothesized to be associated with malformations during embryogenesis, specifically during the early stages of pregnancy at approximately 8 weeks of gestation. Embryogenesis is divided into two phases: blastogenesis and organogenesis. During blastogenesis (the first 28 days of

development), global gene expression influences the development of all embryonic components. The highly integrated and interdependent nature of early embryogenesis may explain defects arising during this phase. Organogenesis, occurring between days 29 and 56 of development, involves the initiation of organ formation. Defects during organogenesis are generally more localized than those during blastogenesis and typically affect a single organ (Pizzo et al. 2013). To diagnose MRKH syndrome, supporting investigations such as ultrasonography, magnetic resonance imaging (MRI), and diagnostic laparoscopy are necessary (‘ACOG Committee Opinion No. 728: Müllerian Agenesis: Diagnosis, Management, And Treatment.’ 2018).

CASE REPORT

Miss NDF, a 24-year-old woman, presented to the Obstetrics and Gynecology outpatient clinic at Zainoel Abidin Regional Hospital with a complaint of never having menstruated despite her age. The patient had not sought medical attention previously, as she initially believed her condition to be normal. At 19 years old, she consulted a gynecologist, and ultrasound imaging revealed the absence of a uterus. However, she did not pursue further evaluation or treatment at that time. Now at 24 years old, she seeks medical advice in preparation for marriage.The patient denied experiencing cyclic abdominal pain or abdominal enlargement. She reported normal bowel and urinary functions, with no significant weight loss, decreased appetite, or other systemic complaints. She has not yet married.

On examination, her general condition was good, and she was fully alert (compos mentis). Secondary sexual characteristics were normal, with breast and pubic hair development corresponding to Tanner stage 5. Hemodynamic parameters and general physical status were within normal limits. Gynecological examination revealed a quiet vulva and urethra. Vaginal probe examination indicated the absence of an introitus vagina. On rectal examination, the anal sphincter tone was normal, the rectal ampulla was not collapsed, and no masses were palpable.

These findings are consistent with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, likely type I, which is characterized by primary amenorrhea, absence of the uterus, and normal secondary sexual characteristics. Further diagnostic imaging, such as MRI, is recommended to confirm the diagnosis and assess the extent of Müllerian agenesis. Counseling regarding reproductive options, potential surgical interventions, and psychological support is advised as the patient prepares for marriage.

Laboratory blood tests for Miss NDF were within normal limits. Abdominal ultrasonography was subsequently performed, revealing the absence of a visible uterus. The right ovary measured 1.66 × 1.38 × 1.69 cm, while the left ovary measured 2.81 × 2.96 × 2.84 cm. The ultrasonography findings concluded with an impression of uterine agenesis, suspected Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. Further diagnostic evaluation and multidisciplinary management planning are recommended to address the patient's condition comprehensively.

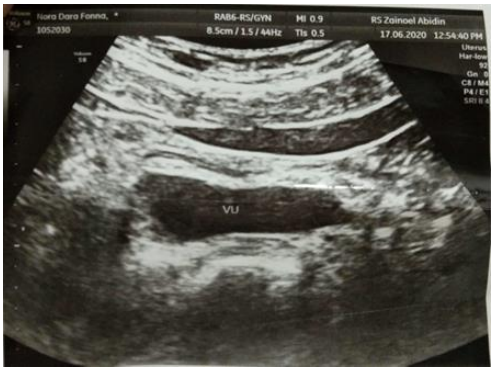

Figure 1 Ultrasonography Examination

The patient subsequently underwent diagnostic laparoscopy. Further exploration revealed both fallopian tubes and ovaries to be within normal limits. The uterus was not visualized, with

findings suggestive of a rudimentary uterus. No bleeding was observed. All instruments and trocars were removed, and the incision site was sutured using 3-0 polyglactin. The laparoscopy procedure was completed successfully.

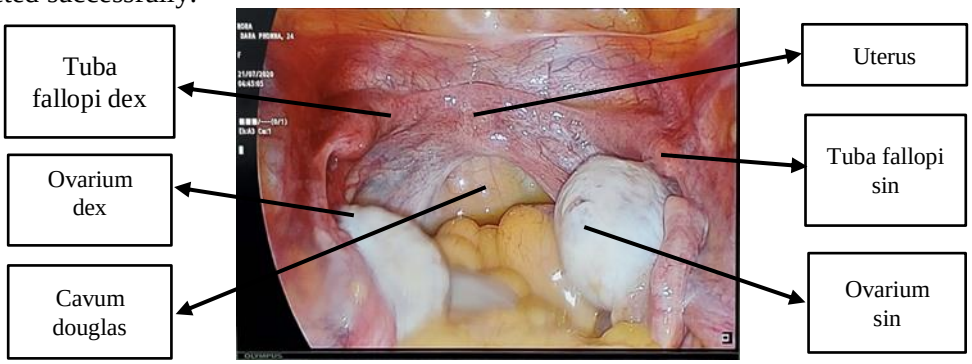

Figure 2 Diagnostic Laparoscopy Results

DISCUSSION

In this patient, physical examination and supporting investigations suggest MRKH as the working diagnosis. Diagnostic laparoscopy findings revealed the absence of a visible uterus, with the impression of a rudimentary uterus. Both fallopian tubes and ovaries were observed to be within normal limits.

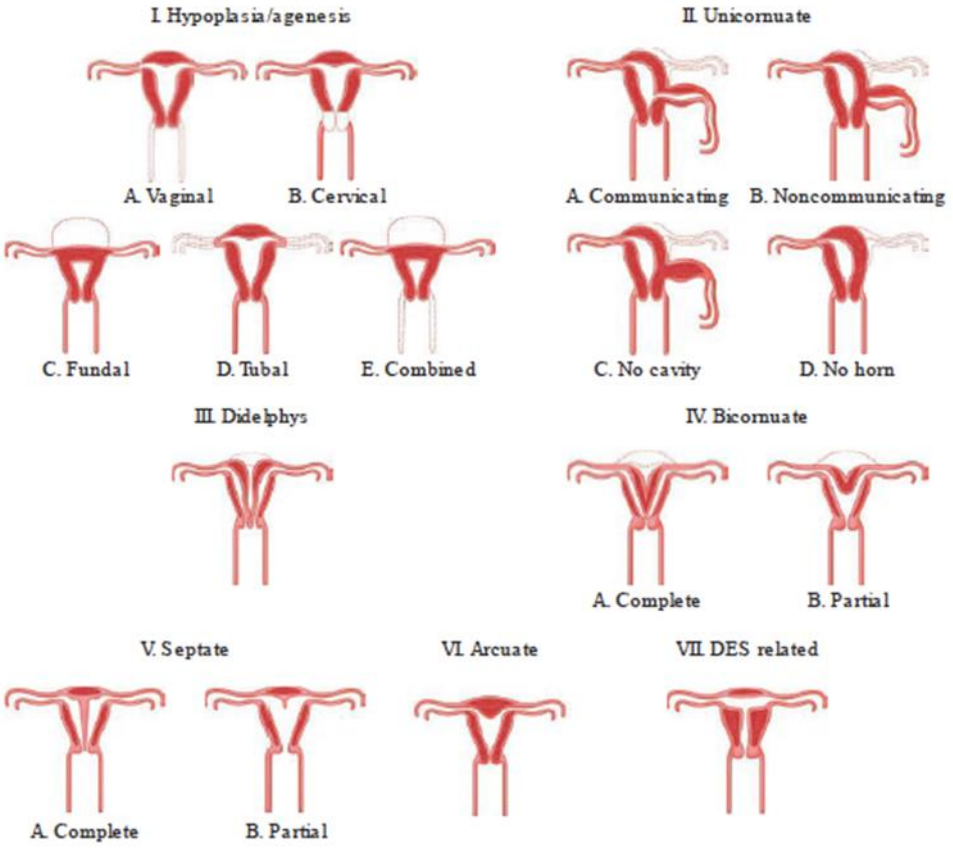

Figure 3 Classification of Müllerian Anomalies

MRKH syndrome occurs in 1 in 4,000 to 10,000 females and is a common cause of primary amenorrhea. MRKH syndrome is caused by an embryological developmental disorder of the Müllerian ducts and is characterized by the absence of the uterus, cervix, and the proximal two-

thirds of the vagina. The ovaries are typically normal as they arise from a different embryological origin, and the distal portion of the fallopian tubes can still be found (Hoffman et al. 2016). During the fifth week of pregnancy, the Müllerian duct (paramesonephric duct) begins to develop. The right and left paramesonephric ducts continue to grow downward and laterally from the Wolffian duct (mesonephric duct), and at some point in the distal region, the Müllerian ducts enter and cross the mesonephric ducts anteriorly. They then fuse distally and eventually come into contact with the urogenital sinus. The fused lower portion of the Müllerian duct undergoes recanalization, forming the vagina, cervix, and uterus. Meanwhile, the two non-fused Müllerian ducts in the proximal region will develop into the fallopian tubes. The fusion of the two Müllerian ducts occurs by the seventh week but is not completed until the twelfth week. At the same time, primordial germ cells migrate from the yolk sac to the genital ridge, leading to the formation of the ovaries. Therefore, Müllerian duct anomalies are not associated with ovarian developmental anomalies. The Müllerian ducts mature into the fallopian tubes, uterus, cervix, and the upper two-thirds of the vagina (the lower third of the vagina originates from the urogenital sinus) (Pizzo et al. 2013; Nunes and Zanatta 2015).

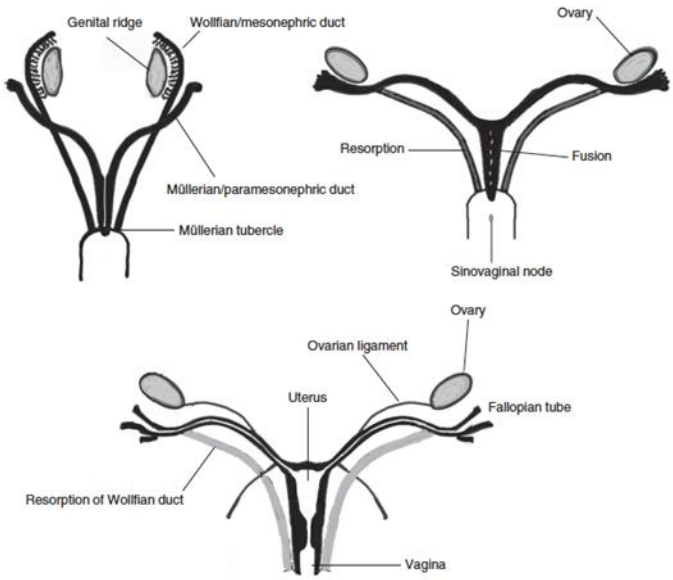

Figure 4 Embryology of the Female Reproductive System

Müllerian agenesis is one of the most common causes of primary amenorrhea in patients with typical thelarche and adrenarche. Upon physical examination, patients with Müllerian agenesis have normal height, breast development, body hair, and external genitalia(‘ACOG Committee Opinion No. 728: Müllerian Agenesis: Diagnosis, Management, And Treatment.’ 2018).

MRKH syndrome is divided into three types: typical (Type I or isolated), atypical (Type II), and MURCS. In typical MRKH, remnants of the Müllerian ducts are found, with normal fallopian tubes and kidneys. On the other hand, atypical MRKH shows agenesis or hypoplasia of the uterus, with or without fallopian tube dysplasia, and is often associated with renal function abnormalities such as renal agenesis, ectopic kidneys, or horseshoe kidneys. Type III, known as the MURCS syndrome, is a type of MRKH associated with bone and vertebral abnormalities, heart defects, and kidney malformations. Vertebral malformations include scoliosis, spinal fusion, and rib malformations. Other associated abnormalities may include facial malformations and digit anomalies (syndactyly, polydactyly), hearing impairments such as deafness, stapedial ankylosis, and pinna dysplasia. Cardiac malformations may include aorto-pulmonary connection defects, ventricular septal defects, pulmonary valve abnormalities, and tetralogy of Fallot (Yasmin and Busby 2018; Nath, Boro, and Naskar 2016; Fontana et al. 2017; Hoo, Norhaslinda, and Reza 2016).

Magnetic Resonance Imaging (MRI) can diagnose MRKH in more than 97% of patients. Computed tomography (CT) is generally avoided as it rarely offers advantages over MRI in this context and involves radiation. Laparoscopy is occasionally required, particularly when pelvic pain is present due to a rudimentary uterus with functional endometrium (Londra, Chuong, and Kolp 2015). The exact cause of MRKH syndrome is still unknown, but analysis of several reported family cases suggests autosomal dominant inheritance. MRKH patients have been reported to exhibit recurrent abnormalities in regions of chromosomes 1q21.1, 16p11.2, 17q12, and 22q11.2. MRKH syndrome is also associated with an increased number of genes (LHX1, TBX6, WNT9B, and WNT4) (Ledig and Wieacker 2018).

Since all MRKH syndrome patients lack a functional uterus, counseling for patients diagnosed with MRKH should include discussion of their reproductive function. MRKH patients can opt for adoption. However, the use of gestational surrogacy (assisted reproductive technology in women with a normal uterus) now allows women who cannot carry a pregnancy but have a genetic connection to the child. Surrogate mothers are often sisters, cousins, or other family members who agree to carry the pregnancy for the patient. Such arrangements usually do not involve financial compensation (Reichman and Laufer 2010)(Friedler et al. 2016; Friedler et al. 2016).

Another reproductive option for MRKH patients can be achieved through uterine transplantation. Uterine transplantation remains an experimental procedure, surrounded by substantial ethical debate. Gestational surrogacy also has ethical and religious pros and cons; however, it is permitted by law in many countries worldwide (Friedler et al. 2016).

In 2015, the first live birth after uterine transplantation in an MRKH patient was reported. The Brännström group performed nine uterine transplants, with four live births and one ongoing pregnancy as of October 2015. Two of the uterine transplants were removed due to uterine artery thrombosis and infection. Five of the seven patients experienced mild immunological reactions. Two patients developed preeclampsia. The Brännström group used living donors and removed the allografts after delivery, thus limiting the need for immunosuppressants. One patient is now pregnant for the second time. Uterine transplants from deceased donors are also possible. The disadvantage of using a deceased donor uterus is the lack of vascularization, leading to uterine ischemia, which reduces the function of the graft or uterine transplant (Brännström et al. 2015).

Ethical issues surrounding uterine transplantation arise because this procedure poses high risks to living donors. These risks can be reduced by using deceased donors. The issue of payment for organ donation also emerges as this procedure becomes more common. In some countries, such as Sweden, surrogacy is illegal, and Swedish law emphasizes that uterine transplantation is solely for research purposes (Farrell and Falcone 2015). In the 2012 annual report of the Society for Assisted Reproductive Technology (SART), there were 38,662 and 19,599 cycles performed for patients aged under 35 and 35-37 years, respectively. The pregnancy rate per cycle was 46.7% and 37.8%, respectively, and the live birth rate per cycle was 40.7% and 31.3%. The implantation rates were 37.5% and 27.6%, respectively (Kupka et al. 2016).

Ovarian stimulation can be performed using the same protocol as oocyte cryopreservation. The response to treatment is assessed by the number of oocytes retrieved, fertilization rates, and embryo quality. The unique pelvic anatomy of MRKH patients requires oocyte retrieval via a transabdominal route. The reported pregnancy rates after IVF in MRKH patients are still low, but IVF remains an attractive option for MRKH patients (Londra, Chuong, and Kolp 2015). Vaginal reconstruction can be performed either through intermittent vaginal dilation (non-surgical method) or with vaginoplasty (surgical method). Non-surgical methods may be useful in cases of certain primary vaginal atresia. However, most patients will require vaginal reconstruction. Patient cooperation is crucial for successful vaginoplasty, and the most important step is to maintain the vagina during the healing period using effective molding devices (Nunes and Zanatta 2015; Chaudhary et al. 2016). Differential diagnoses for MRKH include gonadal dysgenesis, androgen insensitivity syndrome, transverse vaginal septum, and imperforate hymen. Management can be delayed until the patient is ready to initiate sexual activity. Treatment can be either surgical or non-

surgical, and the chosen method depends on the individual needs and motivations of the patient. Non-surgical options in some cases include the Frank technique, Ingram technique, or regular coitus. Surgical techniques include options such as McIndoe technique, Williams vaginoplasty, neovagina construction with bowel tissue, and the Vacchietti technique (Nath, Boro, and Naskar 2016; Fontana et al. 2017; Hoo, Norhaslinda, and Reza 2016).

Androgen Insensitivity Syndrome (AIS), also known as testicular feminization syndrome (OMIM 300068), is a form of male pseudohermaphroditism caused by mutations in the androgen receptor gene. AIS is an X-linked recessive disorder, where affected males have external female genitalia, breast development like females, a short vaginal introitus, absent uterus and ovaries, and undescended testes or inguinal testes. Partial androgen insensitivity syndrome results in hypospadias, micropenis, and gynecomastia (Morcel et al. 2007).

Table 1 Differential Diagnosis between MRKH (Mayer-Rokitansky-Küster-Hauser Syndrome) and AIS (Androgen Insensitivity Syndrome)

Feature	MRKH Syndrome	Androgen Insensitivity Syndrome (AIS)
Genotype	XX	XY
Estrogen Hormone	Normal	Normal testosterone for males
Pubic Hair and Axillary Hair	Normal	Normal
Height	Similar to normal female height	Taller than normal female height
Ovaries	Normal	Intra-abdominal testes (undescended)
Risk of Gonadal Malignancy	No increased risk	Recommended gonadectomy after puberty due to increased risk of malignancy
Breast Development	Normal	Normal

CLOSING

Conclusion

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a form of Müllerian agenesis and one of the causes of primary amenorrhea in women. It is characterized by the aplasia of the uterus and the upper two-thirds of the vagina, while phenotypic development and karyotype (46, XX) remain normal. Vaginal reconstruction can be performed either through intermittent vaginal dilation (non-surgical method) or vaginoplasty (surgical method). Management during childhood is generally not recommended. Reproductive function in MRKH patients can be supported through gestational surrogacy or assisted reproductive technology. Another option is uterine transplantation. Both of these options remain subjects of debate in various countries..

Suggestions and Acknowledgments (if any)

It is essential for healthcare providers to promote early diagnosis and counseling for MRKH patients. This can greatly improve their psychological well-being and provide them with the necessary information regarding their reproductive options. Support groups and counseling for both patients and their families can be beneficial in reducing anxiety and promoting a positive outlook. Continued research into the underlying genetic causes of MRKH syndrome and the development of more refined reproductive technologies such as uterine transplantation and improved surrogacy options will help in enhancing the quality of life for MRKH patients. A multi-disciplinary approach involving gynecologists, psychologists, geneticists, and other specialists can provide MRKH patients with comprehensive care that addresses both physical and emotional aspects of the condition.

We would like to express our gratitude to the healthcare professionals, researchers, and Zainoel Abidin Regional Hospital. Their dedication to advancing understanding and providing innovative solutions is invaluable. Additionally, we acknowledge the patients and their families for their courage in sharing their experiences, which contribute to the ongoing progress in this field.

Finally, we thank the medical and ethical committees that continue to evaluate and guide the implementation of reproductive technologies for MRKH patient.

REFERENCES

'ACOG Committee Opinion No. 728: Müllerian Agenesis: Diagnosis, Management, And Treatment.' 2018. *Obstetrics and Gynecology* 131 (1): e35–42. https://doi.org/10.1097/AOG.0000000000002458.

Brännström, Mats, Liza Johannesson, Hans Bokström, Niclas Kvarnström, Johan Mölne, Pernilla Dahm-Kähler, Anders Enskog, et al. 2015. 'Livebirth after Uterus Transplantation.' *Lancet (London, England)* 385 (9968): 607–16. https://doi.org/10.1016/S0140-6736(14)61728-1.

Chaudhary, Rachna, Vandana Dhama, Shakun Singh, and Renu Azad. 2016. 'Vaginoplasty in Mayer Rokitansky-Kuster-Hauser Syndrome Using Amnion: A Case Series'. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology* 5 (11): 3832–39. https://doi.org/10.18203/2320-1770.ijrcog20163849.

Farrell, Ruth M, and Tommaso Falcone. 2015. 'Uterine Transplant: New Medical and Ethical Considerations.' *Lancet (London, England)* 385 (9968): 581–82. https://doi.org/10.1016/S0140-6736(14)61792-X.

Fontana, L, B Gentilin, L Fedele, C Gervasini, and M Miozzo. 2017. 'Genetics of Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome.' *Clinical Genetics* 91 (2): 233–46. https://doi.org/10.1111/cge.12883.

Friedler, Shevach, Leonti Grin, Gad Liberti, Buzhena Saar-Ryss, Yaakov Rabinson, and Semion Meltzer. 2016. 'The Reproductive Potential of Patients with Mayer-Rokitansky-Küster-Hauser Syndrome Using Gestational Surrogacy: A Systematic Review.' *Reproductive Biomedicine Online* 32 (1): 54–61. https://doi.org/10.1016/j.rbmo.2015.09.006.

Hoffman, B.L, J.O Schorge, K.D Bradshaw, L.M Halvorson, J.I Schaffer, and M.M. Corton. 2016. *Williams Gynecology, 3rd Edition, Philadelphia: Mc Graw Hill*. Philadelphia: Mc Graw Hill.

Hoo, P S, A R Norhaslinda, and J N Shah Reza. 2016. 'Rare Case of Leiomyoma and Adenomyosis in Mayer-Rokitansky-Kuster-Hauser Syndrome.' *Case Reports in Obstetrics and Gynecology* 2016: 3725043. https://doi.org/10.1155/2016/3725043.

Jain, Deepak, Ashima Mittal, Aniket Mittal, Shivraj Goyal, and Promil Jain. 2018. 'Mayer-Rokitansky-Kuster-Hauser Syndrome'. *The Indian Practitioner* 71 (3): 39–42.

Kupka, M S, T D'Hooghe, A P Ferraretti, J de Mouzon, K Erb, J A Castilla, C Calhaz-Jorge, Ch De Geyter, and V Goossens. 2016. 'Assisted Reproductive Technology in Europe, 2011: Results Generated from European Registers by ESHRE.' *Human Reproduction (Oxford, England)* 31 (2): 233–48. https://doi.org/10.1093/humrep/dev319.

Ledig, Susanne, and Peter Wieacker. 2018. 'Clinical and Genetic Aspects of Mayer-Rokitansky-Küster-Hauser Syndrome.' *Medizinische Genetik : Mitteilungsblatt Des Berufsverbandes Medizinische Genetik e.V* 30 (1): 3–11. https://doi.org/10.1007/s11825-018-0173-7.

Londra, Laura, Farah S Chuong, and Lisa Kolp. 2015. 'Mayer-Rokitansky-Kuster-Hauser Syndrome: A Review.' *International Journal of Women's Health* 7: 865–70. https://doi.org/10.2147/IJWH.S75637.

Morcel, Karine, Laure Camborieux, Daniel Guerrier, and Programme de Recherches sur les Aplasies Müllériennes (PRAM). 2007. 'Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome'. *Orphanet Journal of Rare Diseases* 2 (1): 13. https://doi.org/10.1186/1750-1172-2-13.

Nakum, Ashok, Kesharmal Kumawat, Hiral C Chauhan, and Jayesh V Parikh. 2015. 'Mayer-Rokitansky-Kuster-Hauser (MRKH) Syndrome Type 2: Atypical Presentation of Rare Case - '. *The Journal of Medical Research* 3: 409–11. https://api.semanticscholar.org/CorpusID:57749306.

Nath, Kamal, Bhanita Boro, and Subrata Naskar. 2016. 'A Rare Case of Mayer-Rokitansky-Kuster-

Hauser Syndrome Presenting with Acute Psychosis.' *Journal of Clinical and Diagnostic Research : JCDR*. India. https://doi.org/10.7860/JCDR/2016/18478.7658.

Nunes, Rodrigo Dias, and Djulie Anne de Lemos Zanatta. 2015. 'Mayer - Rokiytansky - Kuster - Hauser Syndrome: A Case Report'. *Obstetrics and Gynaecology Cases Reviews* 2 (3): 144–45. https://doi.org/10.36347/sjmcr.2024.v12i09.002.

Pizzo, Alfonsa, Antonio Simone Laganà, Emanuele Sturlese, Giovanni Retto, Annalisa Retto, Rosanna De Dominici, and Domenico Puzzolo. 2013. 'Mayer-Rokitansky-Kuster-Hauser Syndrome: Embryology, Genetics and Clinical and Surgical Treatment.' *ISRN Obstetrics and Gynecology* 2013: 628717. https://doi.org/10.1155/2013/628717.

Reichman, David E, and Marc R Laufer. 2010. 'Mayer-Rokitansky-Küster-Hauser Syndrome: Fertility Counseling and Treatment.' *Fertility and Sterility* 94 (5): 1941–43. https://doi.org/10.1016/j.fertnstert.2010.01.036.

Yasmin, Ephia, and Gail Busby. 2018. 'Primary Amenorrhea in Pediatric and Adolescent Gynecology Practice: Mayer-Rokitansky-Kuster-Hauser Syndrome'. In *Pediatric and Adolescent Gynecology: A Problem-Based Approach*, edited by Sarah M Creighton, Adam Balen, Lesley Breech, and Lih-Mei Liao, 99–108. Cambridge: Cambridge University Press. https://doi.org/DOI: 10.1017/9781316691502.012.