Journal of Fertilization : In Vitro, IVF-Worldwide, Reproductive Medicine, Genitics & Stem Cell Biology

Arleo and Troiano, J IVF Reprod Med Genet 2013, 1:3
DOI: 10.4172/2375-4508.1000115

Case Report

Complex Mullerian Duct Anomalies Defying Traditional Classification: Lessons Learned

Elizabeth Kagan Arleo* and Robert N Troiano

New York -Presbyterian Hospital / Weill Cornell, 425 East 61st Street, 9th floor, NY, NY 10065, USA

Abstract

The purpose of this pictorial review is to provide a visual portrayal of complex Mullerian Duct Anomalies (MDAs) which do not fit into the classification system developed by the American Fertility Society (AFS), the most widely known and utilized schematization. Having recognized these cases of rare manifestations of MDA in our practice, a tertiary referral center with a major center for reproductive medicine and infertility, we have presented them together in order to clearly communicate the useful reminder that classification, in some cases, may be impossible.

Introduction

Congenital anomalies of the uterus may be asymptomatic and unrecognized, or present clinically during puberty due to amenorrhea or childbearing years due to infertility or recurrent miscarriage. The Obstetrician/Gynecologist evaluating a patient in either clinical scenario takes a detailed history, performs a pelvic examination, and orders laboratory tests including a comprehensive hormonal profile. Imaging modalities available for evaluation include ultrasound and Hysterosalpingogram (HSG), but ultimately, the non-invasive diagnostic gold standard, especially for complex cases, is Magnetic Resonance Imaging (MRI) [1] because of its superior level of soft tissue detail.

If a congenital anomaly is present, the primary goal of MRI is to classify the malformation into one of the seven classes (I-VII) of Mullerian Duct Anomalies (MDA) outlined in 1988 by the American Fertility Society (Figure 1) [2], because classification directs treatment. Occam's razor, the idea that simplest explanation is usually the correct one, is an important idea in medicine. However, the cases presented in this pictorial review run counter to this cherished principle and provide a useful reminder that classification, in some cases, may be impossible.

Mullerian Duct Anomalies (MDAs): General Information

Robins et al. have described the embryologic development of the mullerian ducts as a three-stage process, which is completed by week twelve of gestation [3]; first, ductal development, with errors and/or interruptions during this phase yielding class I MDAs; second, ductal fusion, with errors and/or interruptions during this phase yielding class II-IV MDAs; and third, septal reabsorption, with errors and/or interruptions during this phase yielding class V and VI MDAs. Specifically, the bidirectional theory of septal regression posits that septal resorption progresses in both the cranial and caudal directions simultaneously, thus providing a possible embryological mechanism to explain some of the more complex mullerian duct anomalies presented in this pictorial review [4]. Maternal ingestion of Diethylstilbestrol (DES) (late 1940s-1971) during first trimester of pregnancy led to birth of daughters with class VII MDAs, among other problems [5].

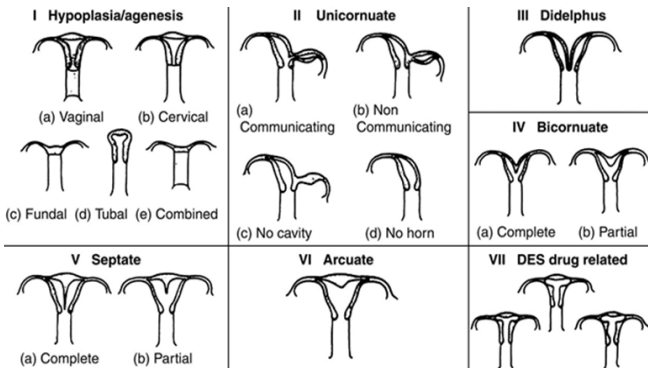

Figure 1: Classification system of mullerian duct anomalies developed by the American Fertility Society (now the American Society of Reproductive Medicine) [2].

Mullerian duct anomalies are associated with other congenital anomalies, such as abnormalities of the renal and skeletal system. Renal anomalies include agenesis, duplication, ectopia, fusion, hypoplasia, and malrotation [6]. Reported skeletal anomalies include spina bifida and vertebral body abnormalities [7]. In addition to such associated anomalies, which have their own set of complications, patients with mullerian duct anomalies may suffer not only from obstetrical complications such as recurrent miscarriage, but an also chronic issue such as endometriosis, as Figure 4 demonstrates.

While the true incidence of mullerian duct anomalies is difficult to determine, it is estimated that they occur in 2-4% of fertile women with normal reproductive outcomes, but with a higher incidence among women with infertility (range, 5-25%) [4,8]. For example, in a recent analysis of 94 observational studies including nearly 90,000 women all together, Chan et al report the prevalence of uterine anomalies in the general asymptomatic population to be 5.5%, in contrast to 8.0% in a population of infertile women, 13.3% in women with a history of miscarriage and 24.5% in those with miscarriage and infertility [9]. However, a small percentage of MDA anomalies seemingly appear defy classification into the traditional I-VII categories, as this pictorial review will now go on to demonstrate.

***Corresponding author:** Elizabeth Kagan Arleo MD, New York -Presbyterian Hospital / Weill Cornell, 425 East 61st Street, 9th floor, NY, NY 10065, USA, Tel: 212-821-0680; Fax: 212-821-0671; E-mail: ela9033@med.cornell.edu

Received August 21, 2013; **Accepted** October 31, 2013; **Published** November 01, 2013

Citation: Arleo EK, Troiano RN (2013) Complex Mullerian Duct Anomalies Defying Traditional Classification: Lessons Learned. J IVF Reprod Med Genet 1: 115. doi:10.4172/2375-4508.1000115

Complex Mullerian Duct Anomalies: Specific Cases Defying Traditional Classification

Cases 1-4: diagnosis in the teenage years

A 17 year-old female was referred to our institution with primary amenorrhea. MRI (Figure 2) demonstrates absence of the uterus and upper two thirds of the vagina; only a small undifferentiated soft tissue remnant within the lower third of the vagina above the introitus is present, consistent with a vestigial sinovaginal bulb. The kidneys were normal in size and location. Thus, this patient has aspects of both a class Ia (vaginal hypoplasia/agenesis) and class Ic (uterine agenesis) MDA. In conjunction with a normal female phenotype and karyotype, these findings are compatible with Mayer Rokitansky Kuster Hauser (MRKH) Syndrome, a rare disorder characterized by congenital aplasia of the uterus and upper two thirds of the vagina in 46 XX phenotypically normal females. MRKH type I demonstrates isolated aplasia of the uterus and upper part of the vagina, as in this case, but is more frequently associated with renal, vertebral, and, to a lesser extent, auditory and cardiac defects (MRKH type II) [10-12]. For this patient, surgical creation of a neovagina is a possibility.

In contrast, MRKH II is demonstrated in Figure 3, images from a 13 year-old amenorrheic female with prenatal history of left-sided hydronephrosis, diagnosed postnatally as a nonfunctioning left ectopic pelvic kidney. MRI demonstrates two divergent uterine converging in the midline but not communicating. In the anticipated site of the cervix, only undifferentiated soft tissue is seen, and the upper vagina is atretic. Thus, this patient had elements of a class Ia and Ib (hypoplasia/agenesis involving both the vagina and cervix) and class IVa (bicornuate, complete) MDA. In conjunction with the history of a nonfunctioning left ectopic pelvic kidney, these findings are most consistent with MRKH, type II variant [10-12].

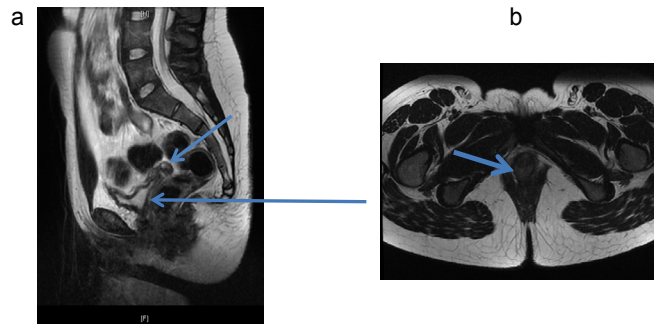

Figure 2: 17 year-old female with primary amenorrhea. a) Sagittal T2-weight MR image demonstrates no evidence of a uterine corpus with only a vestigial cervix (short arrow) and absent vagina (long arrow) evident. b) Axial T2-weight MR image shows a small undifferentiated soft tissue remnant within the lower third of the vagina above the introitus (arrow), consistent with a vestigial sinovaginal bulb.

Another 13 year-old female with primary amenorrhea was referred to our institution and evaluated with MRI. Figure 4 demonstrate a blind-ending unicornuate configuration with hematometra, with the lower uterine segment abutting the medial wall of the cervix without communication. A rudimentary horn with noncommunicating endometrial segment distended with blood is also present. The cervix is normal in configuration with the superficial margin ending blindly at the level of the internal os. Thus, this patient had elements primarily of a class IIb (unicornuate, noncommunicating) MDA, but the dissociation of the uterine corpus from the uterine cervix with no communication of the endometrial and endocervical cavities was beyond classification, and surgically-proven.

Hematometra secondary to outflow track obstruction is also seen in Figure 5, however in this case due to a complex congenital anomaly involving vaginal agenesis. This was also a young female (11 years-old) with primary amenorrhea, with MRI demonstrating a right unicornuate uterus with large associated hematometros. A left rudimentary horn with endometrial segment is present but does not communicate with right unicornuate uterus. Agenesis of the vagina without soft tissue remnant was identified. Thus, this patient had elements of both a class Ia (vaginal agenesis) and a class IIb (unicornuate, noncommunicating) MDA. The patient was initially treated medically with the Gonadotropin-releasing hormone agonist Lupron, with the goal of suppressing the menstrual cycle to prevent retrograde menstruation and the development of endometriosis; she was then lost to follow-up.

Cases 5 and 6: diagnosis during infertility workup

A 26 year-old female with multiple failed IVF cycles and ultrasound suggesting a uterine anomaly was referred for MRI (Figure 6), which demonstrates the uterus to have a complete septum as well as focal duplication of the cervix at the level of the external os. In addition, a blind-ending, tubular left Wolffian duct remnant extending to the

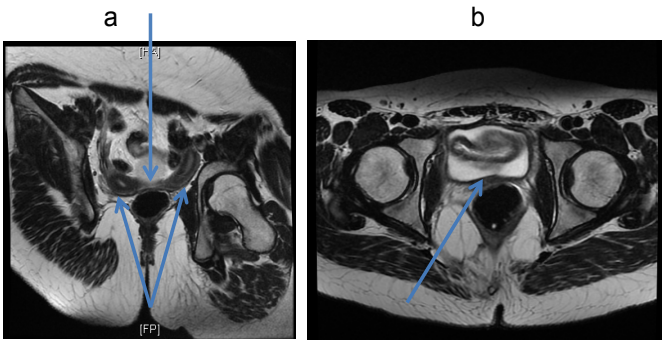

Figure 3: 13 year-old female with primary amenorrhea and prior left nephrectomy for a nonfunctioning pelvic kidney. a) Axial oblique MR image demonstrates bilateral divergent uterine horns with noncommunicating endometrial segments (double arrow) with undifferentiated soft tissue at the anticipated site of the cervix (single arrow). b) Axial T2 weighted-MRI image demonstrates an atretic upper vagina (arrow) as well.

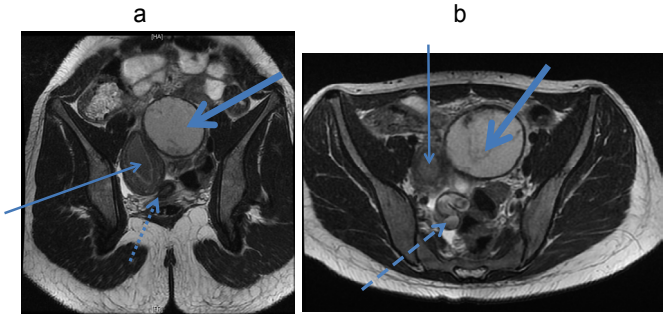

Figure 4: 13 year-old female with primary amenorrhea. a) Coronal oblique T2-weighted and b) axial T2-weighted MR images demonstrates a unicornuate uterine configuration (thin arrows) with an associated obstructed rudimentary horn with a non-communicating endometrial segment (thick arrows); there is dissociation of the uterine corpus from the uterine cervix (dotted arrow) with no communication of the endometrial and endocervical cavities. A hematosalpinx (dashed arrow) is also present.

level of the atretic/absent vagina along the left pelvic sidewall is seen. Thus, this patient had elements of both a class Va (septate, complete) and class III (didelphus) MDA; the wolffian duct remnant was beyond classification, but confirmed surgically when reunification of uterine cavity space with septal resection was attempted.

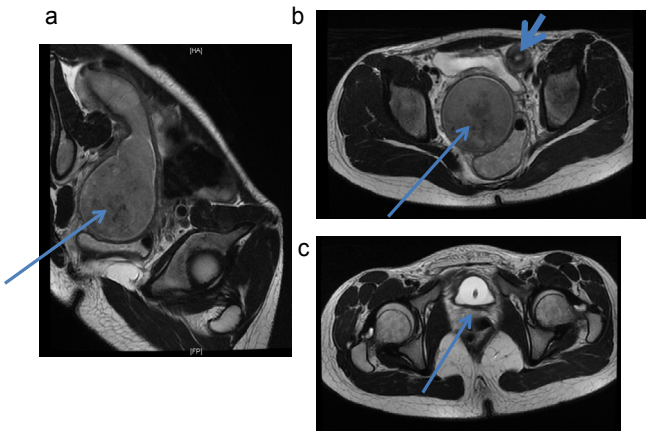

Figure 5: 11 year-old female with primary amenorrhea. a) Short axis T2 oblique and b) axial T2-weighted MR images demonstrates an obstructed right unicornuate uterus secondary to an atretic/absent upper vagina (long thinner arrows); a rudimentary horn is also present, with noncommunicating endometrial segment displaced anteriorly (short thick arrow). c) Axial T2 weighted MR image demonstrates a Foley catheter in the urinary bladder, with arrow pointing to anticipated site of the vagina, which is atretic/absent.

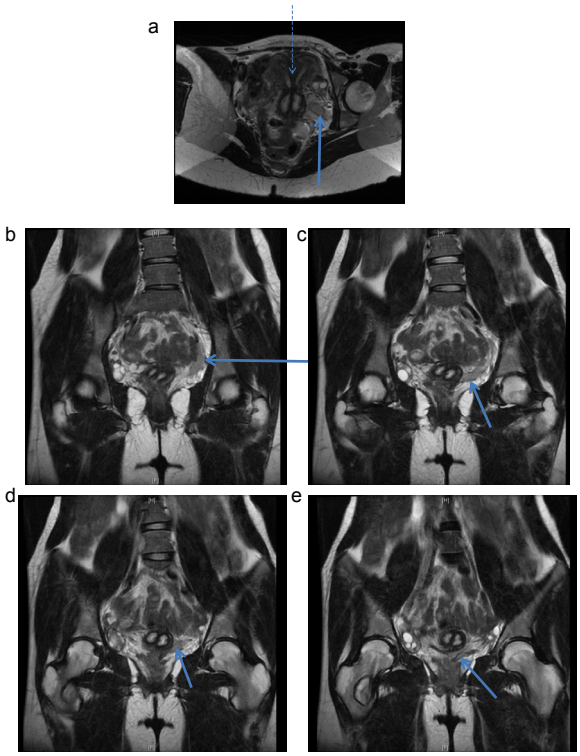

Figure 6: 26 year-old female status post multiple failed IVF cycles. a) Short axis T2 oblique and b) axial T2-weighted MR images demonstrates an obstructed right unicornuate uterus secondary to an atretic/absent upper vagina (long thinner arrows); a rudimentary horn is also present, with noncommunicating endometrial segment displaced anteriorly (short thick arrow). c) Axial T2 weighted MR image demonstrates a Foley catheter in the urinary bladder, with arrow pointing to anticipated site of the vagina, which is atretic/absent.

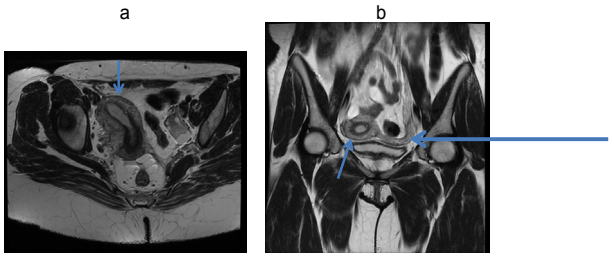

Figure 7: 29 year-old female with unexplained infertility. A) Oblique and b) coronal T2-weighted MR images demonstrate a right unicornuate uterine configuration (short arrows) and an associated undifferentiated mullerian duct remnant tracking up the left pelvic sidewall (long arrow).

Detection of a mullerian duct anomaly, straightforward or complex, does not necessarily preclude the possibility of future successful pregnancy. The 29 year-old female with unexplained infertility in Figure 7 had an MRI demonstrating a right unicornuate configuration (volume = 50 cc) with evidence of a small rudimentary horn without an associated endometrial segment. The rudimentary horn is in continuity with an undifferentiated mullerian duct remnant which tracks laterally up the left pelvic sidewall. Thus, this patient had elements of a class IIc (unicornuate, no cavity) MDA as well as an undifferentiated mullerian duct remnant which defies classification. However, the uterine volume was considered potentially sufficient for pregnancy, and the patient is pursuing IVF.

Conclusion

In conclusion, when the complex mullerian duct anomalies presented here are considered together, they provide the important reminder that classification, in some cases, is impossible. As Behr et al. write in their recent review, "even with today's state-of-the-art imaging techniques, classification of MDAs may be challenging; when a specific designation cannot be made, it is best to describe the anatomy rather than to force the MDA into a category" [1]. In such clinical scenarios, albeit rare, a careful description of morphology, in conjunction with an interdisciplinary review of the actual images, may be the best course of action in order to optimize the care of these complex patients.

References

1. Behr SC, Courtier JL, Qayyum A (2012) Imaging of müllerian duct anomalies. Radiographics 32: E233-250.
2. The American Fertility Society (1988) The American Fertility Society classifications of adnexal adhesions, distal tubal obstruction, tubal occlusion secondary to tubal ligation, tubal pregnancies, mullerian anomalies and intrauterine adhesions. Fertil Steril 49: 944-955.
3. Robbins JB, Parry JP, Guite KM, Hanson ME, Chow LC, et al. (2012) MRI of pregnancy-related issues: müllerian duct anomalies. AJR Am J Roentgenol 198: 302-310.
4. Troiano RN, McCarthy SM (2004) Mullerian duct anomalies: imaging and clinical issues. Radiology 233: 19-34.
5. Herbst AL, Ulfelder H, Poskanzer DC (1971) Adenocarcinoma of the vagina. Association of maternal stilbestrol therapy with tumor appearance in young women. N Engl J Med 284: 878-881.
6. Li S, Qayyum A, Coakley FV, Hricak H (2000) Association of renal agenesis and mullerian duct anomalies. J Comput Assist Tomogr 24: 829-834.
7. Gell JS (2003) Müllerian anomalies. Semin Reprod Med 21: 375-388.
8. Acién P (1997) Incidence of Müllerian defects in fertile and infertile women. Hum Reprod 12: 1372-1376.
9. Chan YY, Jayaprakasan K, Zamora J, Thornton JG, Raine-Fenning N, et al. (2011) The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review. Hum Reprod Update 17: 761-771.
10. Chandiramani M, Gardiner CA, Padfield CJ, Ikhena SE (2006) Mayer - Rokitansky - Kuster - Hauser syndrome. J Obstet Gynaecol 26: 603-606.

11. Pittock ST, Babovic-Vuksanovic D, Lteif A (2005) Mayer-Rokitansky-Küster-Hauser anomaly and its associated malformations. Am J Med Genet A 135: 314-316.

12. Oppelt P, Renner SP, Kellermann A, Brucker S, Hauser GA, et al. (2006) Clinical aspects of Mayer-Rokitansky-Kuester-Hauser syndrome: recommendations for clinical diagnosis and staging. Hum Reprod 21: 792-797.