

# Evidence-Based Management of a Complex Mullerian Anomaly

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## ABSTRACT

**Background:** Because of inaccuracies in classification of Müllerian duct anomalies (MDAs), subsequent diagnostic and treatment errors have occurred. We present a case of a woman with an MDA that was misclassified.

**Case:** A woman with a recent spontaneous abortion and chronic dyspareunia was diagnosed with a complete didelphys by magnetic resonance imaging. Her initial treatment plan was based on an incorrect diagnosis. With reevaluation of the magnetic resonance imaging scan, both the appropriate diagnosis was obtained and the appropriate treatment performed.

**Conclusion:** MDAs have been incorrectly diagnosed because of outdated and incorrect classification systems. Because of outdated and incorrect theories about the embryogenesis of the female genital tract, many women are being incorrectly diagnosed and treated with these abnormalities.

**Teaching Points:** We will focus of the evidence-based diagnosis and treatment of MDAs with a focus on cooperation between the radiologists who assist in diagnosis and the physicians who care for the patients.

**Key Words:** Müllerian Duct Anomalies, Diagnosis, Treatment.

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Conflicts of Interest: All authors declare no conflict of interest regarding the publication of this article.

Informed consent: Dr. Pritts declares that written informed consent was obtained from the patient/s for publication of this study/report and any accompanying images.

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## INTRODUCTION

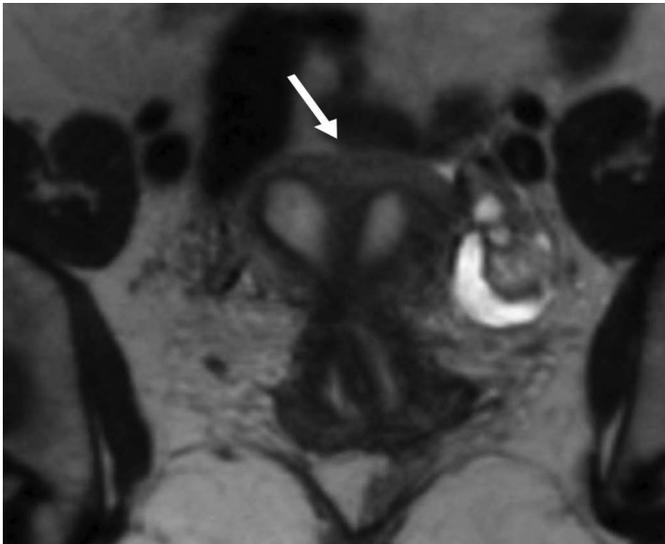
The incidence of Müllerian duct anomalies (MDA) has been reported at 3%–4% in women, with the septate uterus the most common at 35%–55%.<sup>1,2</sup> Additionally, of all the MDAs, a septate uterus is associated with the poorest reproductive outcome.<sup>3</sup> These anomalies tend to present with varying manifestations, resulting in frequent misdiagnoses. This carries the potential for inappropriate or inadequate treatment, all of which impact reproductive performance.<sup>4</sup> Definitive diagnosis is based on the use of hysteroscopy with concomitant laparoscopy, three-dimensional ultrasound, or magnetic resonance imaging (MRI).<sup>5,6</sup> Treatment can be empiric, medical, or surgical.<sup>7</sup> We performed a review of all reported cases of a uterine septum, double cervix and a longitudinal vaginal septum,<sup>2,8–14</sup> and the available data on diagnosis and management.

## CASE REPORT

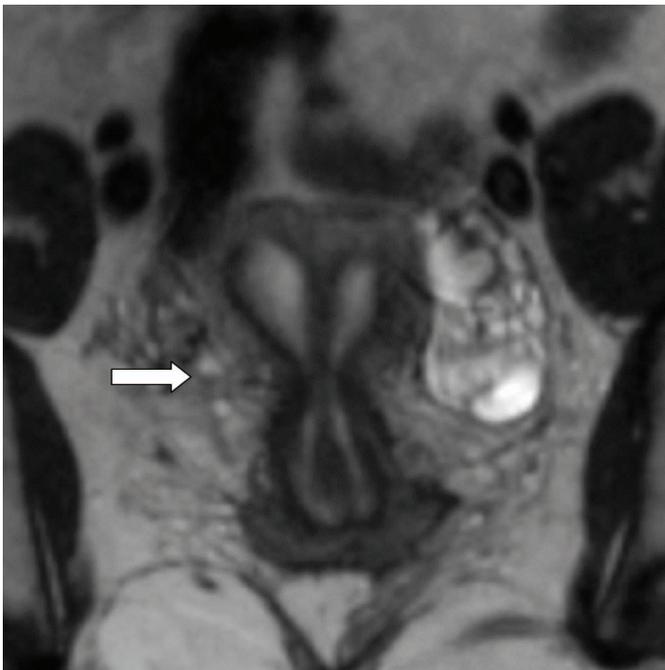
A 30-y-old G1P0010 female presented with severe, chronic pelvic pain and dyspareunia, wanting to conceive. She was diagnosed via MRI with a complete uterine didelphys, with two cervixes and a longitudinal vaginal septum.

In collaboration with the radiology department, the MRI was reevaluated. Indeed, there appeared to be two cervixes and a longitudinal vaginal septum. The fundal, coronal aspect of the uterus had a convex contour noted, consistent with a uterine septum (see **Figure 1**).

Upon further discussion, it was apparent that an outdated classification scheme had been utilized for the diagnosis. Based on previous theories of embryological development of the female genital tract, it was presumed that if a uterine anomaly with two separate cavities was identified concomitant with a longitudinal or transverse vaginal septum and



**Figure 1.** Fundal and coronal MRI with convex uterine fundus (see white arrow).



**Figure 2.** Fundal and coronal MRI with dual cervixes (see white arrow).

two cervixes, it was a didelphic uterus (see **Figure 2**). The revised diagnosis for our patient was a complete septate uterus with two cervixes and a longitudinal vaginal septum.

At surgery, the vaginal septum was excised, and the uterine septum was incised hysteroscopically with abdominal ultrasound guidance. A final postoperative examination

revealed a single vagina, and a sonohysterogram revealed a normal uterine cavity. The patient no longer has pain and is currently attempting conception.

## DISCUSSION

### Embryological Development

Normal development of the female reproductive tract follows a series of events including Müllerian duct elongation, fusion, canalization, and septal resorption, and failure of any one of these steps results in a congenital abnormality.<sup>7,15</sup> Additionally, Müllerian development coincides with development of the urinary tract, so anomalies of the kidney and ureter are commonly seen concomitantly. Conversely, ovarian development occurs as a separate process, so women with Müllerian anomalies usually have normal ovarian development.<sup>3,16</sup>

The most established theory for Müllerian development, described in 1962, follows three stages: 1) development, 2) fusion, and 3) resorption. Development begins when the paramesonephric (Müllerian) ducts, identifiable around week 6 of development, arise along the lateral walls of the urogenital ridge, elongate caudally, and fuse midline. The caudal end of these ducts connects with the urogenital sinus and canalizes, resulting in two channels divided by a septum. This septum is resorbed in a caudal to cephalad direction.

The caudal portion of the Müllerian ducts become the uterus and upper vagina; the cephalad portion becomes the fallopian tubes.

Next, the Müllerian ducts and the urogenital sinus connect, forming a vaginal plate. The center of the vaginal plate degenerates in a caudal to cephalad direction to form the lower vagina. This event is completed by week 20 of gestation.<sup>17–20</sup>

In many women, however, the genital anomalies seen do not quite fit the above theory of caudad to cephalad progression. There is also support for a different theory of uterovaginal development, which is the bidirectional regression theory of Müllerian development. This alternative theory attempts to explain the existence of anomalies that do not fit into the currently accepted classification schemes.<sup>18</sup> It maintains the three-stage process (development, fusion, and resorption) but with varying degrees of directionality. It suggests that the medial aspects of the Müllerian ducts begin to fuse in the middle and proceed in both the cephalad and caudad directions simultaneously.

This is then followed by rapid cellular proliferation between the ducts, forming the uterine corpus and cervix, and septal resorption, all of which occur in both directions simultaneously. According to this theory, a dual vagina/cervix septum could be explained by failed fusion of the Müllerian ducts in the caudal direction beginning at the uterine isthmus. The septate uterus and vagina could be explained by complete failure of normal septal resorption after normal fusion.<sup>8</sup>

### Classification

The varying types of MDAs have not been easy to categorize based on the current classifications systems. That said, attempts are underway to rectify this problem. The push for proper classification of these anomalies arose from the need for proper diagnosis, management, and better ability to predict obstetrical outcome.

The most established and widely used classification system is that by the American Fertility Society,<sup>20</sup> which divides Müllerian developmental abnormalities into seven groups but is focused on the uterus, with anomalies of the cervix, vagina, ovaries, fallopian tubes, and urinary system addressed separately. The problem with this scheme is that it does not include data regarding the diagnostic methods or the criteria utilized to determine the type of anomaly.

Now, with more clinical experience and updated literature, other classification systems have been proposed, such as that by Acien and Acien (2011).<sup>21</sup> They offer an updated embryological-clinical classification that includes six main groups. This classification scheme offers a more detailed description combining all components of the genital tract.

A classification system has emerged from the European Society of Human Reproduction and Embryology/European Society for Gynaecological Endoscopy and American Society for Reproductive Medicine, which attempts to provide a comprehensive description and categorization of most of the currently known anomalies that could not be properly classified by the American Fertility Society system.<sup>22</sup> Most recently, the European Society of Human Reproduction and Embryology/European Society for Gynaecological Endoscopy and American Society for Reproductive Medicine Congenital Uterine Anomalies Working Group is also developing a consensus statement.<sup>23</sup>

### Diagnosis

Currently MRI is the gold standard for diagnosing Müllerian anomalies, and it can distinguish between bicornuate,

didelphic, and septate uteri.<sup>24</sup> This, however, can be done only if a coronal view of the uterus is obtained during the test. Other examples of diagnostic modalities include combination hysterosalpingogram (HSG) and laparoscopy, laparoscopy with concomitant hysteroscopy, and three-dimensional ultrasound. In our case example, the septate uterus was better distinguished by MRI despite the original diagnosis of didelphic uterus.<sup>4–6,10,24</sup> Additionally, an MRI can assess the myometrial indentation into the endometrial canal, which differentiates an arcuate uterus (defined as a normal variant) from a septate uterus.<sup>5</sup> An arcuate uterus has a curved, concave contour of the uterus toward the fundus, and the indentation on an arcuate uterus is <1 cm, in which the myometrium of a septate uterus has an indentation of >1 cm. Furthermore, a uterus didelphys or bicornuate uterus will have a deep fundal cleft instead of a normal convex external fundal contour, whereas a septate or arcuate uterus will present with the normal convex external fundal contour.<sup>6</sup>

Proper management depends on reliable assessment and is essential in guiding therapy in difficult cases.<sup>19</sup> Clinical findings, proper diagnostic methods, and a clear classification system can lead to optimal management of symptomatic patients experiencing, or at risk for, poor reproductive outcome.

### Management

When discussing management, here are two questions that must be asked; 1) is the condition injurious, and 2) will treatment of the abnormality resolve the problem? Management of genital anomalies is complex and not well studied. Most of the studies are biased because of their observational, retrospective study designs, lack of control groups, or the use of historical control groups. In addition, the lack of a consistent and appropriate classification method further confounds the situation. We cannot say with authority that surgery is the standard of care, even for women with obstructive anomalies because hormonal suppression can suffice at least for a time.<sup>25</sup> However, there is little debate that obstructive abnormalities most often require surgery, either for treatment of pain or aesthetic reasons.<sup>26</sup>

There does appear to be some evidence that miscarriage reproductive outcomes are worse for women with uterine septae compared with the general population. Most publications show a higher spontaneous abortion rate in women with uterine septae when compared with controls. When pooling all of the available data, there is also

an increased rate of preterm delivery, intrauterine growth retardation, abruption, and even fetal mortality rates.<sup>27</sup>

Based on these data, one would expect that incision and removal of the septum would improve outcomes for these women. Currently there are no randomized controlled trials addressing this question. There was only one study that included data that were prospectively collected that also included a control group. When addressing spontaneous abortions, the rates were higher compared with the general population as a control group. After incision of the septae for their patients, the spontaneous abortion rate was the same as controls. The live birth rate data followed suit in the study, with lower rates before surgical incision and normal rates afterward.<sup>28</sup>

In a meta-analysis, spontaneous abortion rates were addressed in women who either underwent surgical incision or had the septae left in situ. In the pooled data, spontaneous abortion rates were lower with surgical correction, although preterm delivery rates were not different.<sup>27</sup>

Does the septate uterus play a role in ability to conceive? Again, the studies are inconsistent and of questionable study design. However, the meta-analysis previously discussed also looked at women with all types of uterine anomalies, and only women with uterine septae had a lower probability of natural conception compared with controls.<sup>27</sup>

To justify surgical intervention, however, you must first show a detrimental effect of the septum, followed by data demonstrating an improvement following surgery. Again, there are no randomized controlled trials to help us answer this question. There were two studies that included matched control groups. One prospective study compared pregnancy rates of women who did have incisions versus women who chose not to remove their septae.<sup>29</sup> In the second study that included a control group, the authors retrospectively looked at women undergoing in vitro fertilization with and without septae and in a subset of women once their septae were removed. Before removal, women with septae had lower pregnancy rates than their matched controls without septae. Once incision occurred, those women now had pregnancy rates equivalent to the controls and higher than those with septum left in situ.<sup>28</sup>

## CONCLUSION

Although a rare anomaly, the 128 reported cases of a uterine septum with a concomitant vaginal septum con-

firm that it may be more frequently encountered than previously realized. The older classification systems do not include all known anomalies, and the older embryological theories are probably not correct. It is encouraging that work to better classify MDAs is in progress. Although previously laparoscopy and concomitant hysteroscopy was necessary to accurately diagnose these anomalies, we can now rely on less invasive modalities such as MRI and three-dimensional ultrasound. Even though the quality of evidence is poor, the best available studies would suggest that fertility is reduced, and spontaneous abortion rates are higher in women with a uterine septum. Removal does appear to confer some benefit.

Lastly, errors in terminology in radiological reports can lead to inaccurate diagnoses and incorrect interventions. Participation in evaluating such studies will aid in proper management and help facilitate improved communication between the radiologist and gynecologist.

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