Müllerian Agenesis: Diagnosis, Management, and Treatment

ABSTRACT: Müllerian agenesis occurs in 1 out of every 4,000–10,000 females. The most common presentation of müllerian agenesis is congenital absence of the vagina, uterus, or both, which also is referred to as müllerian aplasia, Mayer–Rokitansky–Küster–Hauser syndrome, or vaginal agenesis. Satisfactory vaginal creation usually can be managed nonsurgically with successive vaginal dilation; however, there are a variety of surgical options for creation of a neovagina. Regardless of the treatment option selected, patients should be thoroughly counseled and prepared psychologically before the initiation of any treatment. Evaluation for associated congenital renal anomalies or other anomalies is also important. Although exact gynecologic screening recommendations are evolving, all women with a neovagina should undergo routine gynecologic care; however, vaginal cytologic screening is not indicated.

Müllerian agenesis also is referred to as müllerian aplasia, Mayer–Rokitansky–Küster–Hauser syndrome, or vaginal agenesis. Given an incidence of 1 per 4,000–10,000 females, most general gynecologists will only encounter müllerian agenesis once or twice during their careers (1). Müllerian agenesis is caused by embryologic growth failure of the müllerian duct, with resultant agenesis or underdevelopment of the vagina, uterus, or both. The vaginal canal is absent or markedly shortened. A single midline uterine remnant may be present or uterine horns (with or without an endometrial cavity) can exist. The ovaries, given their separate embryologic source, are normal in structure and function.

Differential Diagnosis

Patients with müllerian agenesis typically present with primary amenorrhea in adolescence with normal growth and development. After gonadal dysgenesis, müllerian agenesis is the second most common cause of primary amenorrhea (2). On physical examination, patients with müllerian agenesis have normal height, secondary sexual characteristics, body hair, and external genitalia. Furthermore, a vagina is either absent or present as a short blind-ended structure without a cervix at the vaginal apex. Patients with müllerian agenesis have a normal 46,XX karyotype and a normal hormonal profile.

The differential diagnosis of müllerian agenesis includes congenital absence of the vagina (with or without uterine structures), a low transverse vaginal septum, an imperforate hymen, as well as 46,XY disorders of sex development, including androgen insensitivity and 17α-hydroxylase deficiency.

In contrast to most patients with müllerian aplasia, the patient with an imperforate hymen will not have the typical fringe of hymenal tissue. The patient with a low transverse vaginal septum will have a normal hymen with more proximal obstruction of the vaginal canal. In addition to presenting with primary amenorrhea, the latter two conditions occur with symptoms of cyclic abdominal or pelvic pain and a pelvic mass due to the obstructed outflow tract and associated hematocolpos. Pelvic imaging may be helpful to distinguish this disorder.

In cases of androgen insensitivity, the gonads are testes, which produce normal androgens. The lack of functional androgen tissue receptors results in sparse or no pubic and axillary hair. Patients with androgen insensitivity typically have normal breast development because of the peripheral conversion of the circulating androgens to estrogens. They may have a small lower vagina or a normal vaginal length; however, no uterus or cervix is present because of the in utero production of müllerian inhibiting substance by the testes. In pubertal females, the diagnosis
between androgen insensitivity and müllerian agenesis can be made by assessing serum testosterone levels, followed by karyotype analysis, if a level in the pubertal male range is indicated in the results. Determining karyotype is helpful in prepubertal children who do not yet have postpubertal sex steroid production.

In cases of 17α-hydroxylase deficiency, individuals will have phenotypically normal female external genitalia, a blind short vaginal pouch, no uterus or fallopian tubes, and dysgenetic intra-abdominal testes. Affected males usually are raised as females, and the underlying disorder is recognized when the patient is evaluated for lack of pubertal development (3, 4). Because of the risk of neoplasm, it is important that gonadectomy be performed in patients with 46,XY disorders of sex development. The individual risk of neoplasm is estimated based on the molecular diagnosis and age (5).

**Evaluation of the Patient With Müllerian Agenesis**

Conventional transabdominal, translabial, or transrectal ultrasonography; three-dimensional ultrasonography; and magnetic resonance imaging can be used to evaluate the müllerian structures and are helpful in definitively characterizing anatomy. Most patients with müllerian agenesis have small rudimentary müllerian bulbs without any endometrial activity. In 2–7% of patients with müllerian agenesis, active endometrium is found in these uterine structures (1). These patients will present with cyclic or chronic abdominal pain. Magnetic resonance imaging has been suggested to assess the reproductive anatomy, although it rarely is needed in the initial evaluation unless ultrasound evaluation for the presence of functional endometrium in a müllerian structure is equivocal (6). Although laparoscopy is not necessary to diagnose müllerian agenesis, it may be useful in the treatment of patients with functional rudimentary uterine horns (7). When obstructed hemi-uteri are identified (uterine horns with the presence of active endometrium without an associated cervix and upper vagina), then laparoscopic removal of the unilateral or bilateral obstructed uterine structures should be performed (8, 9). Endometriosis can develop from retrograde menstruation from the obstructed uterine horn, which presents as dysmenorrhea and pelvic pain. In most cases, surgical excision of the uterine horn results in resolution of the endometriosis (10).

Evaluation for associated congenital, renal, or other anomalies is essential because up to 53% of patients with müllerian agenesis have concomitant congenital malformations, especially of the abdominal wall, urinary tract, and skeleton (11). Ultrasonography can be used to screen for the more common findings of renal agenesis or a pelvic kidney. Scoliosis is the most common skeletal abnormality associated with müllerian agenesis (11). It also should be noted that there is an increased, but small, rate of hearing impairment in patients with müllerian agenesis (11). A variety of uterine anomalies, including müllerian agenesis, can be seen in association with other anomalies and syndromes, such as VATER/VACTERL and anorectal malformations (12).

**Management of Patients With Müllerian Agenesis**

Management of patients with müllerian agenesis includes psychosocial counseling to address the functional and emotional effects of genital anomalies as well as correction of the anatomical defect. After the diagnosis of müllerian agenesis, the adolescent should be offered counseling to emphasize that healthy sexual relationships are possible. Future fertility options should be addressed with adolescents and their parents or guardians. Discussion of assisted reproductive techniques and use of a gestational carrier (surrogate) is appropriate. Female offspring of women conceived by assisted reproductive technology typically have normal reproductive tracts; although familial aggregates of müllerian agenesis have been documented, the mode of inheritance is unclear (13, 14). This information allows adolescents and young women to understand their reproductive potential for becoming a biologic parent and may help them deal with the diagnosis and its implications. The best predictor of good emotional outcome after diagnosis and vaginal creation is a good relationship between the patient and her parent(s) or guardian(s) and the ability to share feelings with family and friends (8). Contact with a support group of young women with the same diagnosis may be helpful (see Resources) (7). Referral to a mental health professional for ongoing support is worthwhile for some patients. Patients should be given a brief, written medical summary of their condition, including a summary of potential concomitant malformations. This information may be useful if the patient requires urgent medical care or emergency surgery from a health care provider unfamiliar with müllerian agenesis.

**Nonsurgical Creation of a Neovagina**

Timing for nonsurgical or surgical creation of a neovagina is elective; however, it is best planned when the patient is emotionally mature and expresses the desire for correction. Nonsurgical creation of the vagina is the appropriate first-line approach in most patients.

Successful self-dilation requires patients to manually place successive dilators on the vaginal dimple for 30 minutes to 2 hours per day. Alternatively, a bicycle seat stool can provide perineal pressure while allowing the patient to participate in other activities (15). Many young women find that sitting on the bicycle seat stool is too uncomfortable or awkward, thus they may have better success using dilators while reclining. Mature, highly motivated patients who wish to avoid surgery and are aware that it will take several months to achieve their goal are likely to be successful with this technique (15, 16). In a recently reported series of patients with müllerian agenesis, 90–95% of the patients were able to achieve
anatomic and functional success by vaginal dilation (17, 18). Health care providers often use peer mentors (other patients with vaginal agenesis who have successfully dilated), as support to the young woman attempting dilation. Sexually experienced patients may present with natural dilation of the vaginal dimple and occasionally require no additional dilation therapy. However, patients who successfully use dilation therapy may require continuation of dilation on an intermittent basis if they are not regularly engaging in vaginal intercourse.

**Surgical Creation of a Neovagina**

Surgery is an option for patients who are unsuccessful with dilators or for patients who prefer surgery after a thorough informed consent discussion with their health care providers and their respective parents or guardians, if appropriate. Surgical creation of a vagina requires ongoing postoperative dilation or vaginal intercourse to maintain adequate vaginal length and diameter.

The aim of surgery is the creation of a vaginal canal in the correct axis of adequate size and secretory capacity to allow intercourse. The timing of the surgery depends on the patient and the type of procedure planned. Surgical procedures often are performed in late adolescence or young adulthood (ages 17–21 years) when the patient is mature enough to be able to adhere to postoperative dilation. Because patient motivation is an important component of successful outcomes, it is wise to delay surgical therapy until the patient is ready to engage in vaginal intercourse.

A number of surgical techniques can be used to create a neovagina. The approach usually is based on the experience of the operating surgeon. Regardless of the technique chosen, referrals to centers with expertise should be considered. The surgeon must be experienced with the procedure because the initial procedure is more likely to succeed than follow-up procedures. Reoperation in these cases increases the chance of operative injury to surrounding tissues and the possibility of a poor functional outcome. At present, there is no consensus in the literature regarding the best option for surgical correction to afford the best functional outcome and sexual satisfaction (19).

Historically, the most common surgical procedure used to create a neovagina has been the modified Abbe–McIndoe operation. This procedure involves the dissection of a space between the rectum and bladder, placement of a mold covered with a split-thickness skin graft into the space, and the diligent use of vaginal dilation postoperatively. Postoperative dilation is essential to prevent significant skin graft contracture; therefore, this technique is inappropriate if the patient has concerns about or objects to dilation. The dilators must be intermittently used until the woman engages in regular and frequent sexual intercourse.

Other procedures for the creation of the neovagina are the Vecchietti procedure and other laparoscopic modifications of operations previously performed by laparotomy (20). The laparoscopic Vecchietti procedure is a modification of the open technique where a neovagina is created using continuous dilation with an external traction device that is temporarily affixed to the abdominal wall (21). Davydov developed a three-stage operation, which requires dissection of the rectovesicular space with abdominal mobilization of a segment of the peritoneum, and subsequent attachment of the peritoneum to the introitus (9, 22–24). Other techniques, such as bowel graft neovagina, use of buccal mucosa, amnion, and various other allografts, are less commonly applied to women with müllerian agenesis.

**General Gynecologic Care**

Women who have a history of müllerian agenesis and have created a functional vagina require routine gynecologic care. Regular pelvic examinations should be performed to examine for vaginal stricture or stenosis. Sexually active women with müllerian agenesis should be aware that they are at risk of sexually transmitted diseases and, thus, should use condoms and be appropriately screened according to guidelines for women without müllerian agenesis. In addition, vaginal speculum examination and inspection should be performed to look for possible malignancies (in cases of skin graft or bowel vaginas), colitis, ulceration (in cases of bowel vaginas), or other problems. Routine vaginal cytologic testing is not recommended. Insufficient evidence is available to guide the decision for human papillomavirus vaccination of women with dilated or surgically created vaginas, although the theoretic risk of vaginal neoplasia and genital warts is present (25).

**Conclusion**

The most important steps in the effective management of müllerian agenesis are correct diagnosis of the underlying condition, evaluation for associated congenital anomalies, and psychosocial counseling before any treatment or intervention to address the functional and emotional effects of genital anomalies. Laparoscopy is seldom required to make the diagnosis but may be appropriate in the patient presenting with pelvic pain. Nonsurgical creation of the neovagina should be the first-line approach. In cases in which surgical intervention is required, referrals to centers with expertise in this area should be considered because few surgeons have extensive experience in construction of the neovagina.

**Resources**

*The following resources are for information purposes only. Referral to these sources and web sites does not imply the endorsement of ACOG. These resources are not meant to be comprehensive. The exclusion of a source or web site does not reflect the quality of that source or web site. Please note that web sites are subject to change without notice.*

MRKH Organization, Inc.  
PO Box 301494, Jamaica Plain, MA 02130  
http://www.mrkh.org
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