A Second Glance on Cervicovaginal Agenesis

Charise Mae C. Malabanan MD; Kesiah Keren Bugante-Mercado MD and Leedah Ranola-Nisperos, MD, FPOGS, FPSRM, FPSGE
Department of Obstetrics and Gynecology, Dr Jose Fabella Memorial Hospital

Mullerian anomalies arise from the failure in the development of Mullerian ducts and their associated structures during organogenesis which confers adverse impact in fertility and reproductive health. Presented is a rare case of a 15 year old nulligravid, who presented with a chief complaint of severe cyclic hypogastric pain associated with primary amenorrhea. Complete clinical history, physical examination and sonographic findings pointed to a diagnosis of cervical hypoplasia associated with functioning uterine corpus and an absent vagina. Patient underwent total abdominal hysterectomy with left salpingectomy and bilateral oophorocystectomy, for hematometra, bilateral endometriotic cysts, and hematosalpinx. This case report discusses the management of cervicovaginal agenesis through a multidisciplinary approach by a team composed of an obstetrician-gynecologist, reproductive endocrinologist, pediatrician, and pediatric surgeon for proper evaluation, diagnosis, and management of this case.

Key words: Cervico-vaginal agenesis, primary amenorrhea, hematometra, hematosalpinx

Introduction

Cervicovaginal agenesis is a congenital disorder of the female genital system that manifests as the absence of the cervix and a poorly formed vagina. This is a very rare case with incidence of 1 in 80,000 live female births with only less than 200 documented cases published. This arises from the failure of development of the Mullerian ducts during organogenesis that results in uterine agenesis or hypoplasia.[1,2]

This condition initially manifests with primary amenorrhea associated with cyclic pelvic pain caused by the accumulation of menstrual blood in a functioning uterus, hence, cervicovaginal agenesis is usually not diagnosed until menarche. Cyclic pelvic pain is brought about by the inability to expel the menstrual blood from the vagina due to outflow tract obstruction.

Presence of functioning uterus with cervicovaginal agenesis is a big challenge for the gynecologist because a successful conservative repair could restore normal menstrual flow and may preserve the patient's fertility.

A prompt, comprehensive assessment is warranted because amenorrhea is often the presenting sign of an underlying reproductive disorder. A delay in diagnosis and treatment may adversely impact the long-term future of such patients.[3]

The Case

This is a case of a 15 year old nulligravid who presented with cyclic hypogastric pain that was temporarily relieved by oral analgesics.

Patient was previously hospitalized in 2016 at a local hospital under the General Surgery Department due to severe hypogastric pain. She underwent exploratory laparotomy, evacuation of hemoperitoneum, right total salpingectomy for a ruptured hematosalpinx, and appendectomy for a congested retrocecal appendix. The uterus was

noted to be enlarged to 12 weeks age of gestation. The left fallopian tube was likewise dilated. Both ovaries were enlarged and had cystic structures. Patient tolerated the procedure well and was discharged after five hospital days. Patient was then referred to Obstetrics and Gynecology service for further evaluation and management on outpatient follow-up. A transvaginal ultrasound done revealed cervicovaginal agenesis, thin endometrium with hematometra, bilateral endometriotic cysts and left hematosalpinx. Patient was prescribed with Dienogest 2 mg/tab daily which relieved the pain temporarily. She was advised elective total abdominal hysterectomy. However, due to the occurrence of severe abdominal pain, she consulted in the emergency room of a nearby government hospital.

At the emergency room, patient was conscious, coherent, ambulatory with stable vital signs. Patient weighed 45 kilograms, with a height of 142 cm (BMI 22 kg/m^2). Breast development was Tanner stage 4 (Figure 1). On abdominal exam, there was a midline incision scar, and a palpable, midline, tender hypogastric mass. On examination of the external genitalia, no lesions nor masses were noted. The pubic hair distribution was Tanner stage 3. The vagina had a small opening approximately 0.3-0.5 cm, which can accommodate the tip of a cotton pledget (Figure 2). Rectal examination revealed a tender, full culdesac. Initial assessment at this time was To consider Mullerian Anomaly, s/p right salpingectomy, appendectomy (May 1, 2016). Patient was then referred to Reproductive Endocrinology and Infertility Service and Pediatric Surgery. A transrectal and abdominal ultrasound done revealed sonographic features suggestive of cervicovaginal agenesis, thin endometrium with hematometra, bilateral endometriotic cysts and left hematosalpinx (Figure 3).

Patient underwent elective total abdominal hysterectomy with left salpingectomy and bilateral oophorocystectomy. On laparotomy, the uterus was symmetrically enlarged to 10cm x 8cm x 5cm with smooth tan brown external surface. Endometrial canal was slit-like measuring 4.0 cm long, lined by soft, smooth, endometrium measuring 0.1 cm thick. Myometrial wall thickness

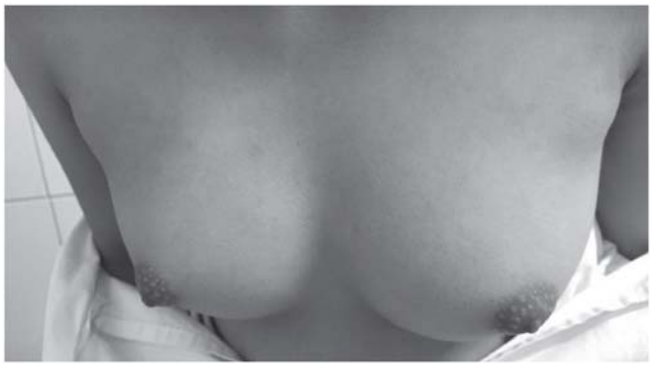

Figure 1. Patient's breasts showing areola and papilla form a secondary mound above level of breast (Tanner Stage IV).

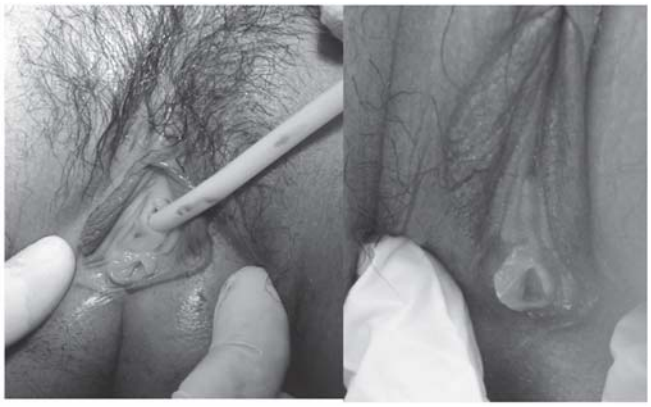

Figure 2. Small vaginal opening noted approximately 0.3-0.5 cm; Can accommodate 0.5 cm of the tip of cotton pledget upon insertion.

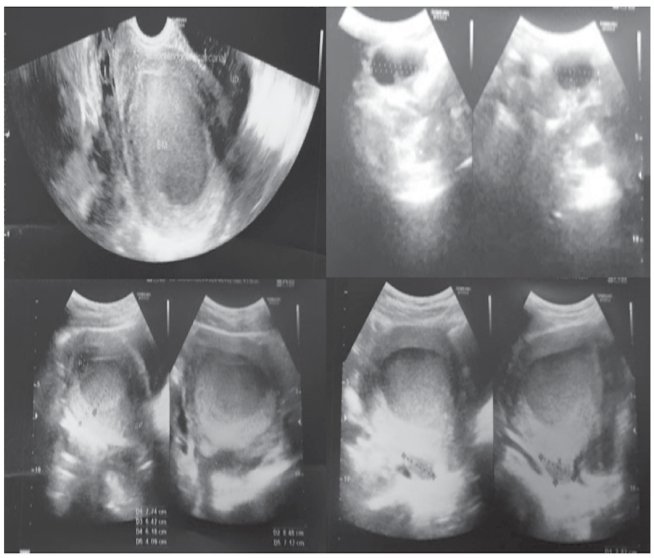

Figure 3. Sonographic features suggestive of cervicovaginal agenesis, thin endometrium with hematometra, bilateral endometriotic cysts and left hematosalpinx.

was 2.5 cm. The delineation between the uterus and cervix was not appreciated (Figure 4). There was a small solid protrusion noted at the caudal portion of the uterus which measured 2.0cm x 0.5cm x 0.3cm. The right endometriotic cyst measured 4.5cm x 1.5cm, while the left endometriotic cyst measured 1.5cm x 1.0cm (Figure 5). The left fallopian tube was dilated, and measured 5.0cm x 2.0cm x 1.0cm (Figure 6).

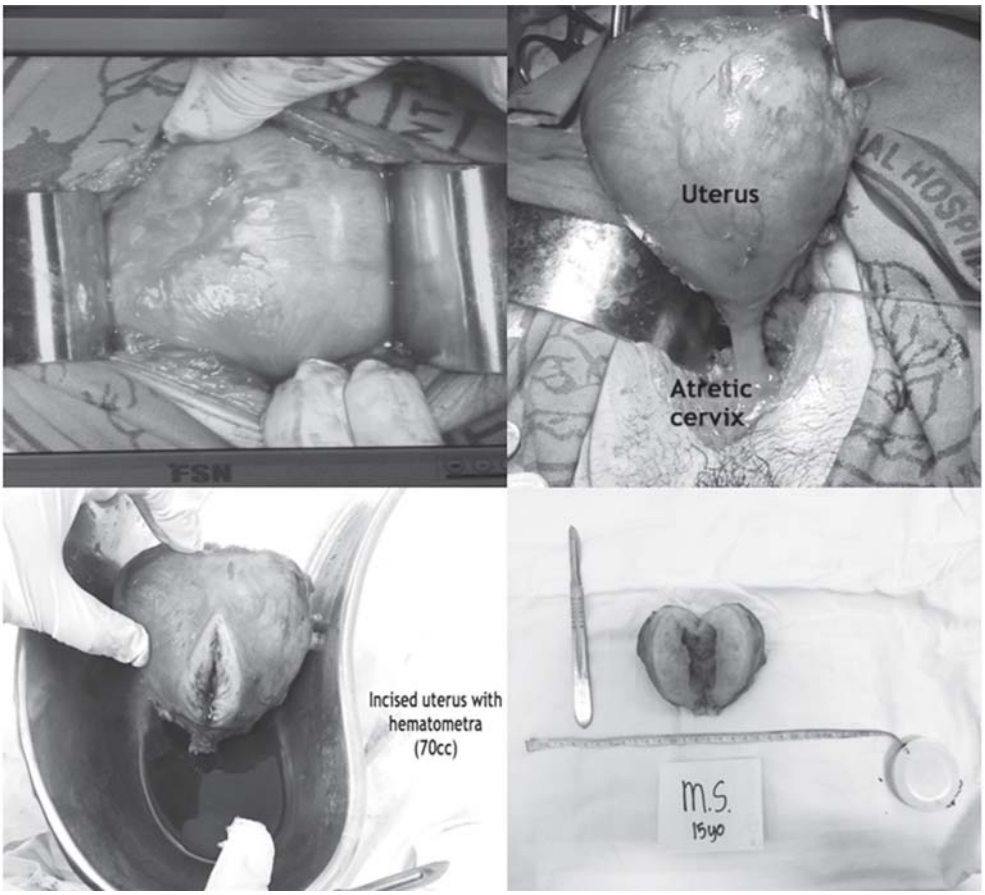

Figure 4. Intraoperative findings of an enlarged uterus with approximately 70cc hematometra, and an atretic cervix.

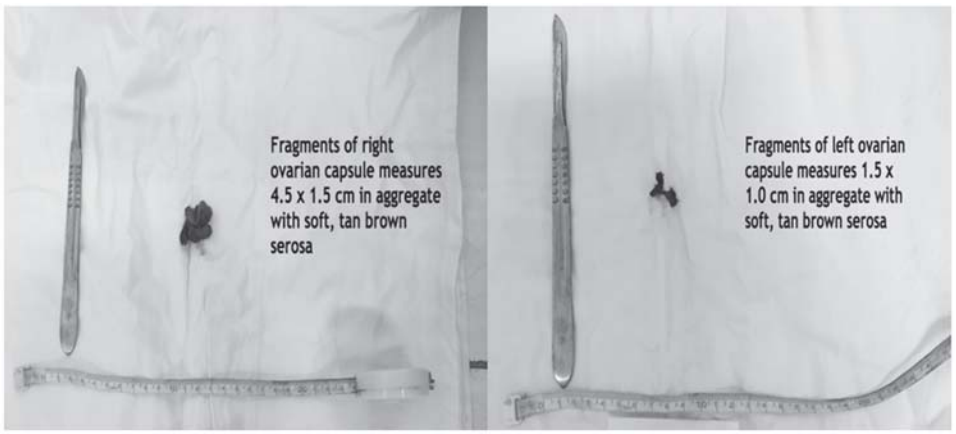

Figure 5. Fragments of right and left endometriotic cysts.

Figure 6. Left Fallopian tube dilated; measuring 5.0cm x 2.0cm x 1.0cm

Post-operatively, patient underwent psychosocial counseling regarding the impact of the surgical management on her future reproductive function.

Discussion

Primary amenorrhea is defined as the absence of menses in a woman who has never menstruated at the age of 15 years old with complete secondary characteristics or who has never menstruated within five years of breast development.[4] Patients with primary amenorrhea associated with cyclic pelvic pain should be carefully assessed and evaluated with considerations of endometrial, ovarian and hypothalamic pathology, outflow tract obstruction, and congenital mullerian anomaly.

A systematic approach to investigate the pathology of primary amenorrhea would be based on the presence or absence of uterus and breast. Examination of genitalia is usually abnormal in approximately 15% of women with primary amenorrhea.[5]

The index patient has a normal female phenotype, normal height, normal size and symmetrical breast classified as Tanner stage 4; Genital examination revealed absence of hymen, empty vaginal canal with a small opening, and Tanner stage 3 pubic hair distribution. The presence of breast development indicates that endogenous estrogen is being produced by the ovary, so this automatically rules out both ovarian and hypothalamic pathologies.[5] A blind or absent vagina with breast development usually indicates Mullerian agenesis, outflow tract obstruction or androgen insensitivity syndrome.[5,6]

Primarily, Androgen Insensitivity Syndrome usually manifests with the absence of pubic hair and with occasional presence of inguinal mass. Moreover, patients usually have facial acne and increased height compared to average females.[7,8] The deprivation of functional androgen tissue receptors results in scanty pubic and axillary hair.[7] Accurate diagnosis of Androgen Insensitivity Syndrome is done by requesting serum testosterone and karyotyping.[7,8] Although testosterone and karyotyping were not requested, Androgen Insensitivity Syndrome can be ruled out clinically by the presence of pubic hair, normal height and absence of inguinal mass or hernia in the index patient.

Lastly, outflow tract obstruction can cause cyclic pelvic pain due to accumulation of products of menstruation behind the defect.[9] There are two possible considerations, imperforate hymen and transverse vaginal septum. Imperforate hymen can be ruled out because it usually presents with

bluish bulging membrane at the introitus which the index patient did not exhibit.[6] Meanwhile transverse vaginal septum usually presents with hematocolpos and can sometimes obstruct the bladder resulting to urinary problems.[6,9]

It is very important to delineate these conditions for the management will depend entirely on the diagnosis. Ultrasound is the modality of choice to visualize the internal genital anatomy which will aid in proper identification of pathology.[6] However, Magnetic Resonance Imaging is still the gold standard of choice in diagnosing pelvic anomalies. In the case presented, sonographic findings pointed to cervicovaginal agenesis which falls under the category of Mullerian anomalies.

Cervicovaginal agenesis is a congenital disorder of the female genital system that manifests as absence of the cervix and poorly formed vagina.[2] Malfunction in the proper development of Mullerian duct is based on the completion of three phases: organogenesis, fusion and septal resorption. Uterine agenesis or hypoplasia is caused by the failure in organogenesis while absence of fusion gives rise to cervical and vaginal agenesis. This happens when there is a failure of development of the distal ends of the Mullerian ducts to form beyond 8th weeks of gestation which results in complete absence of the uterus and vagina.[6] In this case, there is simultaneous development of Mullerian and mesonephric ducts from the mesoderm layer, Consequently, abnormal differentiation of Mullerian ducts will arise to anomalies of urinary system. Evaluation for associated congenital, renal, or bone anomalies is essential because up to 53% of patients with Müllerian agenesis have concomitant congenital malformations.[2] The index patient's KUB ultrasound was unremarkable.

A standardized approach in characterizing Mullerian anomalies is based on American Fertility Society Classification (Figure 7). The index patient can be classified as IA and IB. IA includes cases with vaginal agenesis and with a functional uterus and endometrium however IB constitutes cases with cervical agenesis. There is no established grouping for exact pathology of cervicovaginal agenesis hence incidence is very rare.

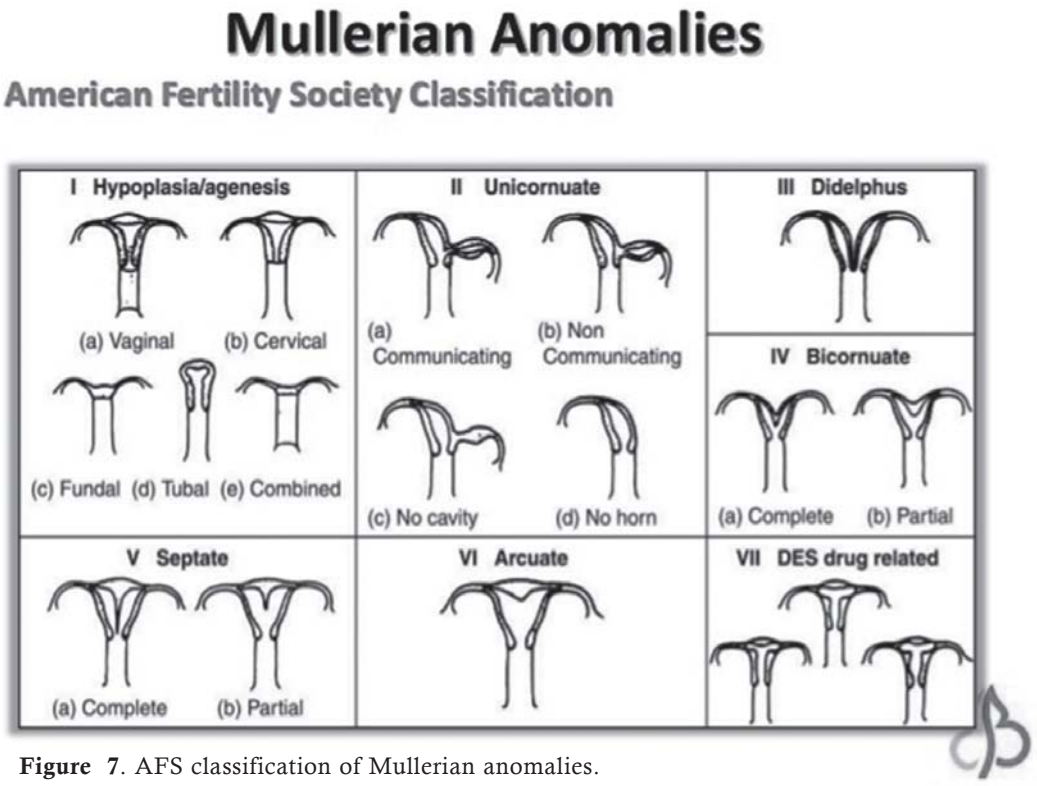

Figure 7. AFS classification of Mullerian anomalies.

Based on recent studies, initial surgical management for patients with cervicovaginal agenesis are uterovaginal anastomosis and creation of neovagina that will restore normal menstruation, fertility and sexual function of the patient. However, due to possible postoperative complications such as pelvic adhesions, recurrent obstruction of uterovaginal canal, strictures or stenosis and intraabdominal infection, many surgeons opt to do hysterectomy which eliminates all the possible surgical complications. Lack of endocervical glandular function and epithelium may be one of the most important contributing factors resulting in stenosis and infertility.[10,11,12,13]

The degree of pelvic endometriosis and adhesions present needs to be considered in recommending a surgical approach to the problem. It must be emphasized that patients, whose chances of fertility would be markedly compromised by the presence of pelvic endometriosis, pelvic adhesions, salpingitis, ovarian endometriotic cysts or advanced maternal age should be advised to consider hysterectomy rather than conservative management.

Patients who underwent total abdominal hysterectomy especially at a young age should receive comprehensive counseling and management. In the index patient, a multidisciplinary management approach was offered by a team composed of the obstetrician-gynecologist, reproductive endocrinologist, pediatrician, and pediatric surgeon.

Conclusion

Management of Mullerian anomalies will rely on the correct diagnosis of the condition of the patient, investigation of other congenital anomalies and psychosocial counseling before any intervention to address the functional and emotional effects of genital anomalies and treatment. Currently, conservative management should be the priority of patients with Mullerian anomalies. However, correct timing for surgical creation of neovagina should be planned carefully. Patients, whose chances of fertility would be markedly compromised by the presence of pelvic endometriosis, adhesions, hematometra, ovarian endometriotic cysts or advanced age, primary hysterectomy rather than conservative management should be considered.

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