Cervicovaginal agenesis: a case report*

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ABSTRACT

Congenital absence of the uterine cervix and vagina in the presence of a functional endometrium is an extremely rare congenital anomaly. Women born with this anomaly present with collection of blood in the uterine cavity or hematometra, disabling pelvic pain and progressively worsening endometriosis. Presented is a case of a 16 year-old girl with severe pelvic endometriosis and hematometra complicated by cervicovaginal agenesis. She was managed by total abdominal hysterectomy with bilateral salpingectomy, left oophorocystectomyandadhesiolysis. Surgical management of congenital cervicovaginal agenesis remains controversial. The decision to do a conservative surgical procedure or a hysterectomy depends on the clinical profile of the patient, the expertise of the surgeon, the extent of the malformation and its association with other mullerian anomalies.

Keywords: cervicovaginal agenesis, endometriosis, hematometra, mullerian anomalies

INTRODUCTION

Developmental anomalies involving mullerianor paramesonephric ducts represent some of the most fascinating disorders in Obstetrics and Gynecology. Normal development of the mullerian duct system involves a series of complex, well-orchestrated interactions that lead to the differentiation of the fallopian tubes, uterus, cervix and the superior aspect of the vagina[1]. Structural malformations in the development of the mullerian duct may result from 1) failure of development of one or both ducts 2) failure or abnormalities in the vertical and lateral fusion of the ducts[2]. Such malformations may be associated with outflow tract obstruction, infertility and recurrent pregnancy loss. The incidence and prevalence of Mullerian anomalies in the general population is unknown because it is unrecognized at birth hence not reported. There is a variation of its incidence from 0.1-3.5%. In one study, its incidence is 4.3 % in infertile women and 13 % in women with recurrent pregnancy losses[3]. However, the exact incidence is difficult to ascertain because of the lack of uniformity in the literature with regards to its classification, diagnosis and management. Vaginal agenesis combined with a functional uterus has a reported incidence of 1 in 4,000 to 10,500 female births; only 7-8% of patients with vaginal agenesis have a functional uterus[4], whilethe incidence of cervical agenesis or lack of uterine cervix is even lower, occurring in 1 in 80, 000-100,000 female births[5]. Thus combined congenital agenesis of the uterine cervix and vagina in the presence of a functional endometrium is an extremely rare mullerian anomaly. At present, there are no local studies citing the mean incidence of mullerian anomalies in the Philippines. The Philippine Journal of Reproductive Endocrinology and Infertility has published two (2) cases of cervical agenesis, one (1) case of cervical agenesis with partial vaginal agenesis, one (1) study describing 2 cases of cervical atresia and one (1) retrospective review of 5 cases of cervical agenesis managed in a tertiary university hospital [6-10].

Cervicovaginal agenesis with a functioning endometrium usually manifest with symptoms of obstructed menstrual flow leading to collection of blood in the endometrial cavity, fallopian tubes and peritoneal cavity. Patients with this condition present with amenorrhea (cryptomenorrhea), disabling cyclic pelvic pain and progressively worsening endometriosis[2]. The decision to attempt a conservative surgical procedure or do a hysterectomy is tailored to the individual cases.

CASE REPORT

The index patient is a 16 year-old gravida 0 who presented at the outpatient department with the chief complaint of primary amenorrhea and 3-year history of cyclic pelvic pain occurring every month and lasting for 3-5 days. The pelvic pain intensified during the third dayof menstruation and was relieved by intake of Mefenamic Acid. There was no family history of menstrual disorder or congenital malformations. The patient had no female siblings. Her mother had begun menstruating regularly at the age of 12 years old. The patient denies any sexual contact.

On physical examination, the patient had normal secondary sexual characteristics (Tanner staging 4 and 5 for breast and pubis). She was not pale and had pink palpebral conjunctiva. She had a soft flat abdomen with direct tenderness of the hypogastric area and no rebound tenderness. Pelvic examination revealed normal appearing

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external genitalia and presence of what seemed to be a hymen. As the patient was a virgin, a bimanual rectal examination was done revealing the presence of a midline mass 6 cm from the anal verge that was compatible with a retroverted uterus approximately 12 weeks age of gestation in size. However, nodularities were noted on the rectovaginal septum. Laterally, on the left, a cystic, tender, slightly movable mass measuring 8 cm in widest diameter was palpated.

Initial working impression was ***Primary amenorrhea probably secondary to outflow tract obstruction probably secondary to transverse vaginal septum; Ovarian new growth, left probably endometriotic cyst.***

Combined transrectal and abdominal ultrasound showed the presence of blood within the endometrial cavity or hematometra (Figure 1), bilateral adnexal masses (Figures 2,3) and the presence of cervix (Figure 4). An intravenous pyelogram showed normal functioning bilateral kidneys and collecting duct system. Preoperative diagnosis was ***Primary amenorrhea probably secondary to outflow tract obstruction secondary to transverse vaginal septum, Bilateral adnexal masses probably endometriotic cysts.***

The patient was scheduled for laparotomy. Examination under anesthesia revealed the absence of any hymen or vaginal canal. What was thought to be the hymen was actually a patulous urethral opening that was dilated to 2cm (Figure 5) Upon laparotomy, adhesions were noted between the omentum and anterior aspect of the uterus and bilateral adnexa. Hence, the patient was referred to surgery for adhesiolysis. The posterior cul de sac was completely obliterated. The uterus was enlarged with no palpable cervix. Approximately 100cc of hematometra was evacuated (Figure 6). The uterus measured 7.0 x 8.0 x 4.0 cm with endometrial implants on the anterior and posterior surfaces (Figure 7,8). The right ovary was grossly normal but adherent to the posterior portion of the uterus and the right fallopian tube. The right fallopian tube was dilated to 11.5 x 6.0 x 3.0 cm containing tar like fluid within (Figure 9). The left ovary was converted into cystic mass with irregular, reddish external surface measuring 15.0 x 10.0 x 8.0 cm containing approximately 700cc of tar like fluid within. The left ovary was adherent to the lateral aspect of the uterus and the left fallopian tube. The left fallopian tube was dilated to 15.0 x 4.0 x 3.0 cm containing tar like fluid within (Figure 10). Total abdominal hysterectomy with bilateral salpingectomy and left oophorocystectomy were performed.

The patient had an uneventful postoperative recovery and was allowed to go home after 4 days. Histopathology showed normal uterus with proliferative phase endometrium; endometriotic cyst on the left ovary; acute and chronic salpingitis, hematosalpinx and endometriosis

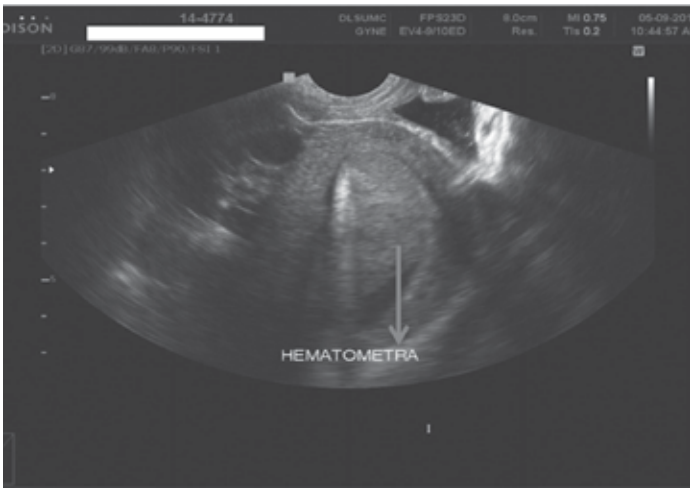

Figure 1. Pelvic Ultrasound showing Hematometra (blood collection within the endometrial cavity)

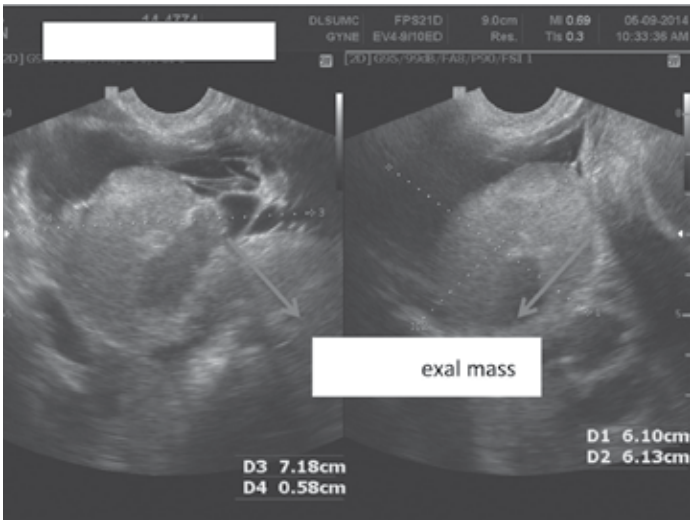

Figure 2. Pelvic Ultrasound showing the Right Adnexal Mass measuring 6 x 6 x 7 cm

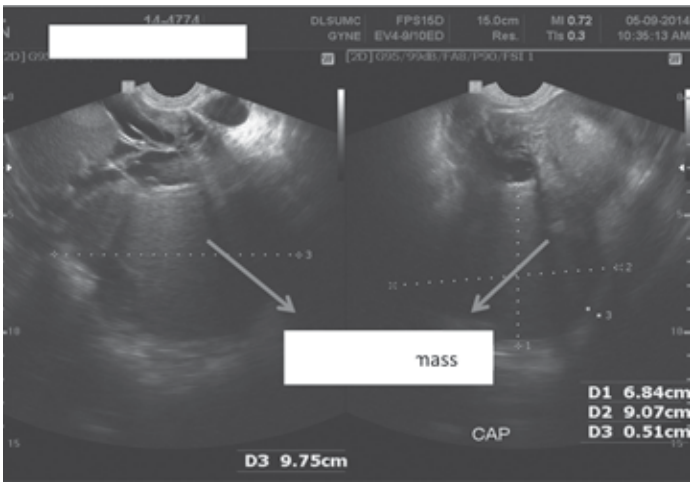

Figure 3. Pelvic Ultrasound showing Left Adnexal Mass measuring 6.8 x 9 x 9.75 cm

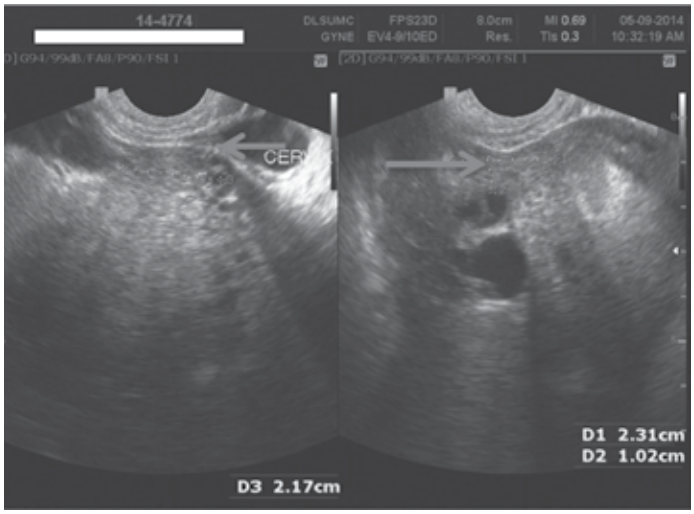

Figure 4. Transrectal Ultrasound showing Cervix measuring 2.31 x 1.02 x 2.17 cm

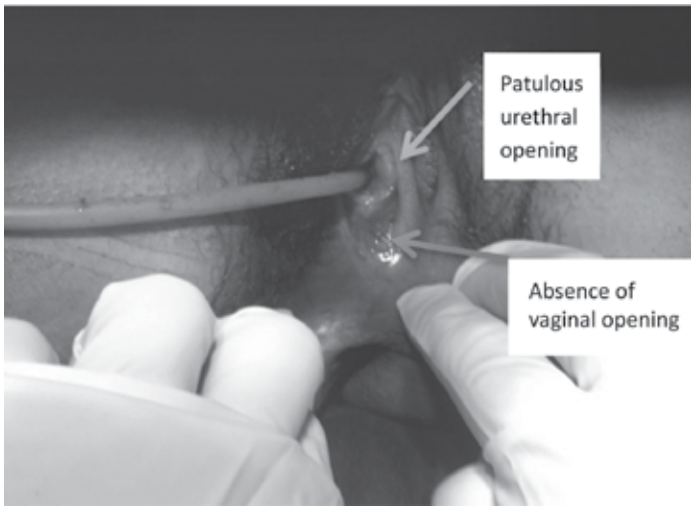

Figure 5. Vulva of the patient showing absence of hymen or vaginal canal

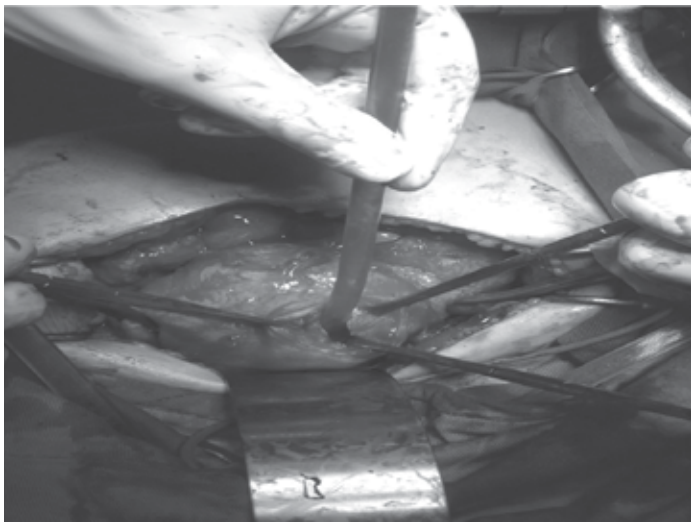

Figure 6. Presence of 100 cc of Hematometra

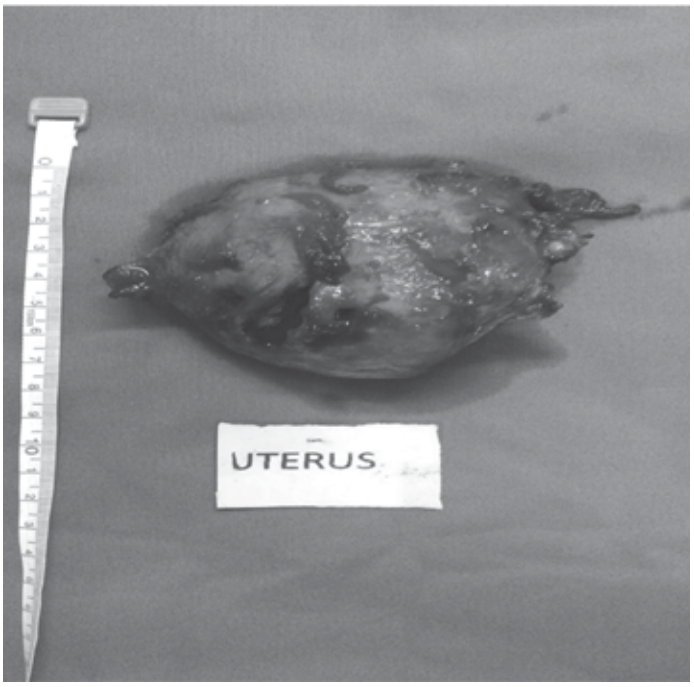

Figure 7. Uterus with absent cervix

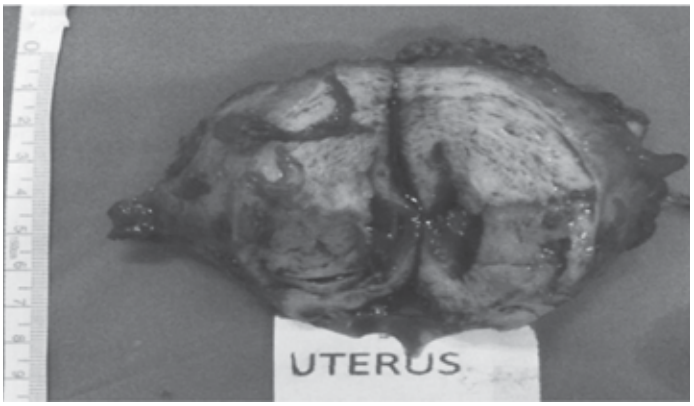

Figure 8. Cut section showing the uterus with absent cervix

Figure 9. Dilated right fallopian tube measuring 11.5 x 6.0 x 3.0 cm (emptied of its contents)

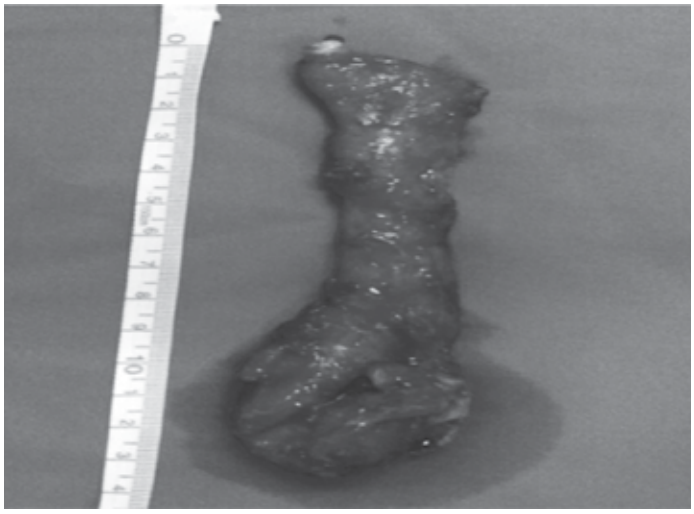

Figure 10. Dilated left fallopian tube measuring 15.0 x 4.0 x 3.0 cm (emptied of its contents)

of the left fallopian tube and acute and chronic salpingitis and endometriosis on the right fallopian tube.

Final diagnosis was ***Cervicovaginal Agenesis; Pelvic Endometriosis, Severe; Endometriotic Cyst, Left Ovary.***

DISCUSSION

This is a case of a 16 year-old gravida 0 who presented with a chief complaint of primary amenorrhea. She also complained of cyclic abdominal pain temporarily relieved by intake of analgesic. She presented with normal development of secondary sexual characteristics. Bimanual rectal examination revealed a slightly enlarged retroverted uterus and a left adnexal mass. Sonography showed the presence of hematometra and bilateral adnexal masses. Preoperative diagnosis was primary amenorrhea probably secondary to outflow tract obstruction probably secondary to transverse vaginal septum.

Differential diagnoses for primary amenorrhea include any disorder involving the outflow tract, uterus, ovary or the central nervous system. The presence of normal secondary sexual characteristics would mean there is presence of endogenous estrogen from normally functioning ovaries. This would clinically rule out an ovarian or central cause of primary amenorrhea. Another cause of primary amenorrhea would be androgen insensitivity syndrome wherein the patient has an XY chromosomal makeup but is phenotypically female. Patients with this syndrome would have presence of breast, absence of uterusand ovaries and absence of pubic and axillary hair. *The index patient had tanner stage 4 for pubis and an ultrasound result confirming the presence of uterus and ovaries*. Primary amenorrhea secondary to an outflow tract obstruction such as transverse vaginal septum or cervical/vaginal agenesis was highly considered.

Different causes of outflow tract obstruction were discussed with the patient and her parents. Treatment options such as excision of transverse vaginal septum and uterovaginal anastomosis and their complications were discussed before the operation. Hysterectomy was also discussed as the last treatment option in case of possibility of presence of any mullerian anomalies such as cervical/vaginal/ or cervicovaginal agenesis being rare causes of outflow tract obstruction. Permission was given for necessary appropriate pictures to be taken during the preoperative and intraoperative period.

Before the procedure, patient was examined under anesthesia and what was thought to be the vaginal opening was actually a patulous urethra. No vaginal canal was appreciated. No bulging mass was noted in the vulva. At this time, vaginal agenesis was highly considered. The surgical team proceeded with exploratory laparotomy. Upon opening, severe pelvic endometriosis was noted and the uterus was enlarged. Hematometra was evacuated amounting to 100cc. Upon further examination, there was no palpable cervix. The condition of the patient was discussed with the parents and consent for hysterectomy was obtained.

Female genital tract malformations are a cause of reproductive problems. The malformations of the female genital tract includes those anomalies affecting the development and morphology of the fallopian tubes, uterus, vagina and of the vulvar introitus, with or without ovarian, urinary, skeletal or other organs associated malformations. Cervicovaginal is characterized by the absence or hypoplasia of the cervix and vagina. *The American Fertility Society subclassified cervicovaginal agenesis as a Class IA, B mullerian anomaly and Class IIB uterovaginalanomaly*[2] (Figure11). In 2013, the European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynecological Endoscopy (ESGE) came up with a new classification of congenital uterine anomalies based on anatomy. Cervical and vaginal anomalies were classified independently into sub-classes. *The index patient falls under sub-class C4 for cervical agenesis and sub-class V4 for vaginal agenesis*[11] (Figure 12).

The steps in mullerian development are elongation, fusion, canalization and septal resorption[12]. Embryologically, congenital cervical agenesis is thought to arise primarily from a failure in the elongation of the mullerian ducts. Vaginal agenesis can be partial or complete. *Complete vaginal agenesis, as in the case of the index patient, is a consequence of developmental failure of the distal portion of the mullerian ducts as well as the urogenital sinus*. Vaginal agenesis is often associated with congenital absence of the uterus in 90-95% of cases[13]. A review of literature by Fujimoto et al. in 1997 revealed that 52% of cervical anomalies were associated with absence

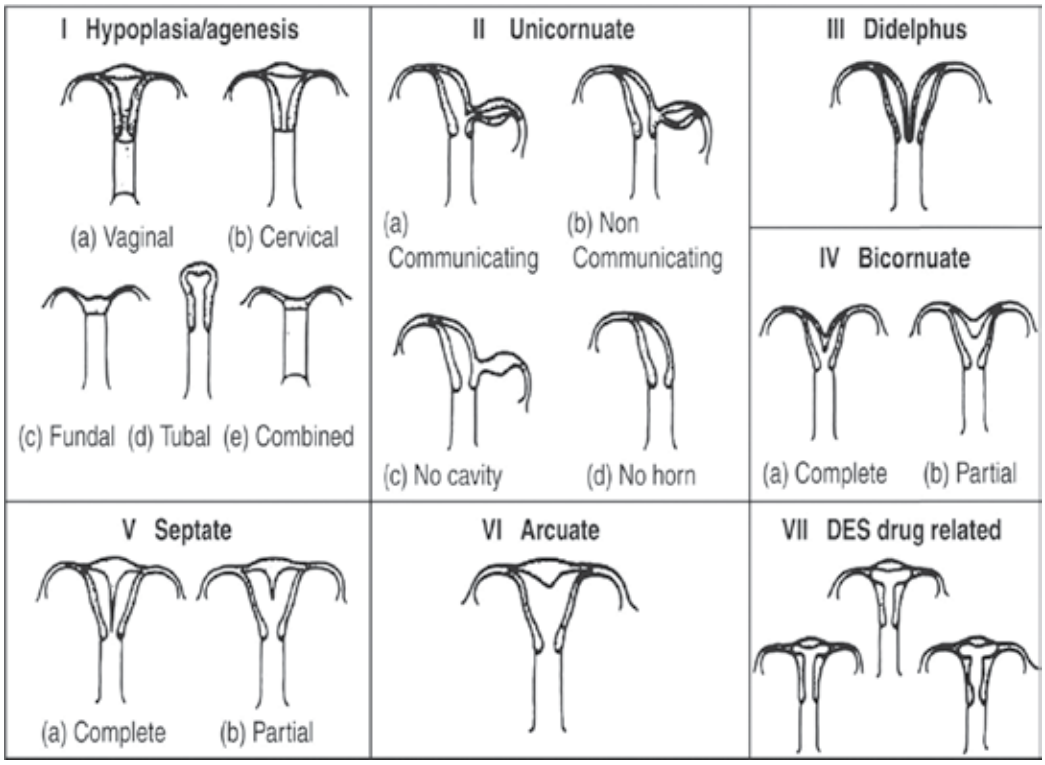

Figure 11. Classification of Mullerian Anomalies. *American Fertility Society. Fertil Streril 1988.*

ESHRE/ESGE classification
Female genital tract anomalies

	Uterine anomaly		Cervical/vaginal anomaly	
	Main class	***Sub-class***	***Co-existent class***	
U0	Normal uterus		***C0***	*Normal cervix*
U1	Dysmorphic uterus	**a.** T-shaped **b.** Infantilis **c.** Others	***C1***	*Septate cervix*
U2	Septate uterus	**a.** Partial **b.** Complete	***C2***	*Double 'normal' cervix*
U3	Bicorporeal uterus	**a.** Partial **b.** Complete **c.** Bicorporeal septate	***C3***	*Unilateral cervical aplasia*
U4	Hemi-uterus	**a.** With rudimentary cavity (communicating or not horn) **b.** Without rudimentary cavity (horn without cavity/no horn)	***C4***	*Cervical aplasia*
U5	Aplastic	**a.** With rudimentary cavity (bi- or unilateral horn) **b.** Without rudimentary cavity (bi- or unilateral uterine remnants/aplasia)		
			V0	*Normal vagina*
			V1	*Longitudinal non-obstructing vaginal septum*
			V2	*Longitudinal obstructing vaginal septum*
			V3	*Transverse vaginal septum and/or imperforate hymen*
			V4	*Vaginal aplasia*
U6	Unclassified malformations			

Figure 12. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Human Reproduction. 2013*

of a portion or the entire vagina.[14]

The urinary and genital systems both arise from a common ridge of the mesoderm. Hence, abnormal differentiation of the mullerian ducts may be associated with anomalies of the urinary system[15]. Among patients with mullerian anomalies, up to 47% were noted to have associated urologic abnormalities[2]. It is mandatory to do renal collecting duct imaging in all patients with mullerian anomalies. *An intravenous pyelogram of the index patient revealed normal kidneys and urinary bladder.*

The skeletal system may also be affected in these mullerian anomalies because it is derived from the mesoderm. Skeletal anomalies such as congenital fusion or absence of the vertebra occur in 12-50 % of cases[1].

Patients with cervicovaginal agenesis are phenotypically and genotypically female. During childhood, most patients with mullerian anomalies are asymptomatic. At puberty, once menstruation starts, the absence of a communicating channel between the uterus and the introitus causes the blood to remain hidden behind the obstruction characterized as cryptomenorrhea. *Clinical presentation usually consist of complaints of primary amenorrhea and cyclic lower abdominal cramping pain commencing between the ages of 11 to 17 as noted in the index patient*. Presence of patent fallopian tubes, functioning endometrium and outflow obstruction caused by the absence of the cervix and vagina prevent menstrual debris from being discharged. Menstrual blood will collect inside the uterus and reflux along the fallopian tubes into the peritoneal cavity. *Endometriosis, as noted in the index patient, and/or pelvic infection may result from the chronic hematometra*. In a study by Olive et al. (1987), endometriosis was present in 77% of women with obstructive mullerian anomalies and a functioning endometrium[16].

Diagnosis of cervicovaginal agenesis is quite difficult and requires a high index of suspicion. Physical examination would reveal the presence of an enlarged uterine corpus distal to the introitus. Adnexal mass and/or tenderness may be present as a consequence of pelvic endometriosis. Since most patients presenting with the clinical profile of mullerian anomalies are adolescents with no previous sexual contact, examination is limited to a bimanual rectal exam making it difficult to differentiate a transverse vaginal septum from a vaginal or cervical agenesis. Hysterosalpingography has no role in the evaluation of mullerian agenesis and hypoplasia. Laparoscopy would be inconclusive and costly. Both ultrasound and magnetic resonance imaging (MRI) are the most helpful diagnostic modalities in preoperative evaluation of cervicovaginal anomalies. Three-dimensional ultrasound has reported higher accuracy rate over conventional two-dimensional scanning when it comes to diagnosing mullerian anomalies. In experienced hands, three-dimensional ultrasound has a sensitivity of 93% and specificity of 100 % when it comes to diagnosis of Mullerian anomalies[15]. MRI is the gold standard in the imaging evaluation of uterine anomalies with a reported accuracy rate of 100% [15,17]. It has the ability to delineate uterine, cervical, and vaginal anomalies. Also, it is not operator-dependent and not limited by bowel loops, which is also an advantage over sonography. *Both 2 dimensional and 3 dimensional ultrasonography were used on the index patient. MRI was not done due to its prohibitive cost*. Both ultrasonography and MRI can help make an accurate diagnosis of the mullerian anomaly when findings are correlated with a complete history and thorough physical examination of the patient. *Despite all the advanced diagnostic modalities, the true nature of outflow tract obstruction is often diagnosed intraoperatively as in the case of the index patient*.

Severe pelvic endometriosis, as seen in the index patient, often complicates obstructive mullerian anomalies and it has a detrimental effect on the anatomical integrity and the fertility potential of patients. Hydrosalphinges, pelvic adhesions, ovarian cysts, and frozen pelvis due to endometriosis often coexist with the obstructive mullerian anomalies like cervicovaginal agenesis. *All of these complications were present in the index patient.*

Management of congenital malformations of the cervix and vagina pose challenging problems to the gynecologist. Experience in the management of cervicovaginal agenesis is still limited. Hysterectomy with ovarian preservation is still the proposed treatment option. But recent advances in reconstructive surgery, laparoscopy and assisted reproductive technology make room for conservative management in carefully selected group of patients who want to achieve pregnancy in the future. Conservative management of cervical agenesis includes canalization, uterovaginal anastomosis and cervical reconstruction[3]. The overall success rate of these techniques is about 60%. There have been 6 reported successful pregnancies after restoration of the uterovaginal route[3]. Creation of a neovagina in patients with vaginal agenesis may be done by several methods. The most commonly used method is the modified McIndoe procedure wherein a cylindrical stent-assisted split thickness skin graft is used. Methods using flaps from the labia majora or thighs have been described[18]. An abdominal approach known as the Vecchietti operation has also been described wherein a device is used to cause upward traction of the retrohymenal fovea. Despite the reported success of all of these advanced surgical techniques, they are limited only to case reports. Complications of conservative surgical management of patients with cervicovaginal agenesis remain substantial with high failure rates and poor functional results. Complications include peritonitis,

recurrent obstruction of the uterovaginal neocanal and persistent infertility[8]. Patients may need to undergo repeated surgical reconstruction and still end up with poor outcomes. Thus, it is not surprising that hysterectomy is still considered the first line approach in patients with agenesis of the cervix and vagina. If the condition is diagnosed immediately and hysterectomy done early enough, the risk of endometriosis can be decreased and the function of the ovaries can be preserved. In local statistics, 9 reported cases of outflow tract obstruction secondary to mullerian agenesis underwent hysterectomy[6-8,10]. One patient underwent 2 failed attempts of uterovaginal canalization before deciding to have a hysterectomy[8].

In the index patient, uterovaginal canalization was not attempted due to the following reasons:

(1) successful canalization would be difficult to achieve due to the absence of an intact cervical body and complete absence of a vaginal canal
(2) prolonged medical suppression and the possibility of repeated surgeries were too costly both psychologically and financially for the patient and her family
(3) the patient's family expressed their anxiety about possible psychological trauma that may be brought about by failure of repeated surgical procedures thus consent for conservative surgery was not given by the family

Postoperative medical management for the index patient's endometriosis was offered as an option but the patient and her family refused. A follow-up pelvic ultrasound 6 months after her surgery revealed no progression of the endometriosis.

The impact of mullerian anomalies on the reproductive and psychological future of patients should not be overlooked. Fertility options after hysterectomy would include adoption and IVF surrogacy. *Once the index patient is ready for sexual contact, vaginal reconstructive surgery may be offered to maintain her sexual function*. Sustained psychosocial support is of utmost importance in patients undergoing either hysterectomy or conservative management, especially since most patients, like the index patient, belong to the adolescent age group and they may not fully comprehend the extent of their condition.

CONCLUSION

Mullerian anomalies represent one of the challenging disorders in Gynecology. Thorough history and physical examination are needed to arrive at a proper diagnosis. Mullerian anomalies such as cervicovaginal agenesis, although a rare cause of outflow tract obstruction, should be considered by any clinician when examining adolescent patients presenting with amenorrhea, cyclic pelvic pain and palpable pelvic mass. Modalities such as MRI and ultrasound will aid in arriving at the correct diagnosis and planning for appropriate management of such patients. However, some are diagnosed intraoperatively as in the case of the index patient.

After an in depth diagnostic evaluation of patients with mullerian anomalies, another challenge for a gynecologist is to come up with the best treatment options. In patients with mullerian anomalies, the goals of management are relief of symptoms such as pain as well as preservation of sexual and reproductive function if possible. Early and accurate preoperative diagnosis, comprehensive treatment plan, careful selection of patients and holistic approach to such anomalies are the cornerstone of management. Although recent technical advances favor pelvic reconstructive surgery for this anomaly, it must be emphasized that these complex operations are not without complications and may result to poor functional outcomes. Surgical management must be individualized and the final decision will depend on the patient and parent's preference, the extent of the malformation and its associated anomalies, the expertise of the surgeon in the field of pelvic reconstructive surgery and assurance of dedicated long-term follow-up. Thus, hysterectomy is still considered the best treatment option.

With an in depth preoperative planning and long term psychosocial support, patient with cervicovaginal agenesis can still live full and normal lives.

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