Cervicovaginal Agenesis with Caudal Regression Syndrome: A Multidisciplinary Approach

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Abstract

This paper describes a multidisciplinary management approach on a case of a 20 year old nulligravid who was diagnosed with both cervicovaginal agenesis and causal regression syndrome (CRS). The index patient mainly presented with complaints of failed vaginal penetration, amenorrhea and cyclic monthly pelvic pain. The coexistence of cervicovaginal agenesis and CRS is extremely rare, and the pathogenesis regarding the association of both conditions is not yet fully understood. This combination poses significant diagnostic and management challenges, requiring a multidisciplinary approach that includes reproductive medicine, radiology, neurosurgery, orthopedics, and psychological support. Surgical reconstruction remains highly complex and individualized due to anatomical and functional constraints.

Key words: Cervicovaginal agenesis, Caudal Regression Syndrome, amenorrhea

Introduction

Mullerian duct anomalies (MDAs) arise from disruptions in the normal development, fusion, or resorption of the paired Mullerian (paramesonephric) ducts. It is a common condition with a prevalence of 4% and 6% of the general population. Mullerian anomalies were initially classified according to the American Fertility Society (AFS) in 1988. The latest modification of

Mullerian anomalies by the American Society of Reproductive Medicine (ASRM) in 2021 is the most widely used clinically. Another known classification system, given by the European Society of Human Reproduction and Embryology and the European Society for Gynecologic Endoscopy (ESHRE/ ESGE) in 2013.[1,3,4]

Cervicovaginal Agenesis is a rare anomaly, which manifests as absent vaginal development, in addition to partial or complete absence of cervical development with an incidence of 1:80,000–1:100,000 live birth.[6] Among these cases, it is estimated that around 7%–8% will have a functioning uterus.[6] At present, there are no documented local studies reporting incidence in the Philippines. The diagnosis is usually delayed until the age of puberty presenting as obstructive symptoms. Consequently, the clinical presentation usually involves amenorrhea, pelvic pain, and presence of an abdominal mass.[8] The pain is consistently experienced on approximately the same date each month.[6] Patients tend to underreport their vaginal agenesis symptoms until they become sexually active, presenting with incapacity to have coitus.[6] On genital examination, patients have no bulge effect but simply a vaginal dimple.

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The imaging of the pelvis, through abdominal and/or transrectal ultrasound along with pelvic Magnetic resonance imaging (MRI), plays a crucial role in confirming the precise diagnosis, describing its anatomy, and guiding proper treatment.[8] A hematometra should be evident on the MRI.[2] The use of standardized classification systems, such as those proposed by the ESHRE/ESGE and the ASRM, facilitates accurate diagnosis and informed treatment planning. In the ESHRE/ESGE classification, cervical agenesis is classified as C4 and vaginal agenesis is classified as V4.[1,3,4]

Significantly, female genital malformations are particularly associated with urinary tract malformation in 40% of cases, and skeletal system abnormalities in 10% of cases.[8] Another rare condition is Caudal Regression Syndrome (CRS), a congenital abnormality where a segment of the spine and spinal cord fails to develop, with noted incidence of 1:60,000 1 to 2:100,000 live births.[9] However, it occurs in about one in 350 infants of diabetic mothers, representing an increase of about 200 times.[9]

The patients usually present with a skeletal malformation which includes a shortened trunk, flexion-rotation-abduction contracture of the hip joints, flexion contracture of the knee joints, and clubfeet. It can also present with multisystemic malformations noted in genitourinary tract, neural tube, and anorectal and cardiovascular systems.[8] There is also a possibility of vesicoureteral reflux, hydronephrosis, fused kidneys, renal agenesis, ectopic ureters, and transposition of external genitalia due to Müllerian duct agenesis that may occur in one patient.[10] The diagnosis can be made in the first trimester via antenatal ultrasound by noting the short crown–rump length, while in the second or third trimester, it can also demonstrate the absence of sacrum and shortened femurs.[11] Mild clinical presentations may even go undetected until adulthood. This condition is often classified using Pang's and Renshaw classification system, which categorizes sacral agenesis into five morphological variants ranging from partial to total sacral agenesis, with varying degrees of vertebral involvement.[12]

The coexistence of cervicovaginal agenesis and CRS is extremely rare, and the pathogenesis with their association is not yet fully understood.8 This combination poses significant diagnostic and management challenges, requiring a multidisciplinary approach that includes reproductive medicine, radiology, neurosurgery, orthopedics, and psychological support. Surgical reconstruction remains highly complex and individualized due to anatomical and functional constraints.

The Case

This is a case of E.L., a 20-year-old, Filipino college student from Tagum City, Davao Del Norte. The patient presented with complaints of failed vaginal penetration, amenorrhea and cyclic monthly pelvic pain.

Four years prior to consult, she started to experience monthly hypogastric pain, described as crampy in character, with a pain score of 2–3/10 lasting for approximately three days. The pain initially responded to Mefenamic acid 500 mg TID. However, the intensity of the pain increased over time, becoming more severe and less responsive to pain reliever. There were no associated gastrointestinal or urinary symptoms.

Two months prior to consult, she and her boyfriend attempted vaginal intercourse for the first time but was unable to achieve penetration despite several attempts. She also reported low back pain that developed during prolonged sitting on hard surfaces, which she believed was related to the same hypogastric discomfort. She also noted absence of menarche, which prompted her to seek medical consultation.

A transrectal ultrasound revealed the following findings: Uterine corpus measured 3.5cm x 3.4cm x 2.8cm. Cervix was not visualized. Endometrium is 12.2 mm, thickened, heterogenous with no color flow. Both ovaries were normal. Posterior to the left ovary was a tubulocystic structure measuring 5.9cm x 3.3cm x 3.1cm, with low level echoes within and no color flow (score of 1), suggestive of hematosalpinx. There was minimal fluid in the cul-de-sac approximately 4 ml. She was thus referred to our institution for further evaluation.

Her medical history was unremarkable. For the family history, both parents were hypertensive, with

noted thyroid disease on maternal side, and diabetes mellitus on paternal side.

The patient had no menarche. Thelarche occurred at 12 years of age, followed by adrenarche at 14. She had one previous sexual partner, with an unsuccessful attempt at coitarche. She is the second of three siblings, currently in her first year of college, and works as a household help. She is a non-smoker, does not consume alcohol, and denies any use of illicit drugs. Her childhood immunizations were completed, and she was born via normal spontaneous vaginal delivery without any reported complications. On physical examination, she has a symmetrically short stature at 139 cm in height, weighed 39 kg with a BMI of 20.19 and an arm span of 135 cm (Figure 1). She is ambulatory with no deformities or deficits upon standing or walking. Her vital signs were stable. On Tanner staging, breast development and pubic hair distributions were both consistent with Tanner Stage V (Figure 2). Abdomen was flabby and soft, with a palpable 4cm x4cm mass in the left lower quadrant. On examination of patient's external genitalia, there was note of an invagination on the vaginal orifice, forming a smooth blind-ending pouch measuring approximately 0.5cm from external orifice (Figure 3). On digital rectal exam, there was a firm, non-mobile, cystic, 4cm x 4cm mass at the left adnexa, which was palpable approximately 8 cm from the anal verge. Neuromuscular function was normal.

The diagnostic examinations included: a complete blood count which revealed a high white blood cell count, with a differential count showing high neutrophils and low lymphocytes; Urinalysis showed slightly cloudy urine with moderate epithelial cells and ketones; Blood chemistry tests revealed normal liver and kidney function; thyroid panel showed normal thyroid function; 12L ECG and 2D echocardiogram showed normal cardiac function; karyotype analysis confirmed 46, XX (Figure 5).

A kidney and urinary bladder ultrasound showed normal kidneys, ureters, and urinary bladder (Figure 6), with an incidental finding of a complex mass in the left adnexal region. A whole abdominal ultrasound revealed a contracted gallbladder and normal liver, biliary tree, pancreas, spleen, aorta, kidneys, and urinary bladder. Wrist X-rays showed normal osseous structures, cortical outline, and trabecular markings. Femur X-rays and a chest X-ray were normal. An MRI of the lower abdomen and pelvis revealed an enlarged anteverted uterus with a distended uterine cavity and fluid demonstrating high T1 signal intensity and low T2 signal intensity . The myometrium appeared normal in thickness and signal intensity. The upper 2/3 of the vaginal canal showed a normal hyperintense signal, but the

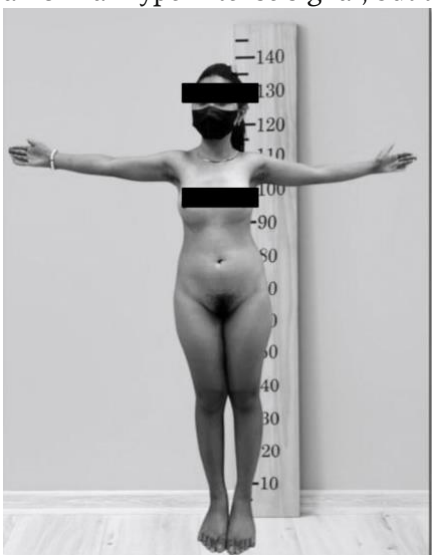


Figure 1. The patient showing short stature with a height of 139cm and arm span of 135cm.

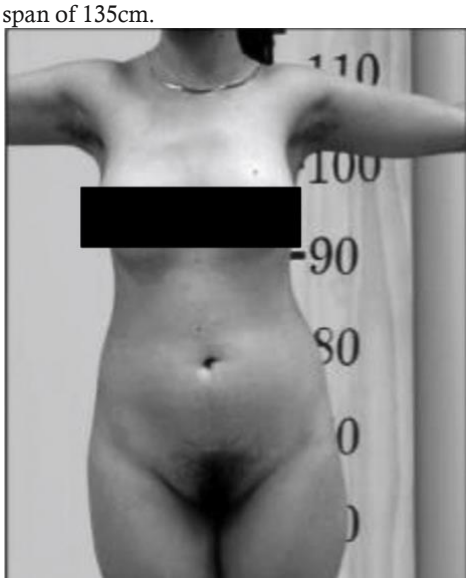


Figure 2. Tanner stage 5 for both breast and pubic hair development.

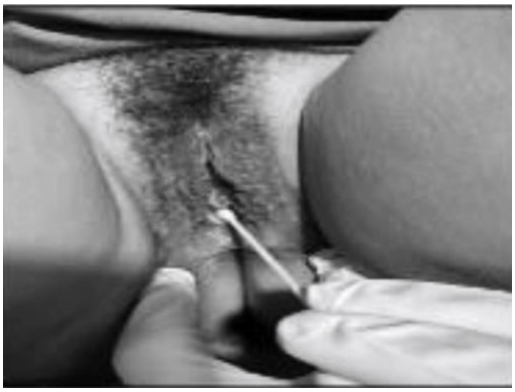
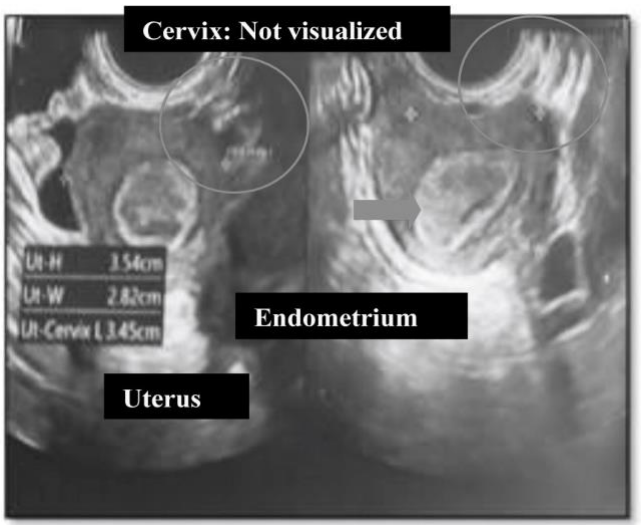
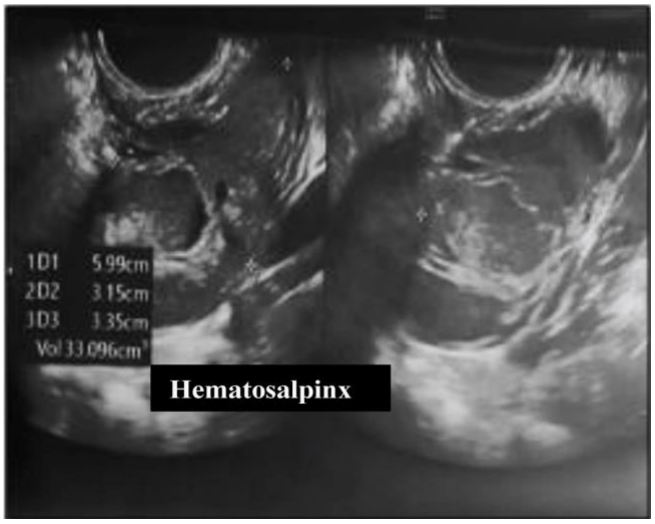


Figure 3. Vaginal dimple measuring 0.5 cm from external orifice

Figure 4. Transrectal ultrasound showing thickened endometrium and not visualized cervix.





Transrectal ultrasound showing left adnexal mass probably hematosalpix measuring 5.9cm x3.3cm x 3.1cm.

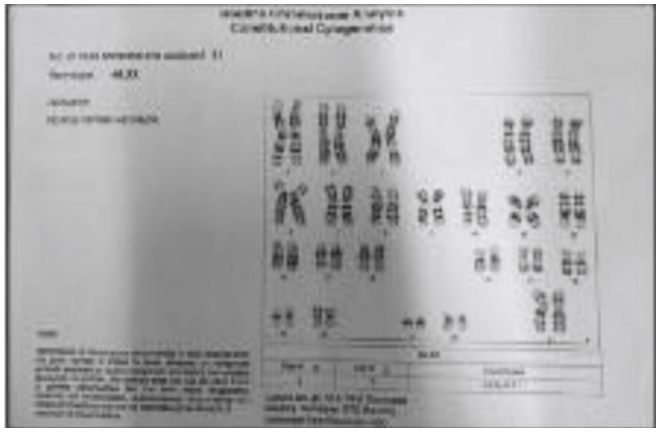


Figure 5. Karyotype 46 XX genotype.

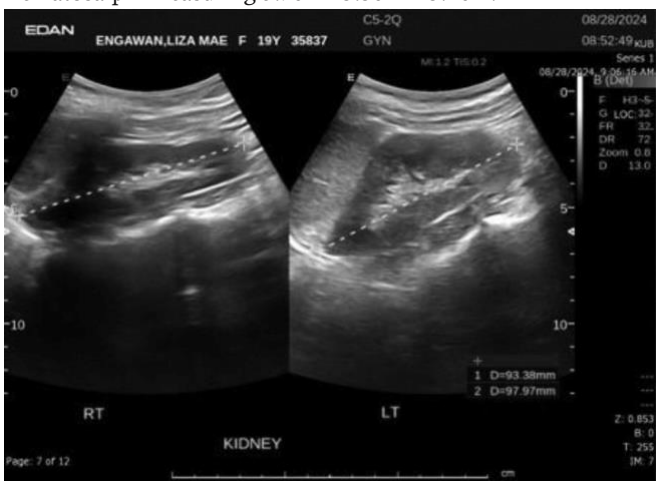


Figure 6. KUB ultrasound showing normal kidneys and urinary bladder.

lower 1/3 was absent. The cervix measured 0.8 cm (Figure 7). A dilated and tortuous tubular structure was noted in the left side of the uterus, suggestive of hematosalpinx (Figure 9). The coccygeal segments were absent, and four sacral segments were noted and oriented posteriorly (Figure 10). The lumbar vertebra

had normal formation and alignment. The spinal cord tapered at the level of L2-L3 (Figure 11), and the nerve roots of the cauda equina appeared normal. The hip and sacroiliac joints were normal, with no evidence of joint effusion or other abnormalities. Minimal free fluid was seen in the pelvis, and there was no lymphadenopathy. The impression was hematometra, left hematosalpinx, distal vaginal atresia, and absent coccyx, with findings suggestive of caudal regression syndrome.

Treatment

The management of our index case's condition requires a multidisciplinary approach. The Section of Reproductive Medicine addressed the patient's concerns regarding sexual function and menstrual suppression. As an initial conservative measure, manual vaginal dilatation was offered to facilitate the creation of vaginal length. Definitive anatomical reconstruction through the creation of a neovagina was discussed. Hormonal therapy using combined oral contraceptive pills was initiated to achieve menstrual suppression and alleviate cyclical pelvic

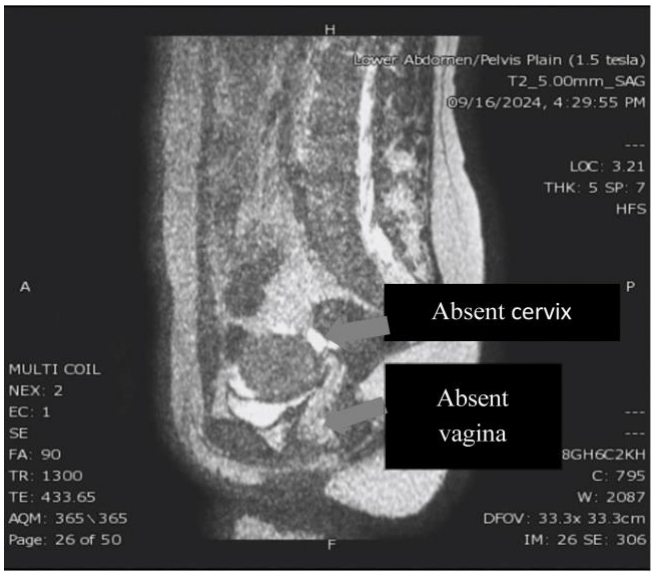


Figure 7. MRI showing normal hyperintense signal on TWI is noted in the upper 2/3 of the vaginal canal with absence of said signal in the lower 1/3.

Osseous structure:

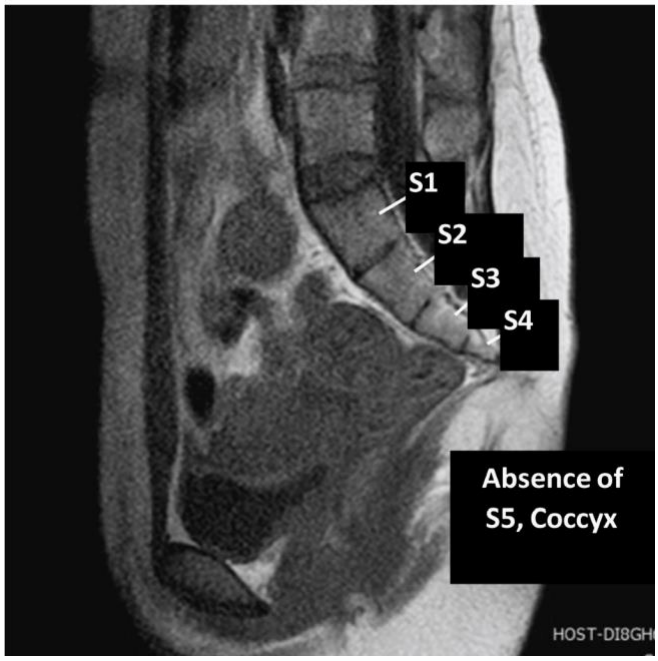


Figure 10. Coccygeal segments are absent. Four sacral segments are noted and oriented posteriorly.

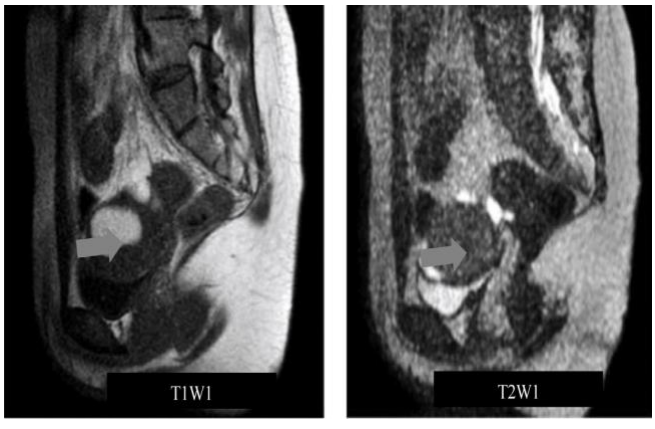


Figure 8. Uterine cavity is distended with fluid demonstrating and low T2 signal intensity (arrows).

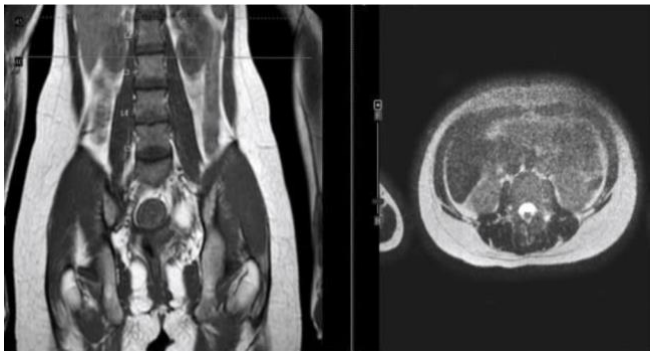


Figure 11. Spinal cord terminates at L2-L3. No evidence of high T1 signal tethering.

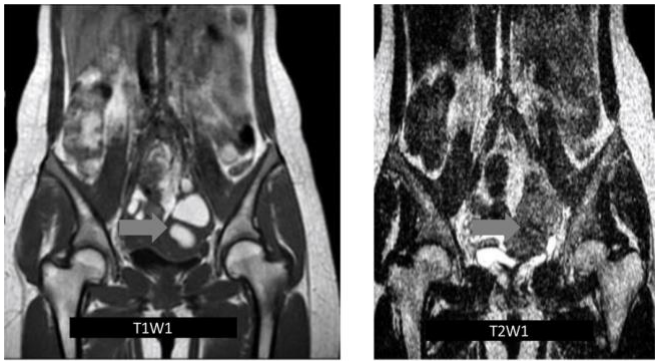


Figure 9. Dilated and tortuous tubular structure in the uterus.

pain associated with obstructed menses. Considering the complete cervical and vaginal agenesis, laparoscopic hysterectomy was also proposed as a definitive surgical option to eliminate the source of hematometra and prevent further complications. For fertility preservation, counseling was provided on assisted reproductive technologies, including in vitro fertilization and the possibility of gestational surrogacy. The Internal medicine team conducted a thorough systemic evaluation to screen for potential metabolic and cardiovascular comorbidities. Orthopedic Spine specialists assessed the structural integrity of the lumbosacral spine, with the primary goal of maintaining spinal stability and preventing progressive deformities that could exacerbate chronic back pain. The Neurosurgical team was consulted to evaluate for possible neurological involvement or spinal cord anomalies contributing to the patient's low back pain, ensuring appropriate long-term monitoring. Additionally, Psychiatric referral was undertaken to address the psychological impact of the diagnosis. The patient was provided with counseling focused on emotional well-being, coping strategies, and fertility-related concerns, with the aim of delivering holistic and patient-centered care.

Patient Follow-up

Currently , the patient has accepted and fully understands her condition. She is not experiencing monthly hypogastric pain and her latest vaginal length was at 2.5 cm. She is compliant with her regular follow-up check-ups, which initially was set monthly, but but when she started her manual vaginal dilatation, the patient comes for check-ups biweekly. The Orthopedic spine and Neurosurgery have advised annual follow-up visits and advised to use pain reliever for low back pain with immediate consultation if symptom worsens. The Psychiatry department has also provided her with scheduled appointments.

Discussion

Embryogenesis of the caudal body axis and urogenital system is a precisely coordinated process. By 15th to 16th day of human development, gastrulation established the three germ layers, ectoderm, mesoderm, and endoderm. The epiblast cells migrate through the primitive streak, with an inward movement to displace the hypoblast to form the definitive endoderm. Once definitive endoderm is established, inward movement of the epiblast forms the mesoderm. The epiblast cells that remain on the surface differentiate into ectoderm.[13] Epiblast cells migrating through specific regions of the primitive streak give rise to distinct mesodermal derivatives: paraxial mesoderm forms skeletal muscles and vertebrae, and Intermediate mesoderm forms the urogenital system, including the Müllerian ducts. Any disruption in this migration can impair development of both skeletal and genitourinary structures. An insult such as maternal hyperglycemia can disrupt mesodermal migration, proliferation, and differentiation. Hyperglycemia leads to tissue hypoperfusion and oxidative stress during organogenesis. Even though the diabetic status in our patient is unknown, this mechanism is well established. . Additionally, mutations in the Brachyury (T) gene impair activation of pathways essential for caudal mesoderm development. An early interruption can result in both Caudal regression and Müllerian anomalies.[13] The female reproductive tract develops from paired Mullerian ducts between 6 weeks and 11 weeks in utero.[1] The Mullerian ducts elongate caudally, then fuse in the midline to reach the urogenital sinus. Then, the central absorption of the cells occurs that will result into two hollow tubes of tissue that remain fused medially. Lastly, the midline septum between the two tubes of tissue undergoes resorption leading to a midline unified structure. The inferior portion of the Mullerian ducts becomes the upper vagina, followed by the cervix and uterus.[7] The lower onethird of the vagina is derived from the urogenital septum.[15]

Cervicovaginal agenesis is a particularly rare form of MDA that results from disrupted development and fusion during canalization the caudal Müllerian ducts and vaginal plate. Approximately 7–8% of these cases present with a functional uterus capable of cyclical endometrial shedding.[6]

Caudal regression syndrome (CRS) is a rare congenital malformation manifested by under development of the lower spine and spinal cord.[12] The clinical features may range from partial sacral agenesis to complete absence of the coccyx, making it a rare but clinically significant condition.[9,11] The coexistence of cervicovaginal agenesis and caudal regression syndrome is extremely rare. In female patients, Caudal regression syndrome has been linked to a spectrum of urogenital anomalies, including renal agenesis, ectopic ureters, and in rare cases, Müllerian agenesis.[8] In fact, it has been reported only once in literature, involving a 13-yearold girl with distal vaginal atresia. Our case involves a 20-year-old woman with cervicovaginal agenesis with Caudal regression syndrome.[8]

In cervicovaginal agenesis patients it typically presents at puberty with primary amenorrhea and cyclic abdominal pain due to outflow tract obstruction. In some instances, diagnosis is delayed until failed attempts at vaginal intercourse reveal the absence of a patent vaginal canal.[8] In this case, the patient also has failed vaginal intercourse. On examination, these patients may show no visible vaginal introitus or only a small vaginal dimple, as was found in this case.

The presence of caudal regression syndrome in this patient further complicates the clinical picture. CRS may cause multisystem malformations, skeletal malformations, urogenital anomalies cardiovascular anomaly, neural tube and anorectal.[8] It often goes undetected until adulthood in mild clinical presentations.[12] In this case, our patient presented with short stature and mild lumbosacral anomalies without major limb deformities but she did presented with chronic low back pain.

In diagnosing cervicovaginal agenesis, pelvic ultrasound is the first-line tool, which can reveal hematometra along with complete absence of the vagina while demonstrating normal ovaries and uterus.[6] In this case, the patient exhibited a functional uterus, but menstrual blood had no path to exit from vagina, as evidenced by cyclic pelvic pain and the presence of hematometra and hematosalpinx on imaging.

While ultrasonography is widely accessible, a 2D ultrasound has low sensitivity (44%) and low specificity (85-92%) as compared to the 3D ultrasound with a sensitivity of 85 % and specificity of 100%. However, MRI is the ideal imaging modality for accurate diagnosis of mullerian anomalies as it gives exquisite information regarding both external contour and internal anatomy1 with a sensitivity and specificity of 96-100%.[16]

In caudal regression syndrome, the diagnosis can be made in the first trimester antenatal ultrasound by noting the short crown – rump length. In adults, MRI is the preferred imaging modality which can yield a high sensitivity and specificity.[11] This condition is categorized according to the Pang's and Renshaw Classification, which is a framework for characterizing the extent and severity of sacral agenesis.[12] In this patient, sacral dysgenesis and complete absence of the coccyx were evident on MRI, consistent with Pang's Type V classification.[12]

Management of Cervicovaginal agenesis with Caudal Regression Syndrome entails a multidisciplinary care which involves Reproductive medicine, Orthopedic Spine, Neurology, Psychiatrist and Internal medicine with the goals of improving sexual function, relieving menstrual obstructive symptoms and offering fertility options.

Reproductive Medicine plays a crucial role in optimizing sexual function, manage menstrual suppression and provide guidance on fertility potential and future reproductive options. The first goal of the management focuses on alleviation of symptoms, which can be achieved either by non-surgical or surgical approach.[17] According to ACOG, for non- surgical options, vaginal elongation by manual dilation is the first-line approach with 90-96% success rate.[18] Initially, the patient should have a examined herself in the mirror so that she can identify her clitoris, urethra, and distal vagina and should be able to demonstrate properly the appropriate location and the angle to place the dilator.[15] There are two technique for manual vaginal dilation that we can offer to the patient , one is the Frank's technique that used hand operated vaginal dilators in the lithotomy position. The other one is the Ingram's method which

uses vaginal dilators placed on a specially designed bicycle seat stool that provides consistent perineal pressure.[16] The patient is instructed to use a dilators for 10–30 minutes one to three times per day, progressing in size. The patient should have a follow up weekly or biweekly to monitor progress, pain and bleeding if present, and to provide encouragement. The success of this intervention is usually measured when anatomically it will achieve a length of 6 cm or longer . Also, the definition of success can be in terms of comfortable sexual activity that is measured by the patients experienced.[15]

Surgery may be performed when the patient is mature enough to understand the procedure and be able to do dilation consistently. The modified Abbe-McIndoe operation is the most common procedure used to create a neovagina, which involves the dissection between the rectum and bladder with subsequent placement of a stent using the splitthickness skin graft. The laparoscopic Vecchietti procedure uses an external traction device that is placed and maintained to the abdominal wall. The Davydov procedure involves the dissection of the rectovesicular space with the use of a segment of the peritoneum that will subsequently be attached to the introitus. Other vaginoplasty graft options include bowel, buccal mucosa, amnion, and various other allografts.[15] Our patient chose conservative management with Frank Manual dilation with current vaginal length of 2.5cm.

In the case of cervicovaginal agenesis, the surgical approach is not well established.[19] In select cases with a functional uterus, surgical reconstruction can be considered to restore sexual function and menstrual outflow. This procedure involves creation of a neovagina, neocervix, and restoration of the continuity between the neovagina, the neocervix, and the uterus.[2] The procedure is performed in two main steps: first, the creation of neovagina; and second, the anastomosis between the uterus and the neovagina through the neocervix.[20] The success rate for this procedure varies depending on the technique, extent of anomaly, surgeons expertise, timing of surgery and adherence to dilation protocols. However, due to high morbidity and mortality of this procedure due to serious complications such as sepsis, endometriosis, and need for multiple surgeries due to restenosis, many authors have concluded that the treatment of choice should be hysterectomy and in canalization alone, 33% is unsuccessful that will eventually require hysterectomy.[20]

For patients who are not ready to undergo surgical intervention, they should be started on menstrual suppression with combined hormones, progesterone injections, or GnRH agonists. At the time of this writing, the patient was still undecided whether to undergo surgery or not. Hence, she was started on continuous hormonal suppression therapy using combined oral contraceptives, to reduce menstrual flow and manage hematometra. Gestational surrogacy using the patient's oocytes remain to be the primary fertility option for patients who may need to undergo hysterectomy.[4,21]

The Psychiatrist should provide essential psychological preparation before a patient undergoes a procedure, including determining the source of emotional support to help the patient adjust to the diagnosis and its implications. For our case, the patient is being seen by the psychiatrist who focuees on psychological well-being, spiritual health and self-body image. For her next consult, the focus will be on addressing her separation from her partner.

For the management of patients with caudal regression syndrome, Orthopedic–Spine specialists assess and monitor skeletal malformations. Their goal is to optimize mobility and prevent progressive deformities that may affect posture, gait, and quality of life. The Neurosurgery plays a key role in surveillance for progressive spinal deformities and evaluating neurological symptoms. They also assess persistent low back pain that may indicate spinal instability or nerve compression.[9]

Our patient was co-managed with orthopedic and neurologic surgery services to monitor for potential spinal instability or neurologic compromise, though active intervention was not required at the time of evaluation. Long-term surveillance remains crucial to anticipate complications, including neurologic deterioration or genitourinary dysfunction.

Conclusion

This case highlights the critical importance of early and comprehensive evaluation in identifying complex congenital anomalies such as cervicovaginal agenesis with caudal regression syndrome. A

comprehensive evaluation is essential, ensuring that clinicians look beyond the gynecologic findings to assess for broader systemic involvement. The successful care of patients with this condition underscores the value of an individualized, multidisciplinary approach that integrates pediatric, surgical, orthopedic, urologic, and gynecologic expertise. Early recognition and coordinated management not only optimize outcomes but also guide long-term planning for functional and reproductive health. This case reinforces the need for holistic, patient-centered strategies when managing rare congenital anomalies.

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