REVIEW ARTICLE

# OHVIRA Syndrome—Diagnostic Dilemmas and Review of Literature

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## Abstract

Obstructed hemivagina, ipsilateral renal agenesis (OHVIRA) syndrome, as well as didelphic uterus, is a rare, obstructed müllerian anomaly, affecting the physical, reproductive, sexual, and mental health of the patient. The diagnosis is often delayed because of unawareness of the fact that even common gynecological complaints like vaginal discharge can be associated with this rare entity. The most common symptoms at presentation, however, include pain in the abdomen and menstrual complaints. Therefore, while evaluating them, the possibility of this rare entity should be kept in mind; hence, emphasizing the importance of local examination. A 3D ultrasound and a magnetic resonance imaging are helpful in confirming the diagnosis. In this article, we report case series of OHVIRA syndrome with extreme clinical symptoms at presentation. We reviewed the literature and discussed various classifications used for this syndrome, including the newer classification based on the type of obstruction. The minimally invasive "vaginoscopic no-touch" technique of surgery is an alternative option available for adolescents where preservation of hymen seems to be important.

**Keywords:** Didelphic uterus, Herlyn–Werner–Wunderlich syndrome (HWWS), Ipsilateral renal agenesis, Obstructed hemivagina, Obstructed müllerian anomalies.

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## Background

Female reproductive function depends on the intact genital tract along with a functional hypothalamic–pituitary–ovarian axis. Aberration in any of the systems may significantly affect a woman's reproductive potential, thereby negatively affecting her quality of life. Müllerian anomalies are congenital developmental anomalies of the female reproductive tract with an overall incidence, including both major and minor müllerian anomalies, of 7–10% while after excluding the minor ones the incidence is 2–3%.[1,2] The incidence of recurrent abortions reaches up to 16%.[3] These anomalies are often associated with one or more extragenital anomalies as well; most common among them are the renal anomalies (17.3%) with renal agenesis contributing to 64.6% of them. Among patients with didelphic uterus, 29.1% had associated renal anomalies with 23.6% diagnosed to have renal agenesis and obstructed hemivagina.[4] Other extragenital anomalies include skeletal anomalies (12–19%), congenital heart disease, and gastrointestinal malformation (12%).[5]

Obstructed hemivagina, ipsilateral renal agenesis (OHVIRA) syndrome or Herlyn–Werner–Wunderlich syndrome (HWWS) is one such complex congenital developmental anomaly of the genitourinary tract characterized by didelphic uterus, obstructed hemivagina, and ipsilateral renal agenesis. It was first reported in 1922.[6] The estimated incidence of obstructed müllerian agenesis is 0.1–3.8% in the general population, which may be underreported due to the associated diagnostic dilemma.[7]

Here, we present two cases of OHVIRA syndrome with two extreme clinical presentations—the most common acute presentation with cyclical abdominal pain in one while an extremely rare delayed presentation with chronic vaginal discharge in the other.

## Case Description

### Case 1

A 21-year-old nulligravid married woman presented with complaints of continuous foul-smelling discharge per vagina for 1 year. She attained menarche at 14 years of age, continued with normal menstrual cycles, and had normal sexual life without any complaints. General and systemic examinations were unremarkable with a normal body mass index (BMI) of 22. Her secondary sexual characters were well developed. Speculum examination revealed copious foul-smelling mucopurulent discharge with an anterolateral bulge on the right side of the vagina. The cervix could not be visualized. On bimanual examination, soft, fluctuant, nontender longitudinal swelling of about 5 × 3 cm was felt on the right anterolateral aspect of the vagina, starting just above the introitus and extending up to the fornix. The discharge was increased on pressing the swelling which raised the suspicion of a small fistula but none was visualized. The cervix felt high up and the uterus was anteverted, bulky, and broad at the fundus with a depression at the middle, firm, nontender, and mobile. Bilateral fornices were nontender. Culture of the mucopurulent discharge showed growth of *Klebsiella pneumoniae*. Ultrasonography raised the possibility of either bicornuate or septate uterus and revealed a hypoechoic collection posterior to the cervix with an absent right kidney. The patient was advised a magnetic resonance imaging (MRI) from an outside facility which

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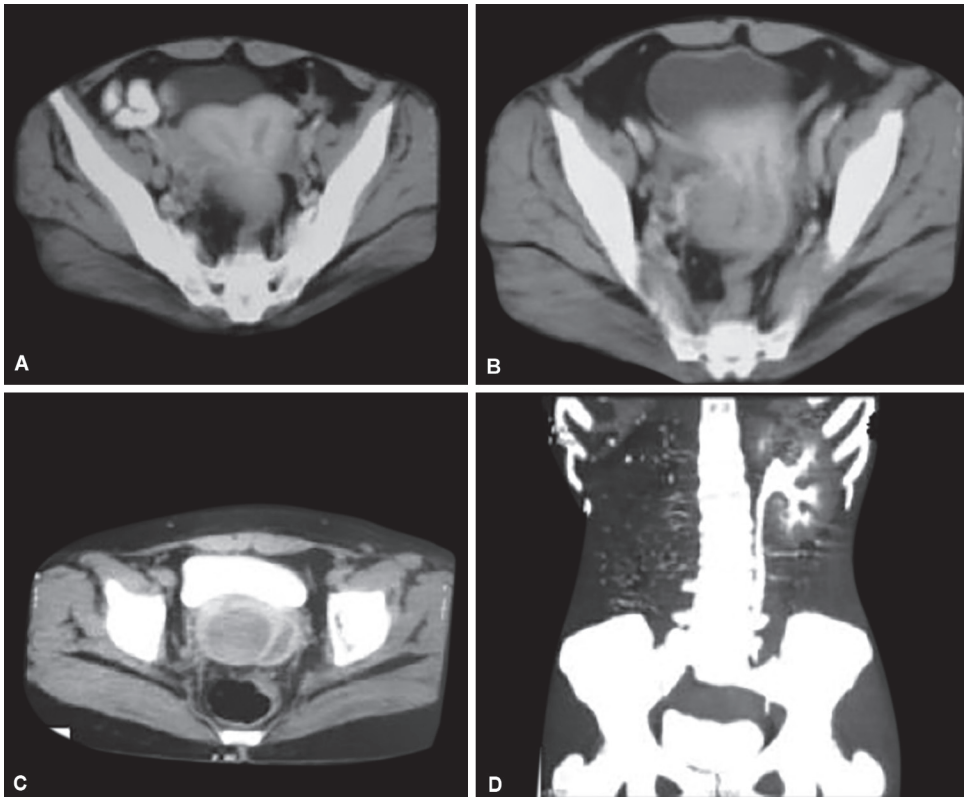



**Figs 1A to D:** (A) and (B) Contrast-enhanced axial CT image of pelvis shows two separate uterine cavities suggestive of didelphic uterus (C) Inferior section of the pelvis showing two vaginal cavities separated by a longitudinal septum with distended right hemivagina suggestive of right hematocolpos (D)-Coronal reconstructed image of CT abdomen with absent right kidney

she refused and got a contrast-enhanced computed tomography scan of the pelvis and lower abdomen which was readily available at our institute. The computed tomography (CT) scan findings revealed two well-defined endometrial cavities along with two hemivaginae, a hypodense collection of 35 x 40 mm present in the right hemivagina with distal obstruction and absent right-sided kidney with compensatory hypertrophy on the left side (Fig. 1).

In view of the above findings, diagnosis of uterus didelphys with **o**bstructed right **h**emivagina with **i**psilateral **r**enal **a**genesis, i.e., **OHVIRA** syndrome was made, and as per the American Society of Reproductive Medicine (ASRM) she was placed under **class III**,[8] as per the European Society of Human Reproduction and Embryology (ESHRE) classification under class **U3b C2 V2**[9] (complete bicorporeal uterus, double "normal" cervix, longitudinal obstructing vaginal septum) and based on the type of obstruction—whether complete or partial, under **class 2.1**[10] (partial resorption of the vaginal septum and communication between two vaginae).

The patient was counseled and underwent a vaginal septal resection with concomitant laparoscopy which revealed no evidence of adhesions, pelvic inflammatory disease (PID), or endometriosis. Postoperatively, there were no complications. She conceived twice within 1 year of surgery; the first pregnancy was a missed abortion and managed medically; the second one was successful with a full-term delivery via cesarean section.

### Case 2

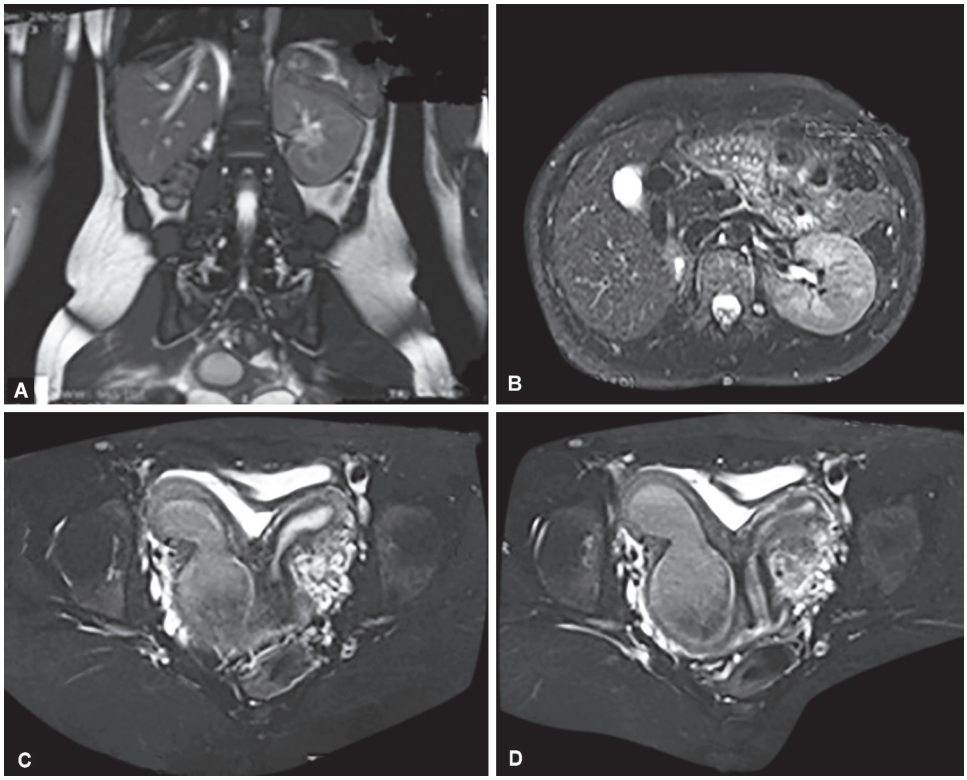
A 14-year-old girl, who attained menarche 1 year back, presented with cyclical abdominal pain and dysmenorrhea for 5 months. Her menstrual cycles were regular. On examination, the general condition was fair, BMI was 21.5, and secondary sexual characters were developed as per the age. On abdominal examination, a tender abdominal lump was palpable just above the pubic symphysis and the external genitalia were normal. Ultrasound showed a large collection behind the bladder with an unclear uterine morphology. MRI findings revealed uterus didelphys, a right-sided hemivaginal obstruction with blood collection, and an absent right-sided kidney (Fig. 2).

Based on the clinical and the imaging findings, a diagnosis of OHVIRA syndrome was made and as per ASRM she was placed under **class III**,[8] as per the ESHRE classification under class **U3b C2 V2,**[9] and based on the type of obstruction under **class 1.1**[10] (blind hemivagina).

Parents were counseled and the patient was planned for an examination under anesthesia (EUA) followed by definitive treatment in the same sitting. EUA confirmed the findings and the vaginal septum was resected. There were no complications in the postoperative period and on follow-up.

## Discussion

Müllerian duct anomalies are the developmental anomalies, resulting from defective development, defective fusion, or defective regression of the septum. Diagnosis of complex malformations is usually delayed, as due to their rarity they are not thought of or considered the cause of women's persistent or recurrent symptoms. OHVIRA syndrome is the result of an embryological arrest of the müllerian and mesonephric ducts at 8 weeks of gestation. The exact etiology of such malformation is unknown; however, genetic, environmental, and endocrine factors may have a role to play.




**Figs 2A to D:** Coronal MR image (A) and axial image (B) showing absent right kidney (C) and (D)-axial view showing two distinct uterine cavities; right-sided uterine cavity and right hemivagina are distended with mixed intensity fluid likely to be blood component suggestive of right hematocolpometra

Wingless integrated (Wnt) genes have been implicated in müllerian duct development but its role in this syndrome is unknown.[11]

The **classical theory** of development of female reproductive organs explains the development of the uterus, fallopian tubes, and the upper one-third of the vagina from the müllerian/paramesonephric duct, and the lower two-thirds of the vagina from the urogenital sinus. According to this theory, however, the complex uterovaginal malformations associated with renal malformation are not explained completely.[12]

In 1992, Pedro Acien proposed a new embryological hypothesis that the vagina is an organ embryologically derived from the mesonephric or Wolffian ducts, mainly with the müllerian tubercle contributing to the vaginal epithelium only. The mesonephric ducts play an inducing role in the development of paramesonephric ducts (müllerian ducts), which fuse to form the uterus including the external cervical os. The caudal portion of the mesonephric ducts enlarges to form the sinovaginal bulbs at the level of cervical os which later fuse to form the vaginal plate. From the mesonephric duct opening in the urogenital sinus, the ureteric bud arises. So, in case of distal agenesis of a mesonephric duct, there will be agenesis of the ureteral bud on that side, hence ipsilateral renal agenesis, and due to its inducing function there will be associated uterine malformations.[13–15] A congenital solitary kidney may undergo compensatory hypertrophy without any functional loss.[16]

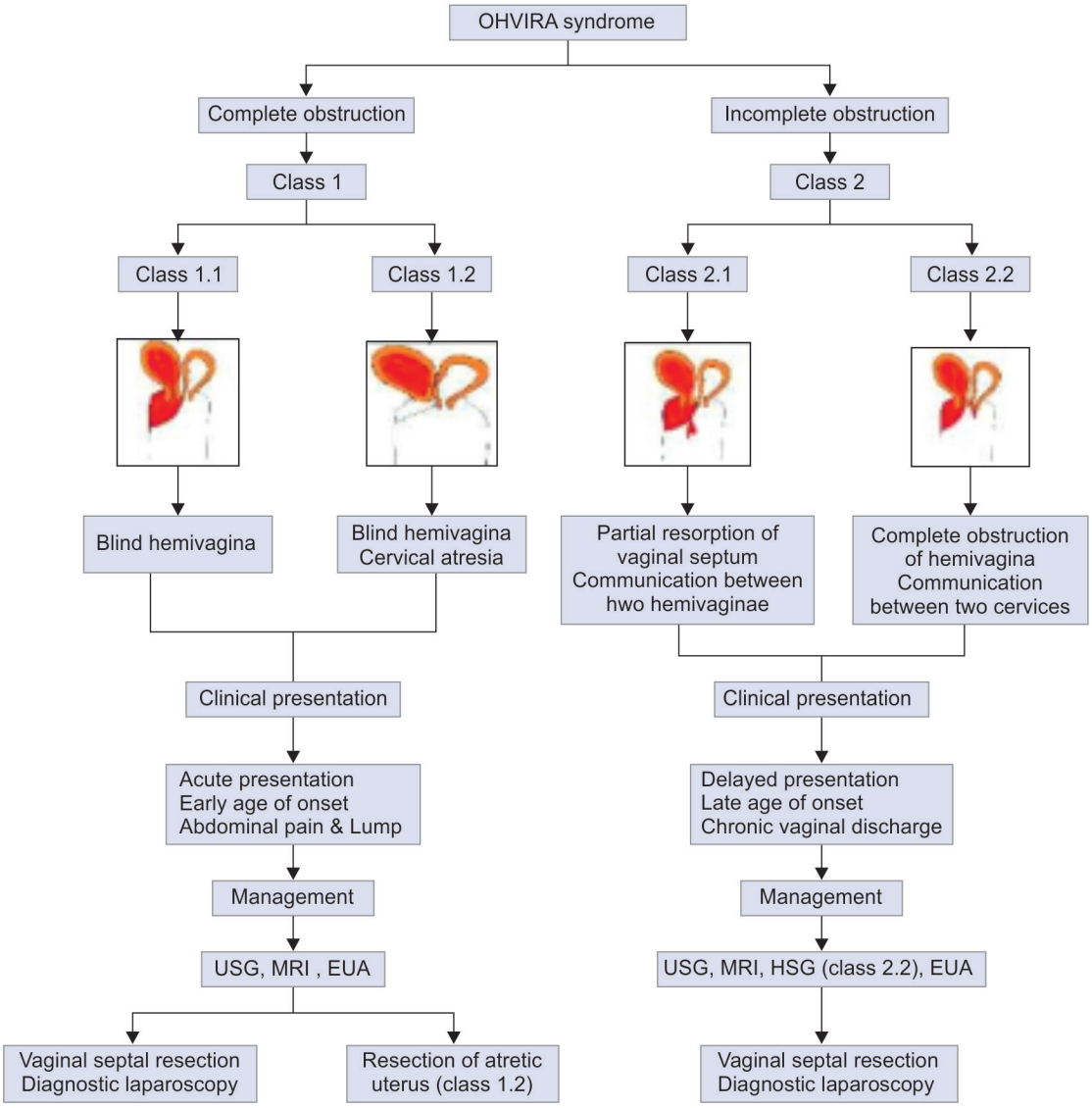
OHVIRA syndrome in the literature has shown varied predilection related to the sides involved—some claiming right-sided abnormality being more common, some left sided, while others claimed equal prevalence on both sides.[17–19]

Taking into consideration the different classification systems of müllerian anomalies, OHVIRA syndrome is classified under class **III** as per the ASRM classification[8] and under class **U3b C2 V2** as per the ESHRE classification.[9] At times, obstructed hemivagina and ipsilateral renal agenesis may be associated with a bicornuate or septate uterus (class U2b as per ESHRE/class IVa or Va as per ASRM); constituting OHVIRA variants. Based on a retrospective study including 70 patients by Zhu et al., OHVIRA syndrome is classified into two classes depending on whether the obstruction of the hemivagina is complete or incomplete (Flowchart 1).[10]

In a completely obstructed hemivagina, i.e., class 1, with the onset of menarche, there is a progressive collection of blood in the vagina, uterus, and fallopian tubes. If the obstruction is still not relieved, reflux of menstrual blood in the peritoneal cavity causes endometriosis, pelvic adhesions, and pelvic infections, leading to infertility. In patients with class 1, HWWS presents early after menarche with abdominal pain, abdominal lump, fever, peritonitis, and urinary tract obstruction. In patients with incomplete obstruction, i.e., class 2, it usually presents late with recurrent and persistent purulent vaginal discharge or PID. Diagnosis is delayed due to the occurrence of normal menstrual flow from the patent hemivagina. Sometimes, muco or hydrocolpos has been reported in infants[20] and rarely vaginal clear cell carcinoma and cervical adenocarcinoma of the obstructed side have been reported.[21]

Diagnosis of OHVIRA syndrome requires a multimodal approach, which includes a detailed history, meticulous examination, and appropriate imaging studies. American Academy of Pediatrics recommends routine examination of the genitalia and EUA (if needed) in adolescents in case of genitourinary symptoms.[22,23] Ultrasound and MRI are the established imaging modalities for diagnosing this condition with the ultrasound being the first-line option. A 3D ultrasound has 93% sensitivity and 100% specificity

**Flowchart 1:** OHVIRA syndrome classification, clinical features and management[10] (USG, ultrasonography; MRI, magnetic resonance imaging; EUA, examination under anesthesia; HSG, hysterosalpingograph)




in the assessment of müllerian duct anomalies, hence a good alternative to MRI. However, expertise is required to diagnose the condition as the problem arises due to the small size of the uterus, nonreactive endometrium, and distended vagina in prepubertal and pubertal girls.[24] MRI is the gold standard investigation available to confirm the diagnosis, providing detailed information of both internal and external uterine anatomy, and to diagnose associated extragenital anomalies. It has 100% accuracy in detecting müllerian duct anomalies.[25]

Uterus didelphys accounts for 5% of all cases of müllerian anomalies and once diagnosed by imaging, it should be a dictum to look for the vaginal septum, as 75% of them are associated with a longitudinal vaginal septum.[26] Also, it is advisable that whenever fetal renal anomalies are diagnosed on the antenatal scan look for obstructed müllerian anomalies in order to detect and treat them at the earliest.[20] Hysterosalpingogram was used in the past quite often but now its role is limited to class 2.2 only to confirm communication between the two cervices. Laparoscopy can help in confirming the diagnosis, detection, and treatment of the associated complications and was considered to be the gold standard in the management of OHVIRA syndrome but due to the availability of better imaging facilities—3D ultrasound and MRI, it is no longer necessary in every case.

Obstructed anomalies, if not treated timely and adequately, may lead to chronic complications and negative psychological impact, thereby impairing a woman's quality of life. Awareness, familiarity, and a high index of suspicion would aid in early diagnosis and timely relief of obstruction with preservation of reproductive potential. Though OHVIRA syndrome is a complex and rare anomaly, its treatment, however, is relatively simple, comprising either resection or excision of the vaginal septum. Only in class 1.2 (cervicovaginal atresia with complete obstruction) would ipsilateral hysterectomy, either abdominal or laparoscopic, be required as in these cases apart from an obstructing vaginal septum, there is obstruction at another higher level, i.e., cervix.[10] For those who refuse partial hysterectomy, the option of uterovaginal canalization but adequate counseling regarding restenosis of the neocervix and future complication is must.[27]

Conventionally, surgical resection of the vaginal septum is done under direct vision. Catheterizing the bladder before starting the procedure helps define the anatomy and avoid accidental injury to the urethra and bladder. Aspiration of accumulated contents in the obstructed hemivagina aids in placing the initial incision. The extent of the obstruction can be demarcated by palpation and the whole septum is resected. The use of electrocautery is convenient and reduces blood loss. Vicryl 2-0 can be used for suturing. Laser is also an option. This conventional approach may cause hymenal rupture and sometimes vaginal tears in adolescents, which leads to postoperative pain and adhesion formation. To overcome these issues, minimally invasive "vaginoscopic no-touch technique" with excellent visualization has been introduced for a longitudinal vaginal septum resection. Using a hysteroscopic L-hook electrode, the vaginal septum is incised followed by placement of a 14/16 Fr Foley's catheter, inflated with 50–80 mL saline in the previously obstructed hemivagina. This technique entails a good surgical outcome.[28]

Because of the associated risk of ascending infection, simple incision and drainage of the obstructed hemivagina are not recommended. Medical management with continuous oral contraceptive pills or medroxyprogesterone can be advised to suppress menstruation until definitive surgery is planned.[29,30] Postoperatively, antibiotics, analgesics, and progestin tablets for menstrual suppression are prescribed. Those who are at high risk for stricture or adhesion formation need bed rest, vaginal molds, indwelling catheter, and deep vein thrombosis prophylaxis. Psychological counseling with respect to the diagnosis, classification of anomaly, consequences, management options, and timing of the surgery is important and should not be underestimated because of the association of this syndrome with the sexual, reproductive, and social stigma.[29]

Differential diagnosis of other causes of outflow tract obstruction should be kept in mind, which includes imperforate hymen, transverse vaginal septum, longitudinal vaginal septum, and cervical atresia. Except imperforate hymen, surgical management in others is complex, demanding expertise.

Follow-up is essential in view of associated risk of adhesions, stenosis, and endometriosis. The patient may complain of mucus discharge as the vaginal epithelium on the side of obstruction is columnar and has not undergone squamous metaplasia, requiring appropriate counseling. Cervical screening by Papanicolaou's smear is recommended separately for each cervix.

In timely and adequately treated patients with OHVIRA syndrome, reproductive performance is consistent with that of a didelphic uterus. Pregnancy rate in obstructed müllerian anomalies varies from 37–40%.[31] In a study of 49 women with didelphic uterus and longitudinal vaginal septum, pregnancy has been reported in up to 94% of cases with 21% resulting in abortion; 24% preterm labor; cesarean section rate, however, was 84%. In this series, 16.3% of patients were having OHVIRA syndrome. Hence, early diagnosis and treatment entail a good reproductive outcome of this rare syndrome.[32] Patients with OHVIRA syndrome are reported to have hypertensive disorders in pregnancy twice as compared to those with isolated uterine anomalies.[33]

## Conclusion

Vaginal discharge, one of the most common gynecological complaints, if persistent and resistant to treatment, can be the manifestation of a rare congenital anomaly—OHVIRA, which should always be ruled out as if left untreated there are serious consequences on the reproductive and mental health. Timely surgical intervention and psychological counseling are of utmost importance. There is a need to sensitize the gynecologist, pediatrician, and radiologist to this rare entity.

## Clinical Significance

Timely diagnosis and treatment of this rare anomaly will help in improving the reproductive outcome and quality of life of the patient.

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