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## Wolffian Origin of Vagina Unfolds the Embryopathogenesis of OHVIRA (Obstructed Hemivagina and Ipsilateral Renal Anomaly) Syndrome and Places OHVIRA as a Female Counterpart of Zinner Syndrome in Males

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### Summary

**Background:**

The classical theory of Müllerian origin of upper vagina fails to explain complex urogenital malformations like OHVIRA syndrome; the Acien's hypothesis, however, unravels the hidden embryopathogenesis. As per Acien, Wolffian (mesonephric) ducts instead of Müllerian ducts and sinovaginal bulbs, give rise to the vagina. The new hypothesis, however, retains the concept of origin of the ureters (with ureters inducing renal development) by the former and the uterus by Müllerian ducts. Thus, a failure of development of mesonephros/mesonephric duct gives rise to absent ureters and hence absent homolateral kidney; blind ending (obstructed) ipsilateral hemivagina and cessation of support to paramesonephric ducts which leads to unfused uterus (uterus didelphys). Hence, the new hypothesis explains all components of OHVIRA syndrome. On a parallel track, unilateral anomalous development of the mesonephros in males causes atresia of the homolateral ejaculatory duct that results in obstruction of the proximally placed seminal vesicle. Besides, there is absence of the ipsilateral kidney (Zinner syndrome).

**Case Report:**

In this manuscript, we describe four cases of OHVIRA syndrome. Case 1 was a 34-year-old nulligravida, married since fourteen years, who presented with a 5-month history of pelvic inflammatory disease and dyspareunia. Regular menses in the patient and azoospermia in her husband delayed the diagnosis. Case 2 was a 14-year-old girl who presented with dysmenorrhea and lower abdominal pain since a few months. Case 3 was a 27-year-old female who presented with infertility and dysmenorrhea. Case 4 was a 15-year-old female who presented with a one-year history of dysmenorrhea and cyclic pelvic pain. In all cases, one of the uterine horns revealed collection due to a hemivaginal septum and an absent ipsilateral kidney; thus, establishing the diagnosis of OHVIRA syndrome. The case 4 additionally revealed homolateral vaginal agenesis.

**Conclusions:**

On the basis of our 4 cases, we support the Acien's hypothesis of Wolffian origin of vagina which explains the development of OHVIRA syndrome. Besides, we emphasize the need to suspect this syndrome in a female with a pelvic mass and absence of homolateral kidney. Finally, we believe that OHVIRA due to its Wolffian origin is a female equivalent of Zinner syndrome in males. Therefore, we propose **OSVIRA (Obstructed Seminal Vesicle and Ipsilateral Renal Agenesis)** as an acronym for Zinner syndrome analogous to OHVIRA.

**MeSH Keywords:**

Dysmenorrhea • Hematocolpos • Infertility • Mullerian Ducts • Wolffian Ducts

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<http://www.polradiol.com/abstract/index/idArt/898244>

## Background

Müllerian (paramesonephric) duct (MD) anomalies have an incidence of 2 to 3% [1]. The ducts originate as invagination of the coelomic epithelium lateral to the mesonephros. Under the influence of the mesonephros, the ducts develop and position themselves anteriorly across it (mesonephros) to lie more medial to it in caudal direction [2]. These medially-located ducts then fuse to give rise to the uterus and upper vagina. Müllerian origin of the upper vagina is, however, debatable [3]. While the classical concept postulates so, complex urogenital anomalies like OHVIRA syndrome challenge the notion. Acien put forth Wolffian (mesonephric) nature of the vagina in the entire length [3,4]. This new hypothesis explains the absence of the ureter (and renal agenesis), blind ipsilateral hemivagina and a uterus didelphys as a result of developmental arrest in the homolateral Wolffian duct (WD) and mesonephros [3]. In this manuscript we describe four cases of OHVIRA syndrome and postulate it to be a female equivalent of Zinner syndrome in males.

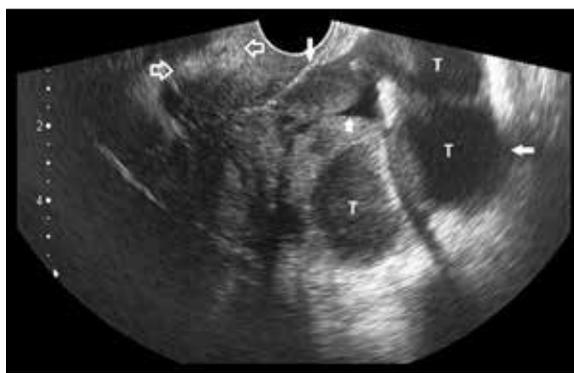
## Case Report

### Case 1

A 34-year-old female, nulligravida, married since fourteen years, presented with a 5-month history of pelvic pain and dyspareunia. There was no history of intermenstrual bleeding, per-vaginal discharge or high-risk behaviour. There was no history of major medical or surgical illness. Menstruation was regular and relatively painless until five months ago. Significant past history included infertility work-up that included pelvic ultrasonography and hormonal profile that showed two unfused uterine cornua and a normal hormonal profile.

The husband had no history of addiction and did not have inguinal hernia, hydrocele or varicocele. The semen analysis revealed azoospermia; however, fructose was present in the semen. His testicular sonogram was normal. The couple was counselled and the husband was advised testicular biopsy. The couple, however, was lost to follow-up.

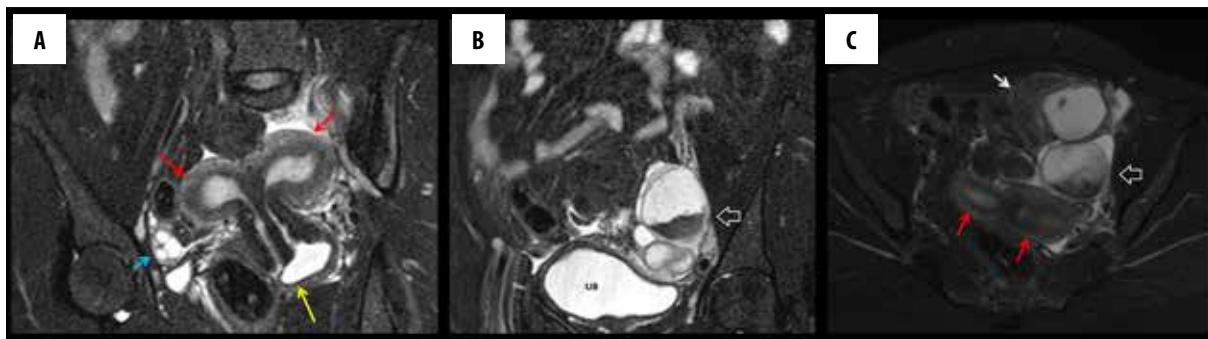
On current admission, the patient was febrile. Remainder of the general examination was normal. Palpation revealed tenderness in the suprapubic region more pronounced on the left side. On per vaginal examination, a cystic mass was felt in the left fornix. The patient underwent CT at a private centre which showed a cystic lesion, reniform in configuration, in the left pelvis (Figure 1A). There was adjacent inflammation (Figure 1A) and the left kidney was not seen in left renal fossa. Also, the two uterine horns were unfused (Figure 1B) with a focal collection on the left side (Figure 1B). The condition was thought of as pyelonephritis in the pelvic (ectopic)



**Figure 2.** PATIENT 1: Endovaginal scan depicts dilated, tortuous left fallopian tube (solid arrows) with echogenic fluid (T) within (Small block arrow – pelvic free fluid; open arrows – two separate endometrial echoes).



**Figure 1.** PATIENT 1: (A) CECT sagittal reformation reveals a reniform cystic lesion (open arrow) in the pelvis with adjacent fat stranding (arrow); (B) Coronal reconstruction shows divergent uterine cornua (red arrows) with focal collection on the left side (yellow arrow). Also noted is the absence of the left kidney (UB – urinary bladder).



**Figure 3.** PATIENT 1: (A) Pelvic MRI in oblique coronal plane demonstrates uterus didelphys with blind left hemivagina (yellow arrow). The blue arrow represents normal right ovary. The left ovary is not seen separately; instead a cystic lesion with fluid–fluid level is seen (open arrows in B and C). The white arrow in C points towards fat stranding (UB – urinary bladder; red arrows – two separate endometrial cavities).



**Figure 4.** PATIENT 2: Serial axial T2 images reveal two unfused uterine cornua (red arrows) with dilated right horn (Blue arrows – normal ovaries; H – hematocolpos; UB – urinary bladder).

kidney on the left side with marked hydronephrosis and was referred to our centre. An ultrasound at our centre demonstrated the same uterine morphology. However, the cystic reniform structure appeared to be dilated and tortuous left fallopian tube, full of fluid with internal echoes (Figure 2). Minimal free fluid was noted in the pouch of Douglas as well. Remainder of the abdomen and pelvic ultrasound examination was normal, except for an absent left kidney. MRI was performed to clearly show the uterine morphology and the status of the tubes. It revealed two separate uterine cavities, two cervixes and two hemivaginae (didelphic uterus). There was presence of retained collection in the left hemivagina limited by a septum (Figure 3A). Also, a cystic lesion with fluid–fluid level with adjacent inflammation was noted. The left ovary was not visualised separately from this cystic lesion (Figure 3B, 3C). The right ovary was, however, of normal morphology. Thus, a diagnosis of OHVIRA syndrome with endometriotic cyst was established. The hemivaginal septum was resected and the patient is on treatment for endometrioma. At two-month follow-up the patient is symptomatically better. Meanwhile, the couple was counselled for adoption and have adopted two baby girls.

#### Case 2

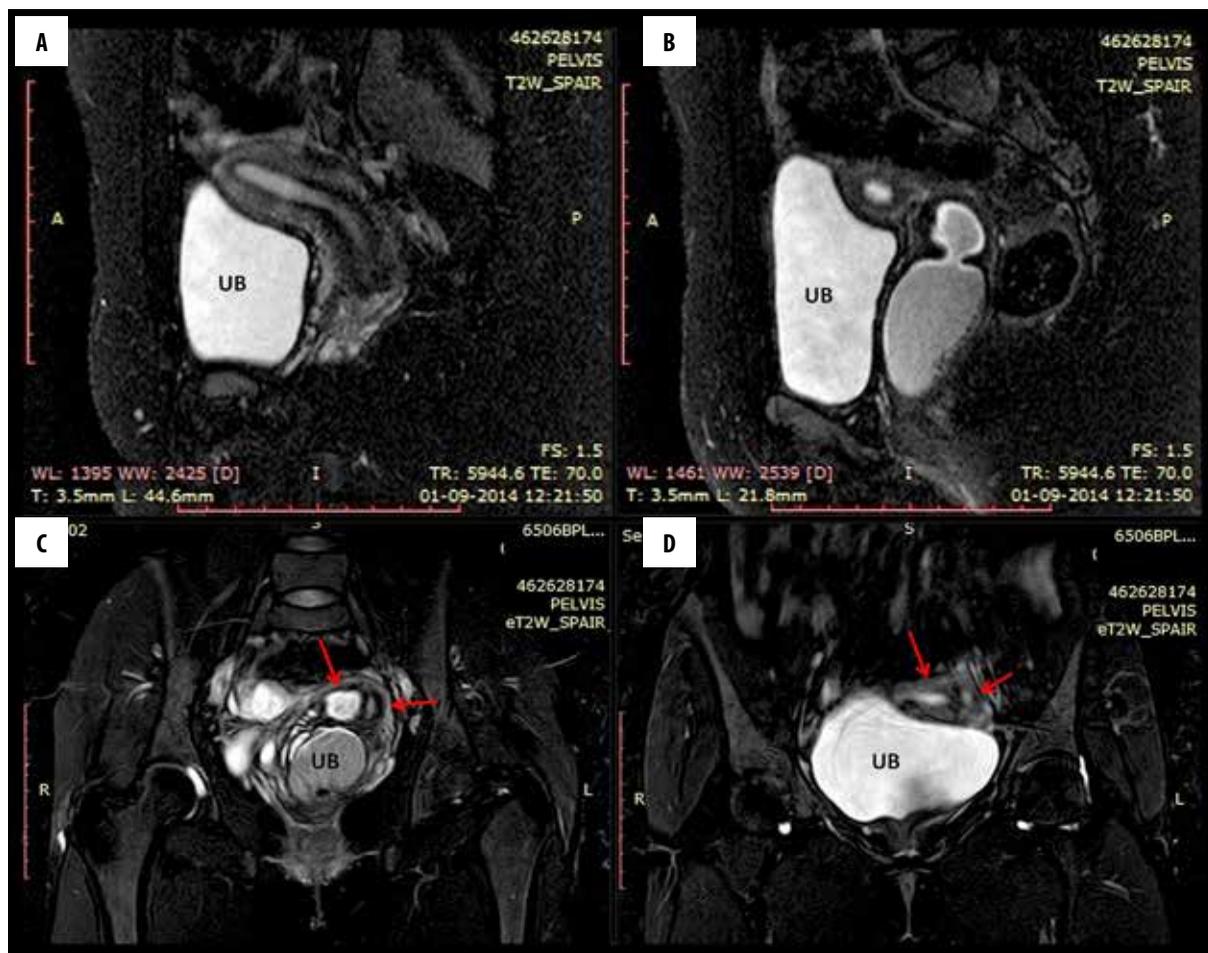
A 14-year-old girl was referred to our services for dysmenorrhea and lower abdominal pain since a few months. The pain was cyclical and appeared during menstruation to begin with; presently, however, it persisted irrespective of menstruation. The patient had attained menarche 2 years ago with regular menstruation.

The general examination was normal. Pelvic examination revealed tenderness and a soft lump on the right side. On ultrasonography, the uterus had two separate cornua. The

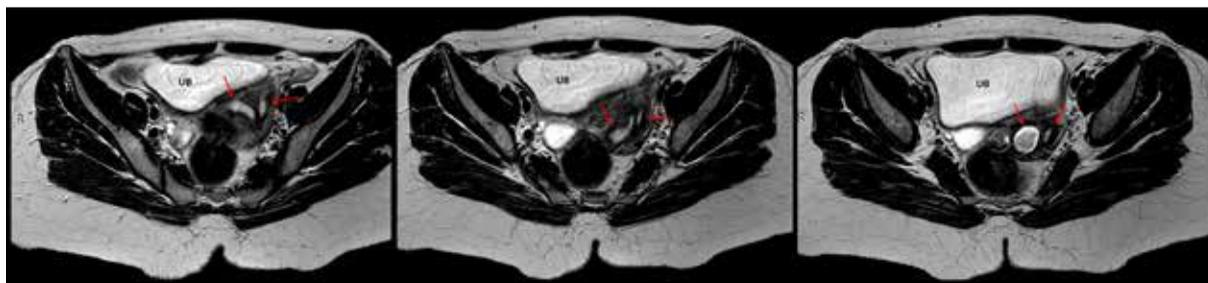


**Figure 5.** PATIENT 2: Coronal T1WI of the abdomen and pelvis shows hematocolpos (H) of the right horn with an absent ipsilateral kidney. The white arrow points towards contralateral normal kidney.

right uterine cavity was dilated and full of fluid with echoes. Besides, the ipsilateral kidney was absent. The left kidney was, however, normal. MRI examination revealed a dilated uterine horn on right (Figure 4) with an absent



**Figure 6.** PATIENT 3: Sagittal T2 SPAIR images reveal normal left uterine cavity (A) and hematometocolpos on the right (B). On coronal images (C, D), two uterine horns (red arrows) are seen separately with a dilated right horn (UB – urinary bladder).



**Figure 7.** PATIENT 3: Serial axial T2WI depict two widely-separated uterine cavities (red arrows) with a dilated right one.

ipsilateral kidney (Figure 5). Thus, a diagnosis of OHVIRA syndrome was established and the uterine contents were drained via resection of the hemivaginal septum. She was discharged on day 7 of surgery and is on follow-up.

### Case 3

A 27-year-old female married since 2 years presented with inability to conceive. The couple had been staying together and coital frequency was 2 to 3 times per week with normal arousal and orgasm. Besides, the patient also complained of dull aching pain in the lower abdomen since a few months. The pain was continuous in nature, aggravated during menstruation and was partly relieved by analgesics.

The infertility work-up of the couple showed normal serum hormone profile of the patient and a normal semen analysis of the husband. However, sonogram of the patient revealed two unfused uterine cornua with collection within the right endometrial cavity. Further, the right kidney was neither seen in the right renal fossa nor elsewhere in the abdomen or pelvis. An MRI was performed which showed a didelphic uterus with hematometocolpos in the right endometrial cavity (Figures 6–8), thus, establishing a diagnosis of OHVIRA syndrome. The patient underwent drainage of the uterine contents leading to a gradual relief of pain in the following months. Three months later, the patient conceived.



**Figure 8. PATIENT 3:** Coronal T1WI shows an absent right kidney. The green arrow depicts a bowel loop occupying the empty right renal fossa (L – liver; S – spine).

**Case 4**

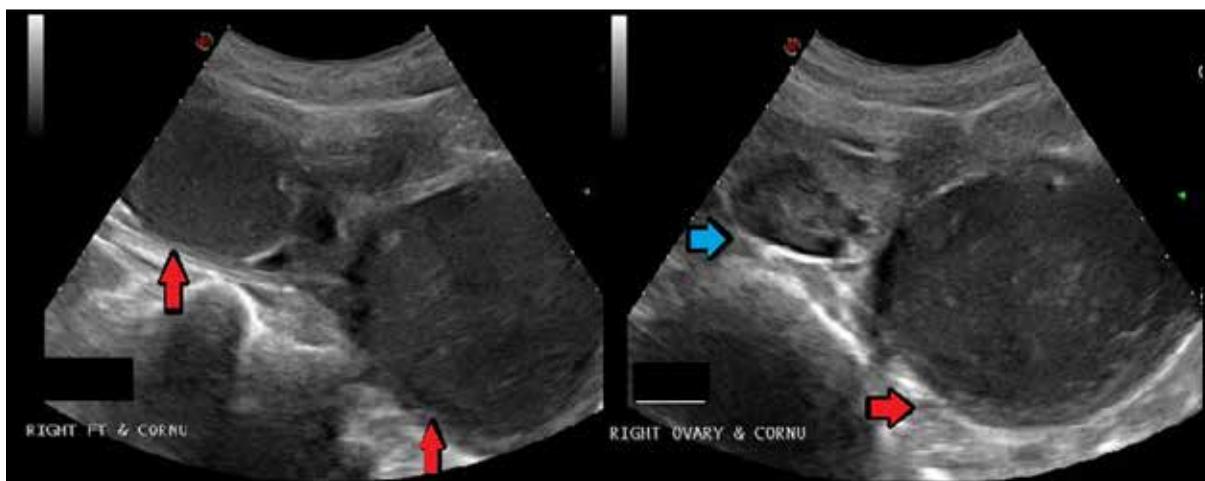
A 15-year-old female presented with complaints of dysmenorrhea and cyclic pelvic pain since a year. She had normal menarche and regular menstrual cycles before this episode. On physical examination, there was tenderness in the right lower quadrant. Ultrasound showed two widely separated uterine horns, a non-obstructed normal-appearing left uterus and cervix and hematometra/hematosalpinx on the right side (Figure 9). These findings were confirmed on MRI (Figure 10). Further, the non-obstructed normal left uterus and cervix was seen to communicate with the vagina. The hematometra and hematosalpinx in the obstructed right uterus and did not show any communication with vaginal cavity suggestive of vaginal agenesis. Additional imaging of urinary system showed right renal agenesis (Figures 10, 11). Thus, a diagnosis of variant of OHVIRA with ipsilateral vaginal agenesis was established which was later confirmed on surgery. The patient

is asymptomatic after drainage of the hematometra and hematosalpinx.

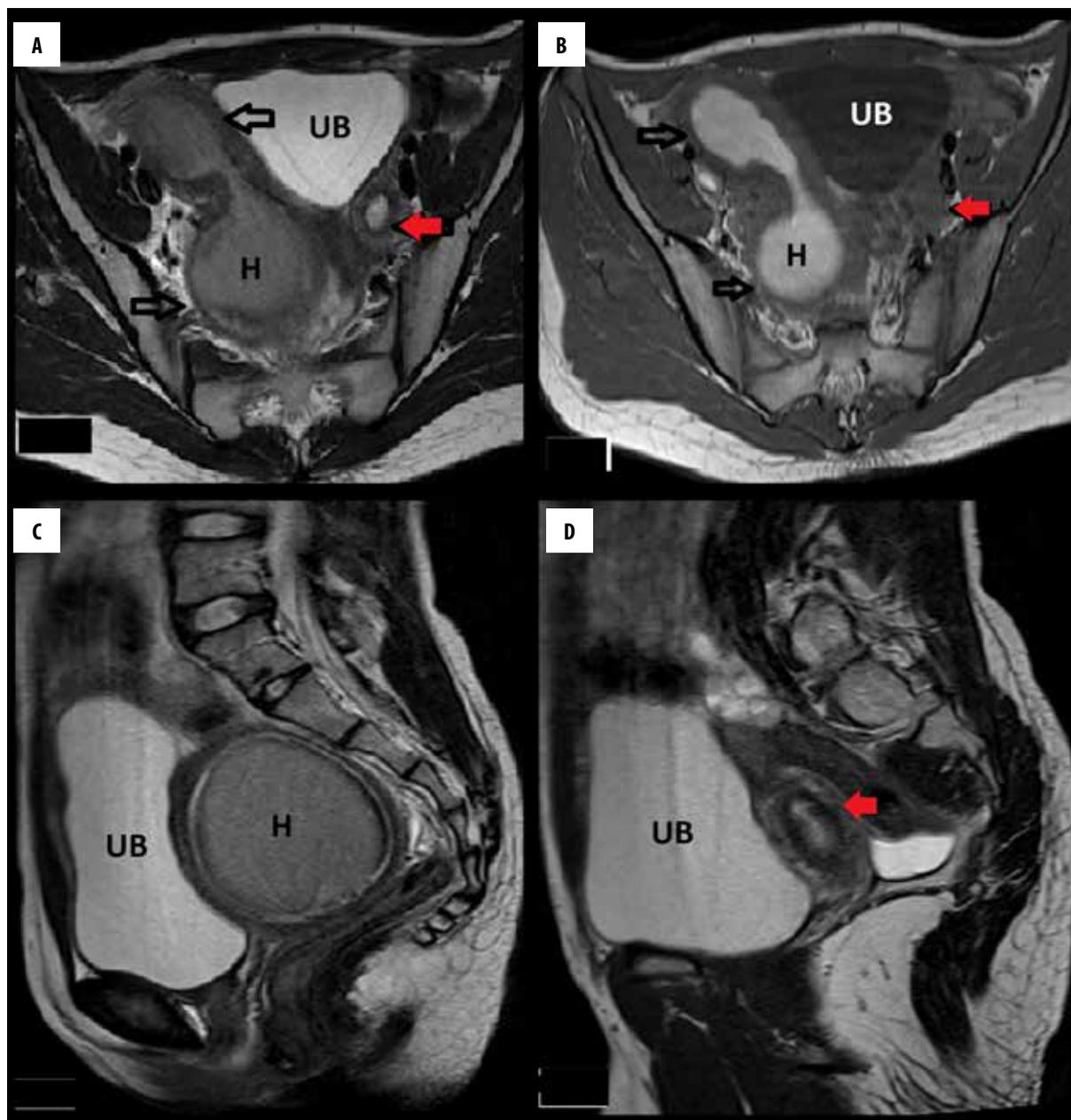
**Discussion**

Herlyn-Werner-Wunderlich is a complex urogenital malformation that comprises of an obstructed hemivagina in a didelphic uterus with homolateral renal agenesis/anomaly [1, 5]. The uterus, however, may be single with two cervixes or may be septated. Hence, the term OHVIRA – obstructed hemivagina, ipsilateral renal agenesis/anomaly (dysplasia, duplication or crossed fused ectopia) with a uterine anomaly better describes the clinical entity [6].

Central to the understanding of OHVIRA syndrome (OS) is a review of embryological development of the urogenital system. Five weeks into embryogenesis, the WD (mesonephric duct) outpouches to form a metanephric diverticulum on each side [2]. The diverticulum soon matures into a ureteric bud that induces metanephric blastema to form a kidney. Beginning in the seventh week, MDs (paramesonephric ducts) originate lateral to the mesonephros and in caudad direction cross the mesonephros anteriorly to lie medially to it [2]. The development, proper positioning and subsequent fusion of these ducts is entirely dependent on factors liberated by the mesonephros [3]. Consequent to the fusion of MD and resorption of the median septum, a normal uterus forms. Traditionally, while the upper vagina is postulated to be a derivative of MDs with the remainder originating from the sinovaginal bulb of urogenital sinus origin, presence of complex malformations like OS challenge this classical concept (Figure 12). The embryogenesis of OS can fully be accounted for on the basis of Acien’s hypothesis [3]. Unlike the classical theory, the vagina is thought to be derived from WDs in entirety (Figure 13). The lining epithelium of the vagina, however, arises from the Müllerian tubercle, a collection of mesenchymal tissue at the junction of MDs and WDs. Thus, a developmental arrest in WD brings formation of both the ureteric bud (ureter and hence ipsilateral kidney) as well as homolateral hemivagina to a standstill. Further, the influence of the mesonephros on positioning and fusion of paramesonephric ducts ceases. Hence, the didelphic uterine morphology [3]. A similar



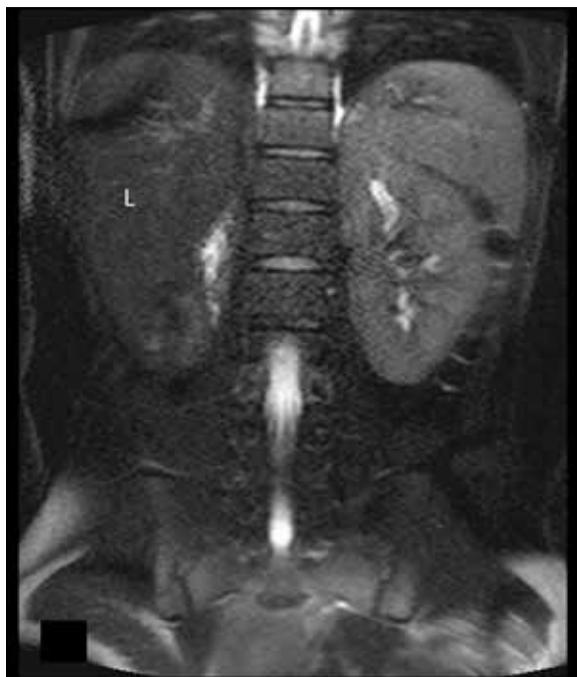
**Figure 9. PATIENT 4:** Ultrasonogram shows hematometra, hematosalpinx (red arrows) in the right uterine cornua and a normal right ovary (blue arrow).



**Figure 10.** PATIENT 4: Axial T2W (A) and T1W (B) images show widely divergent uterine horns, non-obstructed normal left uterine horn (red arrow), hematometra and hematosalpinx (black arrows) in the obstructed right uterus (H – hematometra; UB – urinary bladder). T2WI in sagittal plane (C, D) reveal similar findings.

sequence of events of halted development of the mesonephros in males presents as atresia of the unilateral ejaculatory duct that leads to obstruction and consequent cystic dilation of the seminal vesicle and ipsilateral renal agenesis (Zinner syndrome) [6]. Thus, on this account we believe that Zinner syndrome is a male counterpart of OHVIRA syndrome in males and not of Mayer-Rokitansky-Kustner-Hauser (MRKH) syndrome as previously thought. While Zinner syndrome arises due to faulty development of the mesonephros, Mayer-Rokitansky-Kustner-Hauser (MRKH) syndrome is a Mullerian anomaly. Also, we would like to propose an acronym **OSVIRA for Zinner syndrome, like OHVIRA, which stands for Obstructed Seminal Vesicle and Ipsilateral Renal Agenesis.**

OS constitute a meagre of 0.1–3% of all MD anomalies. Patients are usually asymptomatic until after attainment of menarche when products of menstruation accumulate due to blind hemivagina [7]. The pain arising out of this cryptomenorrhea is cyclical to begin with but later becomes continuous. Persistence of blood products in the vaginal/uterine cavity/tubes provides a nidus for microbial growth [7,8]. Later, pyocolpos and/or tubo-ovarian mass may ensue [7,8]. The patient may also present with foul-smelling mucopurulent discharge and dyspareunia. Alternatively, uterine contractions divert and expel the contents in a retrograde manner causing endometrial implantation into the peritoneum (endometriosis) [9,10]. Further, a didelphic uterus may not support pregnancy [11], cause frequent abortions or preterm labour [12].



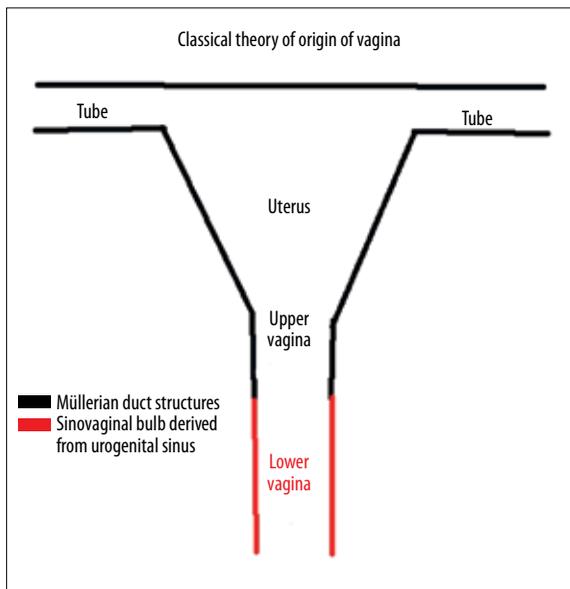
**Figure 11.** PATIENT 4: Coronal T2WI of the abdomen shows renal agenesis on the right side (L – liver).

Owing to the rarity of OS and nonspecific symptomatology (like acute urinary retention [11], calcified vaginal mass [12] or intrapartum rupture of the vagina [5] – all have been described in cases of OHVIRA), the diagnosis is often delayed. Besides, regular menstruation from the contralateral side and gradual extension of hematometrocolpos in the obstructed hemivagina further confound the diagnosis [1]. Imaging is quintessential for diagnosis and ultrasonography is the initial investigation. MRI supersedes as a modality on account of its multiplanar capabilities, wide field of view and excellent soft tissue resolution [1]. Also, MRI is informative about the presence of endometrioma, pelvic inflammation and presence of adhesions [1].

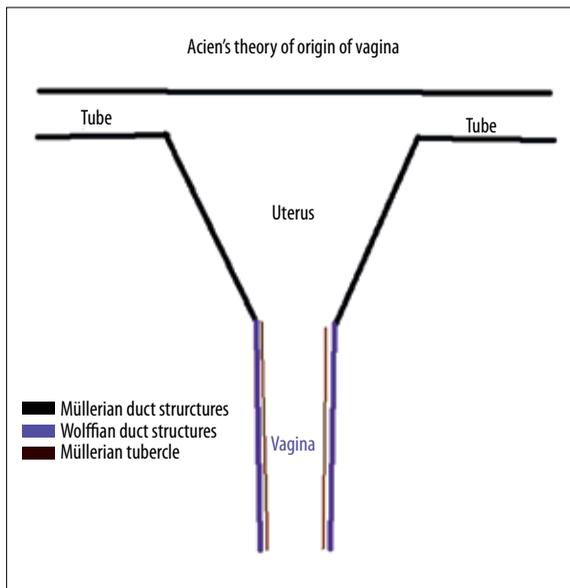
The treatment of OS is surgical excision of the hemivaginal septum with vaginoplasty [1]. Since the syndrome is most commonly encountered 1 to 2 years after menarche, preservation of integrity of the hymen can be achieved by hysteroscopic resection under transabdominal USG guidance [13]. Resection of the septum benefits by relieving obstruction and drainage of the previously accumulated products of menstruation [14]. Besides, the chances to conceive (post resection) increase (to as high as 87%) and parallel to that in uterus didelphys without renal agenesis. Also, the incidence of pregnancy has been reported to be equal in both uterine horns. Thus, previously employed hemihysterectomy is no longer recommended [14].

**Conclusions**

To conclude, OHVIRA syndrome should be suspected in a female with a pelvic mass and homolateral absent kidney. Knowledge of this syndrome is essential to arrive at



**Figure 12.** Schematic diagram of classical concept of vaginal development.



**Figure 13.** Line diagram of the Acién's hypothesis of embryogenesis of the vagina.

its diagnosis and timely treatment is the key to favourable outcome. Besides, in cases of uterine anomaly, kidneys should be assessed for possible malformations. Finally, on account of similar embryopathogenesis we believe that OHVIRA is a female equivalent of Zinner syndrome in males and thus Zinner syndrome may also be renamed as OSVIRA (Obstructed Seminal Vesicle and Ipsilateral Renal Agnesis).

**Final supports/conflicts of interest**

None.

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