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Case Report

OHVIRA Syndrome: From Prenatal to Puberty

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Abstract

A 13-year-old girl was diagnosed with OHVIRA syndrome (obstructed hemivagina and ipsilateral renal anomaly). In the antenatal period, a multicystic dysplasia of the ectopic pelvic right kidney was diagnosed. During puberty, she consulted for dysmenorrhea and the exams concluded to a didelphys uterus with obstructed hemivagina. The OHVIRA syndrome, also known as Herlyn-Werner-Wunderlich syndrome, is rare. Urinary and genital malformations are often associated because of their close relation during embryogenesis. The symptoms are unspecific. Depending on the subtype of the obstructed hemivagina, the symptoms and the age of onset can vary greatly, making the diagnosis challenging. However, it is vital to correctly diagnose this malformation and treat it to avoid complications such as pelvic inflammatory disease (PID), endometriosis, and infertility. The treatment consists of surgery: ideally a surgical resection of the vaginal septum in one step.

It is important to put in place a protocol to screen Mullerian anomalies when renal anomalies are diagnosed because of the high association between the two, and the risk of complication if left untreated.

Keywords: *OHVIRA Syndrome; Mullerian Duct Anomalies; Early Detection; Renal Anomalies*

Abbreviations

OHVIRA: Obstructed HemiVagina and Ipsilateral Renal Anomaly; PID: Pelvic Inflammatory Disease

Introduction

The OHVIRA syndrome is rare and defined as a combination of a uterus didelphys with a renal anomaly, the latter being either renal agenesis or dysplasia in the majority of cases [13] (Figure 1). This article aims to put forward the close relation between renal and genital malformations and to encourage the development of a protocol to combine gynaecological screening when renal malformations are diagnosed.

Case Report

A 13-year-old patient came to the emergency room complaining of abdominal pain.

Figure 1: *Schematic view of OHVIRA syndrome.*

Her medical history started antenatally. Her mother was monitored during pregnancy for an ectopic pelvic right kidney with multicystic dysplasia with mild cortico-medullary differentiation and suspicion of ureterocele (Figure 2). They also confirmed a unique umbilical artery. The left kidney was normal.

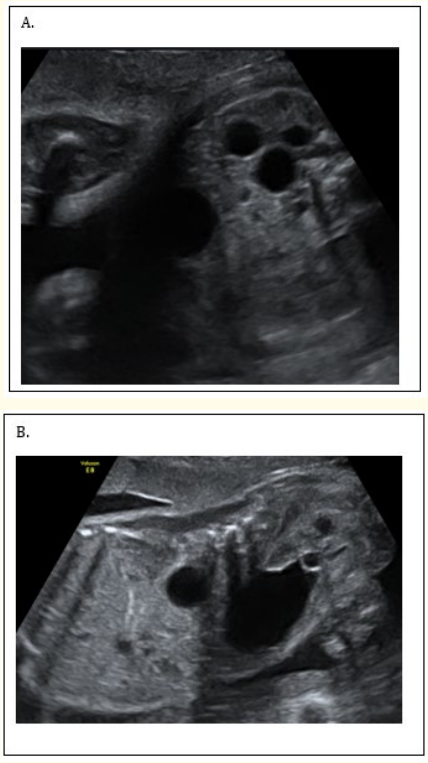

Figure 2: *Ultrasound of antenatal diagnosis.*

A: Ectopic kidney with multicystic dysplasia.

B: Suspicion of ureterocele.

The delivery went through without complications. A pediatric urologist monitored her closely and a blood test was performed at the maternity and showed a normal renal function. An ultrasound confirmed the multicystic dysplasia of the hypotrophic ectopic pelvic right kidney, but the ureterocele was not observed.

The cystography did not reveal vesicoureteral reflux and the scintigraphy showed the absence of function of the right kidney. Usually, the prognosis is excellent and there is a spontaneous disappearance of the kidney and compensatory hypertrophy on the contralateral side. The follow-up ultrasound at 9 months revealed a ureterocele with a dilatation of the retrovesical ureter. For that reason, she was put on prophylactic nitrofurantoin therapy. 3 months later, the ultrasound showed a dilatation of the ureterocele. Considering the risk of urinary infection, a right nephrectomy with aspiration of the ureterocele was undergone with no after-effect on the bladder. The contralateral kidney had undergone compensatory hypertrophy.

Her follow-up mainly consisted of consultations for abdominal pain since the age of 10 years old and the diagnosis of yellow nail syndrome. This rare syndrome, with a prevalence of 1/1000000, is characterised by two of the three following clinical manifestations: yellow nail, lymphedema and chronic lung manifestations or sinusitis [17].

Around 13 years old, a hydrocolpos without any repercussion on the uterus was observed during a kidney ultrasound. At this time, she was asymptomatic, and observation was decided.

One month later, she came to the emergency department for abdominal pain and pyrexia. She was on her period for the fourth time since her menarche. She had no other complaints other than lower abdominal pain and one fever episode.

Her physical examination revealed a normal vulva. Her vaginal examen revealed a turgid mass on the right anterolateral side of the vagina. The ultrasound showed a hematocolpos of 11 x 5 cm with two separate uterine horns (Figure 3A1). One was normal with a height of 6 cm and a normal endometrium. The other had a centimetric hematometra (Figure 3A2). There were no signs of superinfection and the pain decreased with painkillers.

At this stage, we diagnosed a Mullerian anomaly: a didelphys uterus with an obstructed hemivagina corresponding to a female genital tract anomaly classified U3bC2V2 according to the new ESHRE/ESGE classification system [6]. With her history of a renal anomaly, we concluded the diagnosis of the OHVIRA syndrome.

Considering her symptoms (pain and fever), we decided to intervene surgically two days later. Under general anaesthesia, we realized a more precise vaginal exam and a vaginoplasty consisting of incision in the vaginal septum to remove the obstruction and release the pain caused by the pressure of the hematocolpos.

The postoperative follow-up was unremarkable, and an MRI was performed a few months later (Figure 3B). This exam confirmed the diagnostic of U3bC2V1 uterine malformation corresponding to a didelphys uterus without residual hematocolpos. Ideally, another surgery should be performed to resect the vaginal septum.

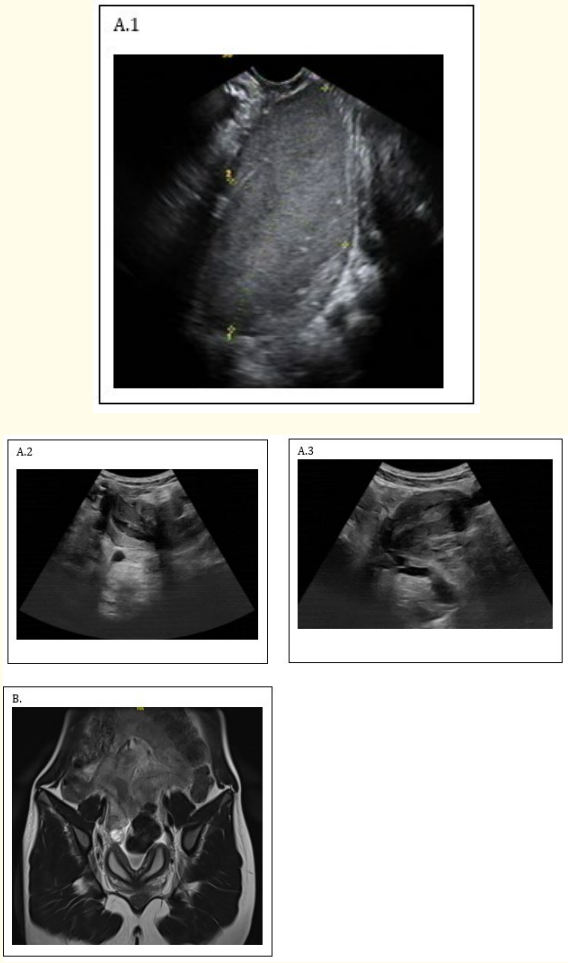

Figure 3: *Imagery of obstructed hemivagina and didelphys uterus. A: Ultrasound. A.1: Obstructed hemivagina. A.2: Right hemi-uterus with hematometra. A.3: Left hemi-uterus. B: MRI.*

Discussion

The OHVIRA syndrome also known as Herlyn-Werner-Wunderlich syndrome is a rare syndrome that appears more often on the right side (as in our case) [16]. The OHVIRA syndrome is a rare syndrome representing 0,16 - 10% of all Mullerian duct anomalies with an incidence of 2 - 3% [13-15]. Because of this low incidence, it is not routinely screened [8]. In this syndrome, the renal anomaly is often agenesis, but it can be also a dysplasic kidney or a duplication [7,8].

Urinary and genital anomalies are often associated because of their intricate connections during embryogenesis. The initial development of the urinary and genital systems begins at around six weeks with two pairs of genital ducts [1].

The Wolffian ducts (mesonephric duct) start from the mesonephros and go down until the urogenital sinus. This last one separates into a urogenital wedge and urorectal septum. At the end of each Wolffian duct, there is the ureteral bud that grows laterally until it reaches the metanephros to create the kidneys [1].

Parallel to the mesonephric duct, Mullerian ducts (paramesonephric) emerge from a coelomic invagination. They descend towards and both will join to form the uterine primordium. Initially, they are separated by a septum, after which they fuse to form the uterus and the fallopian tubes [1]. The end of the paramesonephric fuses with the mesonephric duct and constitutes the Mullerian tubercle. The vagina is derived from the fusion of the Mullerian tubercle with the urogenital sinus [12].

The regression of the Wolffian duct results in renal maldevelopment. The malpositioning of the Mullerian ducts induces a failure to fuse and leads to uterine didelphys. The obstructed hemivagina is explained by the absence of fusion of the Mullerian tubercle with the urogenital sinus [2-15].

Given that both anomalies often coexist, Mullerian anomalies should be routinely screened if renal anomaly is diagnosed, to prevent complications from occurring (abdominal pain, endometriosis, or infertility) [11]. In patients with renal anomaly, around 30% of them have a Mullerian anomaly [11]. There is an equal prevalence of genital anomalies between renal agenesis and dysgenesis [11]. The prevalence of renal anomalies in patients with Mullerian anomalies varies greatly, ranging from 17 to 100% [5-10].

The OHVIRA syndrome has been described by Lan Zhu., *et al*. in two classifications depending on the obstruction of the hemivagina and each classification is separated into two types (Figure 4). The classification 1 corresponds to a completely obstructed hemivagina (Figure 4A and 4B). The 2 correspond to an incompletely obstructed hemivagina (Figure 4C and 4D). According to the type of malformation, the symptoms and their time of onset can vary rendering the clinical diagnosis challenging [18].

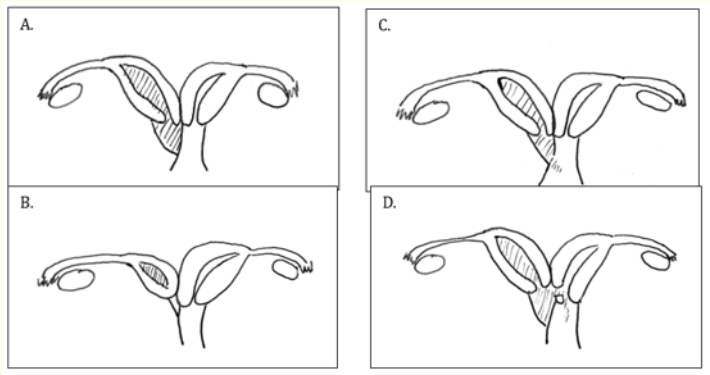

Figure 4: *Classification of the OHVIRA syndrome according to by Lan Zhu., et al. [8]. A: Blind hemivagina. B: Cervicovaginal atresia. C: Partial reabsorption of the vaginal septum. D: Communication between uteri.*

The main symptoms are abdominal pain and dysmenorrhea which are frequent and non-specific symptoms, which delay correct diagnosis. Other symptoms may be present like 2-step menstruation, intermittent mucopurulent discharge, metrorrhagia, and an abdominal mass [3]. However, the most important is to diagnose and treat as quickly as possible to avoid potential complications: endometriosis, pelvic adhesion, acute pelvic inflammation, and infertility [8-10].

The diagnosis is based on the ultrasound and above all on the MRI. The MRI is the most precise to characterize the shape of the uterine cavity, the contours, any vaginal or cervical anomaly, the septa, and the contents of obstructed hemivagina and to detect if there is a renal-associated anomaly [10].

The recommended treatment consists of surgical intervention to remove the vaginal septum by a transvaginal approach and suture the mucosa between the two sides after excising the septum [9,10]. It is recommended to do the surgery in one step. Two-step surgery is

needed in cases of infection or virgin patients because of the narrow vaginal opening: the first step consisting of incision of the septum to release the hematocolpos and the second to resect the septum. It can be interesting to do a laparoscopy at the same time to exclude any complications and if necessary, treat them [10]. Zaki Sleiman., *et al*. describe a laparoscopic procedure to preserve the integrity of the hymen (in conservative societies). It starts with a colpotomy to drain and wash the hematocolpos. Next, they push the high septum downwards revealing the vaginal septum behind the hymenal ring and they continue with the classical resection of the septum outside the vagina. The remaining septum is then resected in a second step through the vaginal cavity [14]. If the intervention has to be postponed, we can stop the menstruation with hormonal treatment such as a contraceptive pill, injection of progesterone or gonadotrophin-releasing hormone agonist [9].

What about fertility and OHVIRA syndrome? It is known that uterine malformations are associated with a high risk of early and late miscarriages, preterm birth, and malposition. However, some studies showed good obstetric outcomes with a didelphys uterus. 64 to 95% of all sexually active patients wishing to conceive had at least one delivery [8]. Another study showed that 56% of pregnancies were born at full term [4]. It is no longer recommended to perform a metroplasty to improve fertility. It may cause more complications such as Asherman's syndrome, uterine rupture, and postpartum hemorrhage [10].

Because of the close relation between the renal and genital anomalies, the non-specific symptom, the potential complications of the obstructed hemivagina and the required surgery, it is essential to establish a protocol to screen for the OHVIRA syndrome or other genital anomalies in the presence of renal malformations.

Friedman., *et al*. proposed an algorithm to screen the Mullerian anomalies in patients with renal anomalies. This algorithm is divided into two timeframes:

- Prenatal: When a renal anomaly is diagnosed, the parents must be informed of the association with Mullerian anomalies. The parents and the paediatrician must be informed about recommended screening during puberty.
- Puberty: Pelvic ultrasound is recommended to detect Mullerian anomalies between the thelarche and the menarche. If the ultrasound is inconclusive, an MRI can be performed [5].

With this approach, we can diagnose before the menarche and initiate early treatment to avoid complications.

Conclusion

Because of the close correlation between genital and urinary malformations, patients presenting with renal anomalies have to be screened for associated genital malformations. In some genital anomalies as OHVIRA syndrome, it is essential to implement early detection and treatment to prevent complications such as PID or infertility. A future line of thought should be dedicated to establishing a clear protocol, such described by Friedman., *et al*. [5].

Conflict of Interest

The authors declare that there is no financial or conflict of interest.

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