CASE REPORT

OHVIRA Syndrome: A Müllerian Anomaly as a Cause of Abdominal Pain in an Adolescent

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Abstract

Obstructed hemivagina with ipsilateral renal agenesis (OHVIRA) syndrome, or Herlyn-Werner-Wunderlich syndrome, is a rare congenital disease, caused by a Müllerian anomaly, characterized by a didelphys uterus, obstruction of the hemivagina and ipsilateral renal agenesis. It usually presents after menarche with progressive abdominal pain and pelvic mass secondary to hematocolpos. When the hemivagina obstruction is incomplete, the diagnosis may be delayed by the reduction of the severity of symptoms and possible regularity of the menstrual cycle. Rarely, it presents in the adult age as the cause of primary infertility. We describe the clinical case of a 15-year-old girl with a neonatal diagnosis of right renal agenesis who presented recurrent abdominal pain associated with abdominal-pelvic mass.

Keywords: Abdominal Pain/etiology; Adolescent; Abnormalities, Multiple; Kidney/abnormalities; Mullerian Ducts/abnormalities; Uterus/abnormalities; Vagina/abnormalities

Introduction

The syndrome characterized by obstruction of hemivagina and ipsilateral renal agenesis was first reported in 1922,[1] with the acronym OHVIRA suggested in 2007.[2] It is a rare Müllerian anomaly caused by the absence of development or fusion of the Müller ducts or due to a defect in the reabsorption of the uterine or vaginal septum.[3] In most cases, it occurs after menarche, presenting with recurrent abdominal pain or dysmenorrhea, associated with abdominal or pelvic mass. The diagnosis of this entity can be difficult given its rarity and heterogeneity of clinical presentation.[1]

Although the accumulation of menstrual blood in the vagina – hematocolpos – may arise early, associated with oligomenorrhea and abdominal pain, in situations of incomplete hemivagina obstruction, menstrual cycles may be regular, and the symptoms may not be typical,[1,4] delaying the diagnosis. Rarely, it can manifest later as a cause of primary infertility,[5] with an increased risk of complications.

Magnetic resonance imaging (MRI) is the most sensitive diagnostic exam and should be obtained for an accurate description.[4-6]

Surgical excision of the longitudinal vaginal septum, is the treatment of choice, allowing symptomatic relief and preservation of fertility, with a success rate superior to 80% in these cases.[7,8]

It is crucial to maintain a strong suspicion in patients with urologic abnormalities that present with menstrual irregularities, cyclical abdominal pain or even infertility, to guarantee a timely diagnosis and treatment, preventing possible complications.

Case Report

The authors present the clinical case of a 15-year-old female, with right renal agenesis, diagnosed in the neonatal period after an identification of a right preauricular ear tag. She had no other relevant medical history or family diseases, and she was on no medication at the time of admission. She presented in the emergency department due to lower abdominal pain that started three days before, on the first day of her last menstrual period. She had no complaints of pruritus or vaginal discharge. Her menarche dated three years back and had regular menstrual cycles, once every 28 days with three to four day duration of menstrual flow. Since the last eight months, she referred mild to moderate dysmenorrhea and hypogastric pain on the second and third of the menstrual period with good response to analgesia with ibuprofen. She denied having a sexual life. In the physical exam, she showed good general condition and state of nutrition. The abdomen

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was soft and depressible, painful to palpation in the suprapubic region and right iliac fossa, where a defined, elastic, spindle-shaped mass of about 8 cm of greater axis was perceptible. No signs of peritoneal reaction were seen. Observation of external genitalia appeared normal. No other changes to the physical exam were seen, except for a right preauricular ear tag.

Laboratory tests showed normal blood count, renal function, hepatic function, ionogram, lactate dehydrogenase, C-reactive protein, and sedimentation rate. Abdominal and suprapubic ultrasound demonstrated a heterogeneous expansive lesion, of approximately 10 x 7.5 cm size, in the right adnexal region (Fig. 1). An abdominal and pelvic MRI was performed in order to obtain more detailed information, revealing (Figs. 2 and 3):

- Uterine malformation, with two completely separated uterine cavities, apparent duplication of the cervix and proximal region of the vagina, admitting dystrophic / bicornous uterus;
- Dilation of the right uterine cavity in relation to hematometrocolpos with reflux for the homolateral fallopian tube, which was ectasized in relation with hematosalpinx, suggestive of distal obstruction, possibly in the cervix or proximal vagina;
- Right renal agenesis with vicarious left kidney.

The determination of tumor markers revealed a slight increase in CA 19.9 (72.1 U/mL, cut off < 37 U/mL) and CA 125 (59.7 U/mL, cut off < 30.2 U/mL). The values of alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) were normal.

She started oral contraceptives continuously and was scheduled for surgical treatment.

The patient underwent laparoscopic surgery that confirmed the findings of the MRI. It was possible to identify the existence of two uterus and a voluminous right hematosalpinx with adhesions to the pelvic cavity and to the fundus of the Douglas' pouch. The right ovary showed no alterations. Lysis of adhesions and

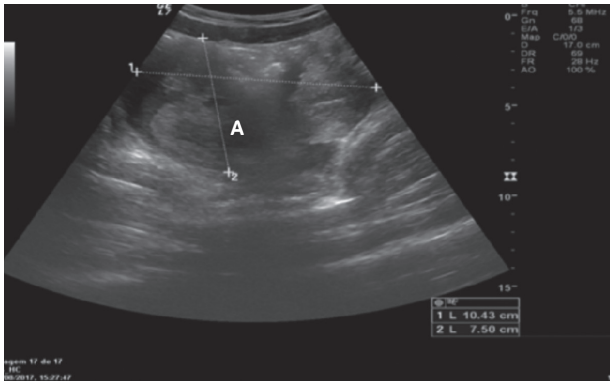

Figure 1. Pelvic ultrasound showing a heterogeneous expansive lesion measuring 10 x 7.5 cm, in the right adnexal region (A).

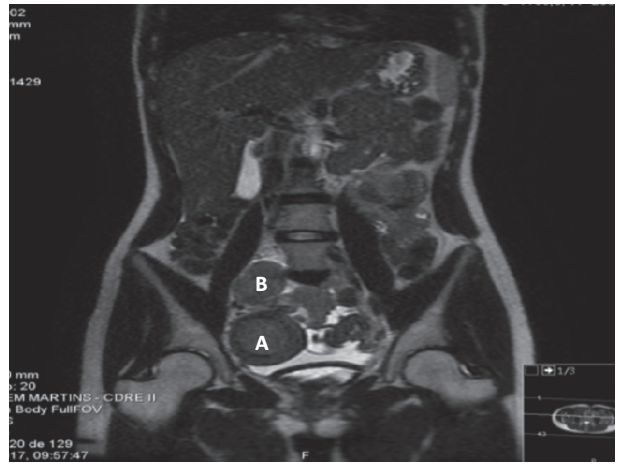

Figure 2. Abdominal-pelvic magnetic resonance imaging, coronal plan, showing dilatation of the right uterine cavity caused by hematometrocolpos (A) and right ectasied Fallopian tube in relation with an hematosalpinx (B).

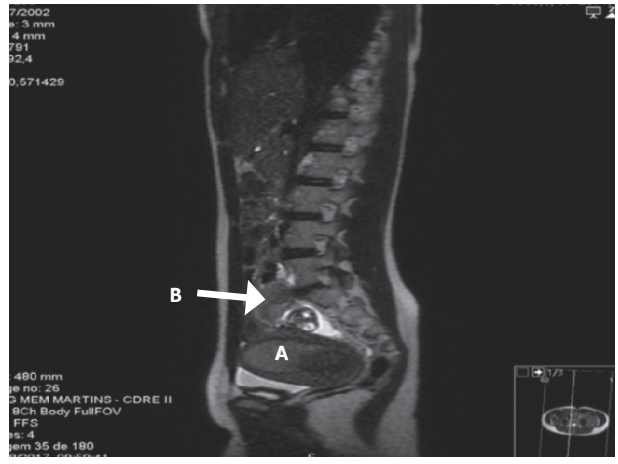

Figure 3. Abdominal-pelvic magnetic resonance imaging, sagital plan, showing the right uterine cavity with heterogenous blood content (A) and a right ectasied Fallopian tube caused by retrograde menstrual flow from the homolateral uterine cavity (B).

a salpingostomy were performed with hematosalpinx drainage. In a hysteroscopy, performed simultaneously with a diagnostic laparoscopy, a single uterine cervix was identified, and the longitudinal vaginal septum was excised. The left uterus, Fallopian tube and ovary were normal. The patient recovered well postoperatively. She maintained follow-up in consultation of gynecology and pediatric surgery, and treatment with oral contraceptives, showing clinical improvement.

Discussion

Congenital malformations of the female genital tract result from anomalies in the embryonic development of the Mullerian or paramesonephric ducts. They represent a benign condition with a prevalence of 4%-7%. According to the European Society of Gynecological Endoscopy and Human Reproduction, uterine malformations are

classified according to the following main classes, expressing uterine anatomical deviations with common embryonic origin[9]:
- U0, normal uterus;
- U1, dysmorphic uterus;
- U2, septate uterus;
- U3, bicorporeal uterus;
- U4, hemi-uterus;
- U5, aplastic uterus;
- U6, still unclassified cases.

These main classes are further divided into subclasses expressing anatomical varieties with clinical significance.[9]
OHVIRA syndrome, consisting of didelphys uterus (belonging to U3 class), obstruction of hemivagina and ipsilateral renal agenesis, has been increasingly recognized within the spectrum of Müller's anomalies. The Wolff ducts not only originate the kidneys but are also necessary elements for an adequate fusion of the Müllerian ducts. Thus, an anomaly in the development of the caudal portion of the Wolff ducts can cause unilateral renal agenesis associated with obstruction of the ipsilateral hemivagina.[2] On the side where the Wolffian duct is absent, the Müllerian duct is displaced laterally and cannot fuse with the contralateral duct, resulting in a didelphic uterus. The contralateral Müllerian duct gives rise to a vagina, whereas the displaced Müllerian duct that cannot come in to contact with the urogenital sinus centrally forms a blind sac, leading to an imperforate or obstructed hemivagina.[10-16]
Associated renal malformations are frequent, with a prevalence of 43%,[2] with renal agenesis as most common, as presented in this case. Pelvic kidney, renal cystic dysplasia, duplication of the collecting system and ectopic ureters may also occur.[10,17] Renal agenesis is predictive of an ipsilateral obstructive Müllerian anomaly in 50% of cases,[8,18] with the right side being affected twice as much as the left one.[2] Given this close relationship, when a renal anomaly is found in an adolescent, the existence of a congenital anomaly of the reproductive system should be investigated, and vice versa, preferably before menarche.[6]
The diagnosis is usually made 12 to 18 months after menarche[8] when abdominal pain secondary to hematocolpus begins, caused by the accumulation of blood in the hemivagina. This syndrome may remain unrecognized, at first, not only the menstrual flow from the unobstructed patent hemivagina gives the appearance of regular menses, but also dysmenorrhea, if present, is a common complaint in this age group.[5]
The use of non-steroidal anti-inflammatory drugs and oral contraceptives also decrease the intensity of symptoms.[4,8] A voluminous hematocolpos or a piocolpos can occur when there is an infection of the retained menstrual blood.[11] Rarely, it has a later presentation in adulthood, with primary infertility.[5]
In gynecological observation, a bulge in the lateral wall of the vagina, corresponding to the obstruction of the hemivagina, and a second uterine cervix is sometimes visualized.[5] A longitudinal vaginal septum is present in 75% of the cases.[16]
Multiple imaging modalities can diagnose the presence of uterine anomalies, such as supra-pubic or gynecological two-dimensional ultrasound or, more recently, three-dimensional gynecological ultrasound.[19,20] They have a sensitivity of 96.7% and specificity of 100%, allowing a better image resolution and accuracy of 97.2% in the diagnosis of uterine malformations.[20] A computed tomography scan or an MRI of the abdominal-pelvic region[3] should also be obtained, with the MRI remaining as the Gold standard test,[4,16] being useful in the characterization of genito-urinary anomalies, accurately demonstrating the structural morphology and liquid elements, with a diagnostic sensitivity of almost 100%.[4-6,13] Laparoscopy is not mandatory in diagnosis, although it is useful in its confirmation and may still be a part of the treatment, at the same operative time.[1,20]
The association between increased levels of CA 19.9 and CA 125 has been described in the literature.[15,21] These are markers expressed by endometrial and endocervical epithelial cells and are increased in benign conditions.
The importance of early diagnosis and treatment relates to, not only, symptomatic relief but also to the prevention of complications such as endometriosis, caused by retrograde menstrual flow, disturbances of the menstrual cycle, infertility, pelvic adhesions, obstetric complications,[5,6] and tumors of the cervix on the obstructed side.[12] A surgical correction usually restores normalcy of menstrual, sexual and reproductive functions.
The overall prognosis is good. The primary concern is related to the preservation of fertility. When diagnosed and treated early, women with this syndrome have a conception rate higher than 80%.[14] If untreated, the spontaneous abortion rate can reach 74% and the prematurity rate 22%. This may be explained by the decreased uterine cavity size, diminished uterine distensibility, or abnormalities of the myometrium and cervix.[16,18] There is a need for cesarean section in 82% of cases,[6,7,15] because of a higher probability of pelvic presentation of fetuses from mothers with this syndrome,[7] with no higher rates of maternal morbidity or uterine rupture.[22]
In conclusion, it is necessary to maintain a strong suspicion for the existence of abnormalities of the female reproductive system, in the presence of

defects of urological development and vice versa. The investigation should be based on a good clinical history, associated with a precise physical exam and a detailed gynecological observation. Magnetic resonance imaging is the most appropriate exam for the description of urogenital malformations. Treatment should take place as soon as possible, providing symptomatic relief and preventing complications.

WHAT THIS CASE REPORT ADDS

- Strong suspicion and knowledge of this anomaly are essential for an accurate diagnosis.
- In the female sex, the presence of urological abnormality requires the investigation of associated genital anomaly and vice versa.
- Early recognition and prompt surgical treatment rapidly relieve the symptoms and prevent most complications.
- Abdominal-pelvic magnetic resonance imaging remains the standard gold test for diagnosis of Müllerian anomalies.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Síndrome OHVIRA: Uma Anomalia Mülleriana como Causa de Dor Abdominal numa Adolescente

Resumo:
A síndrome de obstrução da hemivagina e agenesia renal ipsilateral (OHVIRA), ou síndrome de Herlyn-Werner-Wunderlich, é uma doença congénita rara, secundária a uma anomalia Mülleriana, caracterizada por útero didelfos, obstrução da hemivagina e agenesia renal ipsilateral. Apresenta-se habitualmente após a menarca com dor abdominal progressiva e tumefação pélvica secundárias a hematocolpos. Quando a obstrução da hemivagina não é completa, o diagnóstico pode ser atrasado pela diminuição da gravidade dos sintomas e possível regularidade do ciclo menstrual. Raramente, surge na idade adulta como causa de infertilidade primária. É descrito o caso clínico de uma adolescente de 15 anos, com diagnóstico neonatal de agenesia renal direita com queixas de dor abdominal recorrente associada a tumefação abdomino-pélvica.

Palavras-Chave: Adolescente; Anomalias Congénitas Múltiplas; Dor Abdominal/etiologia; Ductos Paramesonéfricos/anomalias congénitas; Rim/anomalias congénitas; Útero/anomalias congénitas; Vagina/anomalias congénitas