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HERLYN-WERNER WÜNDERLICH OHVIRA SYNDROME (OBSTRUCTED HEMI-VAGINA AND IPSILATERAL RENAL ANOMALY), DIFFERENT FORMS OF CLINICAL PRESENTATION AND HOW TO INTEGRATE 2D AND 3D ULTRASOUND FOR PROPER MANAGEMENT. CASE SERIES

SÍNDROME DE HERLYN-WERNER WÜNDERLICH OHVIRA (HEMIVAGINA OBSTRUIDA Y ANOMALÍA RENAL IPSILATERAL), DIFERENTES FORMAS DE PRESENTACIÓN CLÍNICA Y CÓMO INTEGRAR EL ULTRASONIDO 2D Y 3D PARA UN MANEJO ADECUADO. SERIES DE CASOS

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Herlyn-Werner Wünderlich Ohvira Syndrome (Obstructed Hemi-Vagina And Ipsilateral Renal Anomaly), Different Forms of Clinical Presentation and How to Integrate 2d and 3d Ultrasound for Proper Management. Case Series

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## ABSTRACT

Introduction: Obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome, is a rare Mullerian duct anomaly with uterus didelphys, unilateral obstructed hemivagina, and ipsilateral renal agenesis. In most cases, Patients who rarely present this structural anomaly, start to experience sympotms such as chronic pelvic pain and mass sensation that usually swap that star wirh menarche and variate with the menstrual cycle. Objective: this is an original article which aims to describe the wide range of symptoms presented by patients with (OHVIRA) syndrome, how their quality of life is affected due to underdiagnosis, and how 2D and 3D ultrasound is an important tool for the diagnosis of an adequate surgical technique. Matherials and methods: narrative describes the case of 2 adolescent patients who were incidentally diagnosed with the syndrome in the city of Cali Colombia at the imbanaco Clinic. information was obtained from their respective clinical histories, and ultrasound images and the respective surgical techniques used for the management of the symptoms were also extracted. the informed consent of both patients was obtained. Results: The diagnosis is usually late or incidental because the clinical presentation only becomes evident once menarche occurs. As the clinical and structural presentation of the pathology comprises a wide spectrum, therefore the diagnosis today is made by means of 2D and 3D ultrasonography, diagnostic imaging such as computed axial tomography and magnetic resonance imaging, the management will depend on the structural anomaly and the intensity of the symptoms. Today surgical method are usually the treatment of choice. Conclusion: OHVIRA syndrome is a rare congenital anomaly that represents a diagnostic challenge because of the regular menstruation and nonspecific clinical presentation. Health care providers should be aware of the different extending symptoms in order to employ different diagnose images such as 2D and 3D ultrasonography operated by highly trained staff (sensibility >90 % y specificity 100% to facilitate early and accurate management and improve patients quality life.

Keywords : uterine didelphys, solitary kidney, ultrasonography, hematocolpos, quality of life

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# Síndrome de Herlyn-Werner Wünderlich Ohvira (Hemivagina Obstruida y Anomalía Renal Ipsilateral), Diferentes Formas de Presentación Clínica y Cómo Integrar el Ultrasonido 2d y 3d para un Manejo Adecuado. Series de Casos

# RESUMEN

Introducción: El síndrome de hemivagina obstruida y anomalía renal ipsilateral (OHVIRA), es una rara anomalía del conducto de Müller con útero didelfo, hemivagina obstruida unilateral y agenesia renal ipsilateral. En la mayoría de los casos, las pacientes que rara vez presentan esta anomalía estructural, comienzan a experimentar síntomas como dolor pélvico crónico y sensación de masa que suele intercambiar esa estrella con la menarquia y variar con el ciclo menstrual. Objetivo: este es un artículo original que tiene como objetivo describir la amplia gama de síntomas que presentan los pacientes con síndrome (OHVIRA), cómo su calidad de vida se ve afectada por el infradiagnóstico y cómo la ecografía 2D y 3D es una herramienta importante para el diagnóstico del síndrome. una técnica quirúrgica adecuada. Materiales y métodos: se describe narrativamente el caso de 2 pacientes adolescentes que fueron diagnosticados incidentalmente con el síndrome en la ciudad de Cali Colombia en la Clínica Imbanaco. Se obtuvo información de sus respectivas historias clínicas, así como también se extrajeron imágenes ecográficas y las respectivas técnicas quirúrgicas utilizadas para el manejo de los síntomas. Se obtuvo el consentimiento informado de ambos pacientes. Resultados: El diagnóstico suele ser tardío o incidental porque la presentación clínica sólo se hace evidente una vez que ocurre la menarquia. Como la presentación clínica y estructural de la patología comprende un amplio espectro, hoy en día el diagnóstico se realiza mediante ecografía 2D y 3D, diagnóstico por imágenes como la tomografía axial computarizada y la resonancia magnética. el manejo dependerá de la anomalía estructural y de la intensidad de los síntomas. Hoy en día el método quirúrgico suele ser el tratamiento de elección. Conclusión: El síndrome OHVIRA es una anomalía congénita poco común que representa un desafío diagnóstico debido a la regularidad de la menstruación y la presentación clínica inespecífica. Los proveedores de atención médica deben ser conscientes de los diferentes síntomas que se extienden para emplear diferentes imágenes de diagnóstico, como la ecografía 2D y 3D operada por personal altamente capacitado (sensibilidad >90 % y especificidad 100 % para facilitar un manejo temprano y preciso y mejorar la calidad de vida de los pacientes.

Palabras clave: didelfo uterino, riñón único, ecografía, hematocolpos, calidad de vida

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#### **INTRODUCTION**

HERLYN-WERNER-WÜNDERLICH (OHVIRA) syndrome is a congenital urogenital malformation characterized by the presence of an obstructed hemivagina, a didelphic uterus and ipsilateral renal agenesis. This syndrome is a rare congenital malformation caused by abnormal development of the Müllerian and Wolffian ducts during embryonic development of the female reproductive system, is very rare, with an undetermined prevalence due to clinical underdiagnosis in many cases; representing less than 10% of all Müllerian malformations; the exact rate is unknown but is thought to range from 1/2000 to 1/28000 women.<sup>1</sup>

Although its pathophysiology is not very clear, it is believed that this type of Müllerian malformation may be the final product of a deficit in the fusion, canalization and reabsorption of the septum of the Müllerian (paramesonephric) and Wolf (mesonephric) ducts. In most cases (30-50%) there are usually concomitant genitourinary anomalies, due to the joint embryonic development of both systems during the early stages of human embryogenesis, which leads to the coexistence of genital and urological malformations.<sup>2,3</sup>

The spectrum of symptoms is usually very broad and will depend on the % of vaginal obstruction, however, in most cases patients experience dysmenorrhea and progressive pelvic pain which are usually the cardinal symptoms. Diagnostic delays are frequent, and are mainly due to the presence of patients with regular menstrual cycles.<sup>4,5,6</sup>

The European Society of Human Reproduction and Embryology in conjunction with the European Society of Gynecological Endoscopy has generated a classification that describes the type of uterine, cervical and vaginal abnormality in order to offer the most appropriate management for each patient.<sup>1,4,7</sup> (Table 1).







Table 1

	Uterine anomaly		Cervical/vaginal anomaly Co-existent class	
Main class		Sub-class		
U0	Normal uterus		co	Normal cervix
U1	Dysmorphic uterus	a. T-shaped b. Infantilis c. Others	C1	Septate cervix
			C2	Double 'normal' cervix
U2	Septate uterus	a. Partial b. Complete	<i>C3</i>	Unilateral cervical aplasia
			C4	Cervical aplasia
U3	Bicorporeal uterus	a. Partial b. Complete		
		c. Bicorporeal septate	vo	Normal vagina
U4	Hemi-uterus	<ul> <li>a. With rudimentary cavity (communicating or not horn)</li> </ul>	V1	Longitudinal non-obstructing
		b. Without rudimentary cavity (horn without cavity/no horn)	V2	Longitudinal obstructing vaginal septum
U5	Aplastic	a. With rudimentary cavity (bi- or unilateral horn)	V3	Transverse vaginal septum
		b. Without rudimentary cavity (bi- or	V4	and/or imperforate hymen Vaginal aplasia
U6	Unclassified malforr	unilateral uterine remnants/aplasia) nations		
U			с	V
J0/ útero	e normal	dismórfico Clase U2/ útero septado	<b>P</b> pleto	Clase U4/ hemi útero
	Clase U3/ útero bicorpóreo	Clare US/	útero aplásico	Clase U6/ casos inclas

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This article describes 2 cases presented in the city of Cali, Colombia in patients of different age groups, with a wide spectrum of symptoms which were diagnosed through the use of gynecologic ultrasonography operated by highly skilled specialists who contributed to a timely diagnosis. The patients are currently undergoing various medical and surgical treatments with a positive prognosis.<sup>8,9</sup>

## Narrative

#### Case 1

The first case corresponds to a 20-year-old female university student, previously diagnosed with congenital renal agenesis since birth in continuous management with nephrology, pregnant 0 para 0, who first consulted the gynecology service at 17 years of age, referred from the emergency department for presenting a clinical picture of approximately 3 months of evolution, consisting of progressive pelvic pain of uncertain etiology associated with dysmenorrhea which did not yield to the use of





antispasmodics or analgesics, the patient referred regular menstrual cycles. Therefore, with the suspicion of a possible appendicitis, which was ruled out, it was decided to refer the patient to the gynecology and obstetrics service, where a transvaginal gynecological ultrasound was performed, which reported a complex cyst adjacent to the cervix and it was suggested to complement it with computed axial tomography or abdomino-pelvic magnetic resonance imaging.

The patient was referred to a specialist in gynecology and obstetrics where the attending gynecologist decided to take the patient to an exploratory laparoscopy with hysteroscopy, where resection of the right hemiuterus and right salpingectomy were performed. (image 1) the operative findings report a vagina without lesions, a single cervix is observed, a 5-6 cm mass is palpated which ablates the posterior fundus lateral to the right cervix (image 2), the only visible ostium is observed in the left cavity, the left hemiuterus looks normal, the right hemiuterus has an elongated shape with hematometra extending from the endometrial cavity to the right endocervix, the fallopian tubes are normal. Normal ovaries. Normal tubes. Resection of the right hemiuterus and salpingectomy (image 3), biopsy of uterine tissue without histological abnormalities with diagnosis of right hemiuterus, proliferative endometrium, myometrium without particularities and uterine tuba with foci of old hemorrhage.

**Image 1** Speculoscopy showing on the right side of the patient the transverse vaginal septum without cervical os and on the right side the cervix of the left hemisphere.







**Image 2**: upper laparoscopic view showing a kind of mass attached to the uterus on the right side of the patient, which is recognized as the right hemi uterus with collection (hematocolpos).



Image 3: Resection of right hemiuterus and right salpingectomy by laparoscopy and hysteroscopy.

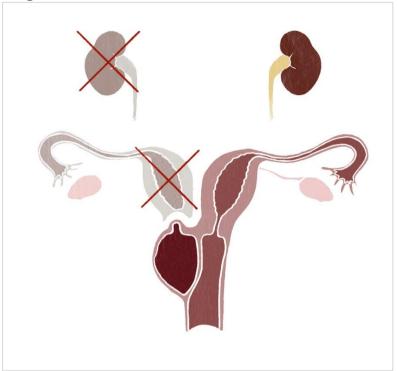


After surgery, the specialist sent a pelvic MRI that reported failure in the fusion of the mullerian ducts, with a didelphic uterus with obstruction of the cervical orifice on the right side and a hematic collection in its interior (image 4).





## Image 4



Animated illustration showing the surgery performed (exploratory laparoscopy with hysteroscopy, where resection of the right hemiuterus is performed, right salpingectomy) source of elaboration Gabriela Quintero Rodríguez, illustrator.

Therefore, he considers that the most appropriate thing to do is to refer the patient to a highly qualified specialist in ultrasound diagnosis, where a 2D transvaginal ultrasound is performed, which reports a normal echogenicity left hemi uterus, measuring 70x32x41 mm with volume 49cc, endometrial echo of 7.9mm menstruating. In the right hemivagina an oval image measuring 49 x 32 mm with ground glass content corresponding to hemicervix with hematocolpos is seen (Image 5). A 2D and 3D reconstruction of the initial ultrasound image is performed (Image 5 and 6). There is marked sensitivity expressed by the patient during the exploration. It is important to emphasize that at this time the patient had already been admitted for surgery and therefore only a uterine cavity with adnexal vaginal mass is observed, thus confirming ultrasonographically the previous diagnosis of OHVIRA U3(b) C2 V2 syndrome (Image 7).

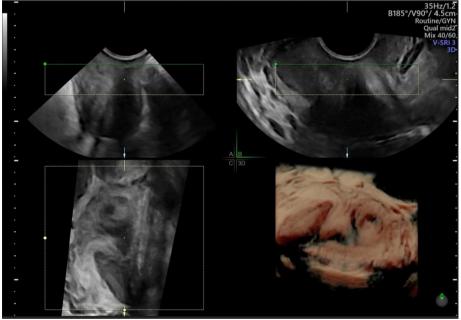




**Image 5**: transvaginal pelvic ultrasound showing on the right side of the image a collection of dense echo content and on the left side a hemi cervix without alterations.



**Image 6**: three-dimensional reconstruction of the previous image showing a collection on the right side and an unaltered hemi cervix on the left side.

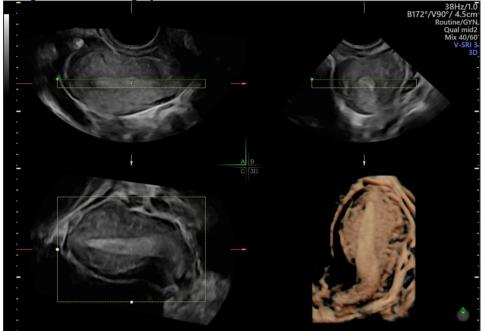








**Image 7**: three-dimensional reconstruction of the residual left hemiuterus with normal appearance (image taken after surgery).



To date, the patient reports that after the first surgery she felt improvement of the mentioned symptomatology, however, approximately two months ago she has presented the same clinical picture again, reason for which she is waiting for a trachelectomy by laparoscopy in order to definitively improve her quality of life and the possibility of possible complications.

#### Case 2

This is a 12-year-old female patient with no personal or family pathological history who consults the emergency department of a hospital in the city, with no personal or family pathological history, who consults for presenting a clinical picture of 3 days of evolution in the lumbar portion with irradiation to the right inguinal area, which did not subside with oral analgesics. In the hospital a diagnosis of renal lithiasis vs. appendicitis was made. A renal and urinary tract ultrasound was performed, reporting a left kidney not visualized in the left lumbar fossa or the rest of the abdomen, uterus of usual ultrastructure, with a mass in the projection of the left ovary suggestive of teratoma and left renal agenesis with right kidney of compensatory aspect, suggesting a CT scan to complement the diagnosis and correlate with clinical symptoms. CA 125, CA 19-9, carcinoembryonic antigen, alpha fetoprotein and qualitative beta subunit chorionic gonadotropin were negative.





It was decided to perform a contrasted abdominal tomography which reported left renal agenesis with compensatory renal hypertrophy, didelphic uterus without the possibility of defining a septum with associated vaginal collection, apparently left hemivagina. The previous findings are suggestive of OHVIRA syndrome, and a contrasted pelvic MRI and evaluation by gynecology are suggested. The contrasted pelvic MRI reports didelphic uterus with duplication of cervix, duplication of vaginal cavities with distension at the expense of liquid content that could indicate a hematic nature (hematocolpos) without ruling out a secretory (infectious) nature. Multifollicular ovaries, scarce free fluid.

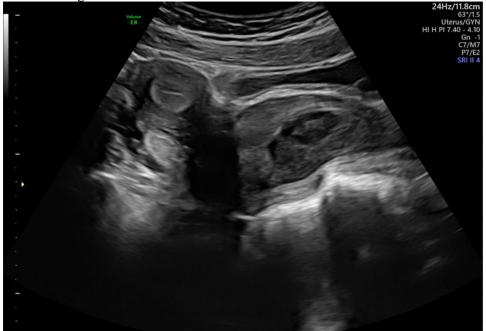
The patient began to refer to her mother the presence of a yellow, fetid vaginal discharge associated with severe pelvic pain which did not yield to the use of painkillers so she consulted the emergency department, where a vaginal smear was performed which reported positive fungal +++ pH 6, negative Gardenella and negative vaginal culture; She is medicated with oral metronidazole for 7 days and is referred to consider surgical management for vaginal and uterine reconstruction at level III in order to reduce symptoms and improve the patient's quality of life.

In consultation with a specialist, surgical intervention is suggested and transvaginal ultrasound is requested by a highly qualified specialist in ultrasonographic diagnosis, which reports: OHVIRA syndrome, didelphic uterus with classification U3 (b) C2, V3 (image 8 and 11), hematocolpos in left hemivagina, vaginal septum, ipsilateral renal agenesis, a 3D virtual reconstruction is generated (image 9 and 10) and an imaging report is sent to the surgical specialist in order to guide the most opportune decision making regarding the various possibilities of medical surgical management indicated for the pathological characteristics of the patient..

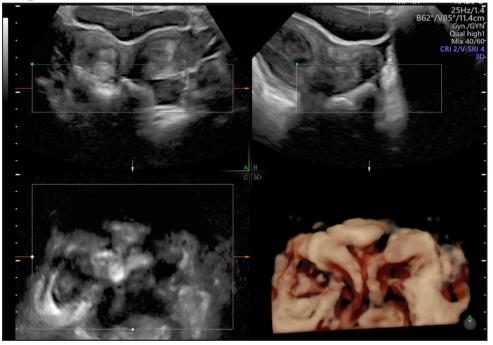




**Image 8**: transabdominal ultrasound in sagittal view showing left hemiuterus with collection at the level of the left vaginal canal.



## Image 9

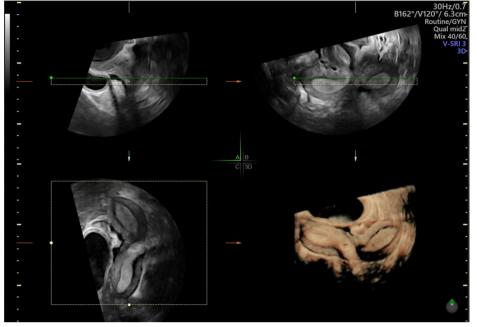


Abdominal ultrasound with three-dimensional reconstruction where the two uterine bodies can be differentiated bi-corporeal didelphic uterus with the presence of distal vaginal hematocolpos corresponding to left hemiuterus.

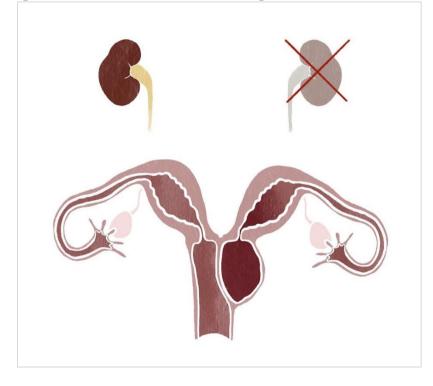




**Image 10:** three-dimensional reconstruction via the abdominal route showing two uterine bodies with bilateral endometrial stimulation.



**Image 11**: illustration showing hematocolpos in left hemivagina, vaginal septum, ipsilateral renal agenesis. source Gabriela Quintero Rodríguez. illustrator.



After the 2D and 3D ultrasound examination the patient is interviewed by the surgeon who after seeing the images decides that the patient is suitable to undergo hysteroscopy in order to drain the hematometrium, dissect the uterine septum and significantly improve her quality of life to avoid possible complications.





#### MATERIALS AND METHODS

A descriptive case report type study was performed, without intervention on the analysis of the two clinical histories compatible with HERLYN-WERNER-WÜNDERLICH syndrome (OHVIRA).

The study was carried out in the city of Cali, Colombia, at the Imbanaco clinic. The respective information was extracted from the clinical histories of the patients, highlighting the appearance of the diversity of clinical symptoms, differential diagnoses, diagnostic methods and some treatment alternatives. Emphasis is placed on the challenge posed by the possibility of a timely diagnosis for health personnel. It should be noted that this case report has the approval of the ethics committee of the Imbanaco clinic in Cali, we consider it of utmost importance to emphasize that the report in question was made under all standards of good clinical practice and following the parameters of the Helsinki declaration of the World Medical Association, also with the respective consent and informed assent for the disclosure of the clinical outcome, imaging and individualized treatment of each patient.

## DISCUSSION

Müllerian malformations characterized by the association of vaginal obstruction with ipsilateral renal anomalies were first reported in the literature in 1922 by Herlyn-Werner and later in 1950 by Wunderlich.8,10

The cases described in this report had in common the presence of a didelphic uterus, a hemivagina with partial or total obstruction and ipsilateral renal agenesis. This characteristic diagnostic triad is now recognized as the OHVIRA syndrome (Obstructed Hemi-vagina and Ipsilateral Renal Anomaly).

The exact incidence of this syndrome is unknown. Some reports suggest that it ranges from 1/2000 to 1/28000 women. With a prevalence of Müllerian anomalies of 7% of women of reproductive age worldwide.1

Approximately 40% of these are associated with renal alterations. Of patients with uterine duplication, 6% have an obstructed hemivagina. Renal agenesis occurs in 63 to 81% of cases of uterine duplication, and in 92 to 100% of cases of obstructed hemivagina.1,7,11

The exact pathophysiologic mechanisms involved in this type of Müllerian anomalies are currently unknown. The theory of a multifactorial etiology has been proposed, including genetic and epigenetic factors. The embryological alteration of the mesonephric or unilateral Wolffian ducts gives rise to renal





agenesis. This alteration in the mesonephric duct lateralizes the ipsilateral paramesonephric Wolffian duct, resulting in a didelphic uterus and an obstructed hemivagina.12

The diagnosis is usually made after menarche, and although its clinical spectrum is usually broad depending on the structural anomaly and the percentage of obstruction, its classic form usually appears as a picture of chronic pelvic pain associated or not with progressive dysmenorrhea and in some cases with the presence of a sensation of a vaginal mass or tumor. Late diagnoses are frequent and are due to multiple causes such as: absence of symptoms prior to menarche, progressive onset of symptoms after the menstrual cycle, however the presence of regular menstrual cycles often distract the health professional.

A prenatal or neonatal diagnosis can be made by exhaustive evaluation of the Müllerian structures in fetuses or neonates diagnosed with renal anatomical alterations 13.

Diagnostic confirmation, as mentioned above, is made by means of imaging techniques both by 3D ultrasound with image reconstruction and by MRI, the accuracy of the latter being close to 100%.8,9,12 Early diagnosis of this syndrome allows the possibility of offering the patient appropriate management to improve her quality of life, reducing the presence of chronic pelvic pain, decreasing the appearance of complications such as pelvic inflammatory disease, endometriosis and infertility.14

For diagnosis, 2D and 3D ultrasound and Magnetic Resonance Imaging (MRI) are useful. To obtain images of the soft tissue anatomy and identify congenital anomalies 15. Once the diagnosis is suspected, it is indicated to perform a tranvaginal ultrasound operated by an expert where the visualization of the hematocolpos (if present) and the uterine malformation is allowed, 3D reconstruction ultrasound is usually of great help for surgical planning and its operative pathway. Magnetic Resonance Imaging is also usually of great help with a sensitivity of 100%. 8,9

It is of substantial importance to perform an exhaustive screening for Müllerian malformations in all patients diagnosed with renal anomalies in order to generate a timely referral to the gynecology service in order to generate a diagnosis and be able to perform an adequate management in order to improve the quality of life of the patients.





## CONCLUSIONS

HERLYN-WERNER-WÜNDERLICH syndrome (OHVIRA) is a complex urogenital müllerian anomaly, which is infrequently seen in clinical practice. Its wide variability of clinical presentation and the lack of knowledge of it lead to a late diagnosis which ultimately increases the possibility of presenting complications that compromise the quality of life of affected patients; altering their quality of life and compromising their sexual and reproductive future; it is of great importance that health professionals, from the first contact with the patient, consider the possibility of the existence of this pathology in order to generate an early clinical diagnosis and to be able to offer the possibility of establishing an adequate therapy; thus reducing the comorbidity related to this syndrome.

## **Confidentiality of data**

The authors declare that they have followed with protocols of their work center on the publication of patient data and images.

## Right to privacy and informed consent

The authors declare that no patient data appear in this article. Informed consent signed by the patient is available.

## **Conflicts of interest**

The authors declare that they have no conflicts of interest.

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