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Case report

Herlyn-Werner-Wunderlich syndrome: A report of three cases in adolescents and adult woman ☆,☆☆

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ABSTRACT

We report three cases with Herlyn-Werner-Wunderlich syndrome in adolescents and young female. The objective of this report was to describe the clinical presentation, ultrasound (US) and magnetic resonance imaging (MRI) findings of Herlyn-Werner-Wunderlich syndrome. The three patients were 12, 13 and 34 years old, respectively. The reason for admission and clinical symptoms varied between the 3 patients, including menstrual cramps, vaginal bleeding, and dull pain in the hypogastric region. Nevertheless, the sonographic and MRI findings of all three cases were typical for HWWS, including didelphys uterus, obstructed hemivagina, and ipsilateral renal agenesis.

Introduction

Herlyn-Werner-Wunderlich syndrome is a combined anomaly of Mullerian and mesonephric ducts which includes a triad of didelphys uterus, obstructed hemivagina, and ipsilateral renal agenesis (Fig. 1) [1,2]. Another synonym is obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome, with or without didelphys uterus [3]. HWWS is rare with a reported incidence in the general population of approximately from 0.1% to 3.8% [4]. Unilateral renal agenesis has an incidence of about 1: 1000 and is usually symptomless and often associated with other urogenital anomalies [5,6]. HWWS is often detected and diagnosed after menarche with the majority of clinical presentation being pelvic pain, menorrhagia, dysmenorrhea, irregular menses, and a palpable pelvic mass following menarche depending on the incomplete or complete obstruction of hemivagina [7]. Surgical resection remains the mainstay of treatment [8,9]. Herein we present three cases of HWWS which were detected on ultrasound and were confirmed by MRI.

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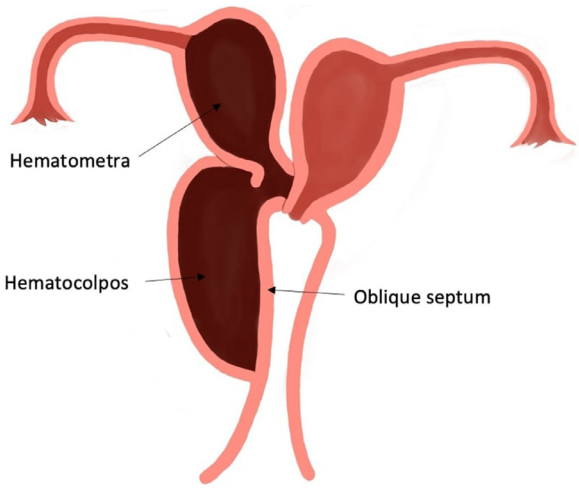

Fig. 1 – Illustration of Herlyn-Werner-Wunderlich syndrome with complete vaginal septum, didelphys, hematometra and hematocolpos on the right (type 1 according to China's classification).

Case series

Case 1

A 12-year-old female patient hospitalized due to menstrual cramps and progressive pain in the hypogastric region. The patient has a history of appendectomy 1 year ago and accidental discovery of left kidney aplasia and didelphys uterine malformation at the same time. She had started menstruating for 8 months. Menstruation is irregular with associated mild pain during menstruation. Physical examination showed no palpable mass in the abdomen, normal vulva, and one hymen hole. Blood cell count showed iron-deficiency anemia (red blood cell count was 3.71 × 10^9/mL, HGB was 103 g/L, MCH was 27.8 pg), beta-human chorionic gonadotropin level and other biochemical indexes were in normal range. Abdominopelvic ultrasound images revealed uterus didelphys with left hematometra measuring 38 × 28 × 51mm, obstructed left hemivagina, and left hematocolpos measuring 95 × 43 × 43mm (Fig. 2). The left kidney was not visualized. Subsequently, an abdominopelvic MRI was performed to better characterize the anatomy and confirmed the presence of above findings, including hematometra, hematocolpos on the left, and the absence of the ipsilateral kidney (Fig. 3). The right ovarian had a dominant follicle measuring 15mm. Vaginoscopic incision of vaginal septum was performed successfully.

Case 2

A 13-year-old girl presented to the outpatient clinic with a history of vaginal bleeding. She had no history of any other medical condition. She had menarche three months earlier and had a regular menstrual cycle with dysmenorrhea and cyclical abdominal pain. She was born at term of an uncomplicated pregnancy and had no family history of any congenital

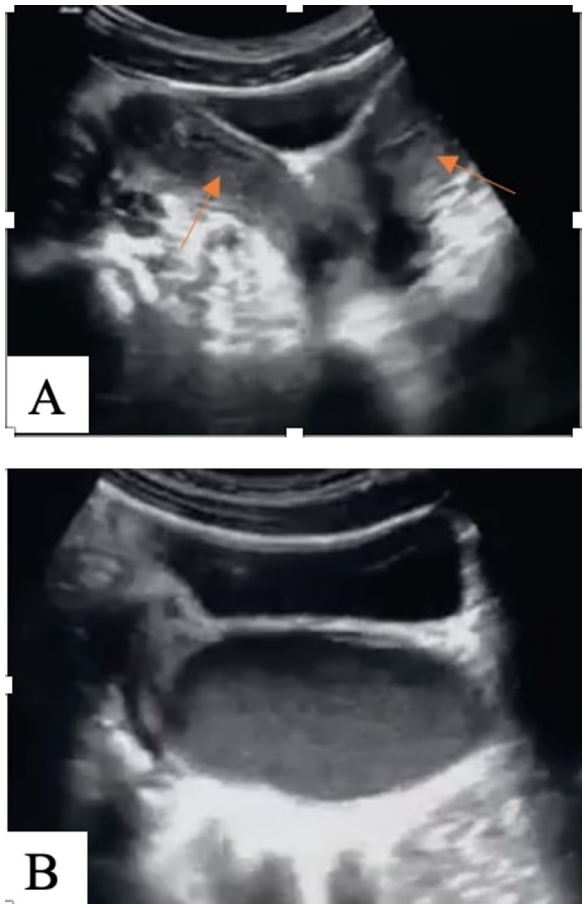

Fig. 2 – Patient 1, a 12-year-old girl. Transabdominal ultrasound showing uterus didelphys and left hematocolpos.

anomalies. Abdominopelvic ultrasound and MRI examination revealed didelphys uterus, bilateral homogeneous thickened endometrium (10mm on the left, 12mm on the right), complete vaginal septum, right hematocolpos with 38 × 31 × 47mm in size, ipsilateral kidney agenesis (Figs. 4 **and** 5). The right ovarian had a 21-mm de Graff cyst. The patient's parents denied further treatment. The patient was discharged without further observation.

Case 3

A 34-year-old female presented to our hospital with dull pain in the hypogastric region. She underwent menarche at age 15 years. Her menses were regular with 7 period days and 40-day intervals with mild dysmenorrhea. She got married 5 years ago and still has no children. She revealed that she was aware of an absent left kidney and cervix malformation 4 years ago. Blood test, CRP, beta-human chorionic gonadotropin levels and kidney function were within the normal range. An abdominopelvic MRI revealed accurately detailed anatomy in the pelvis including duplication of uterus, cervix and vagina, left hematocolpos and absent kidney on the same side (Fig. 6). MRI did not show other related complications such as

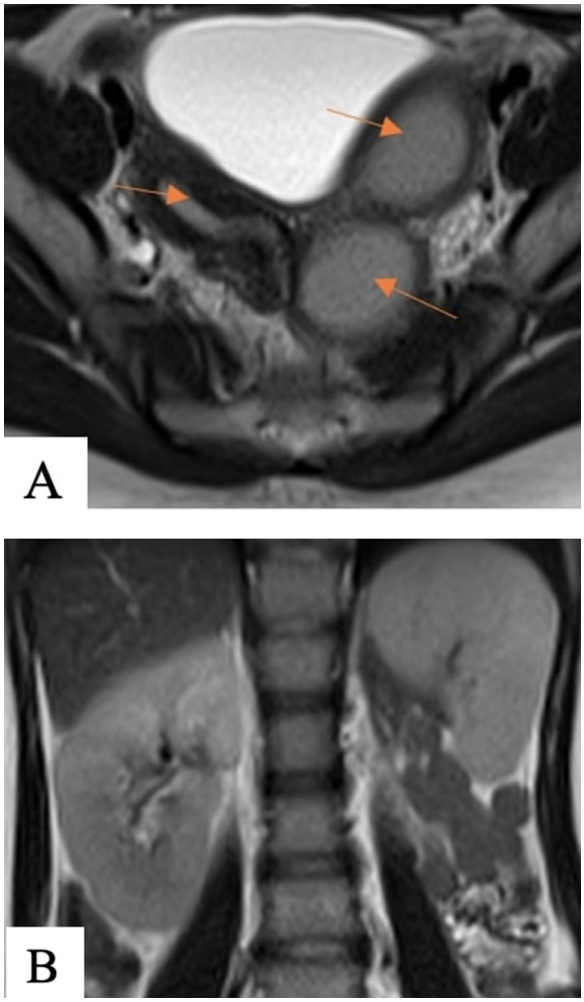

Fig. 3 – Patient 1, a 12-year-old girl. Axial and Coronal T2-Weighted, (A) uterus didelphys, hematometra, and hematocolpos on the left (arrows), (B) ipsilateral kidney agenesis.

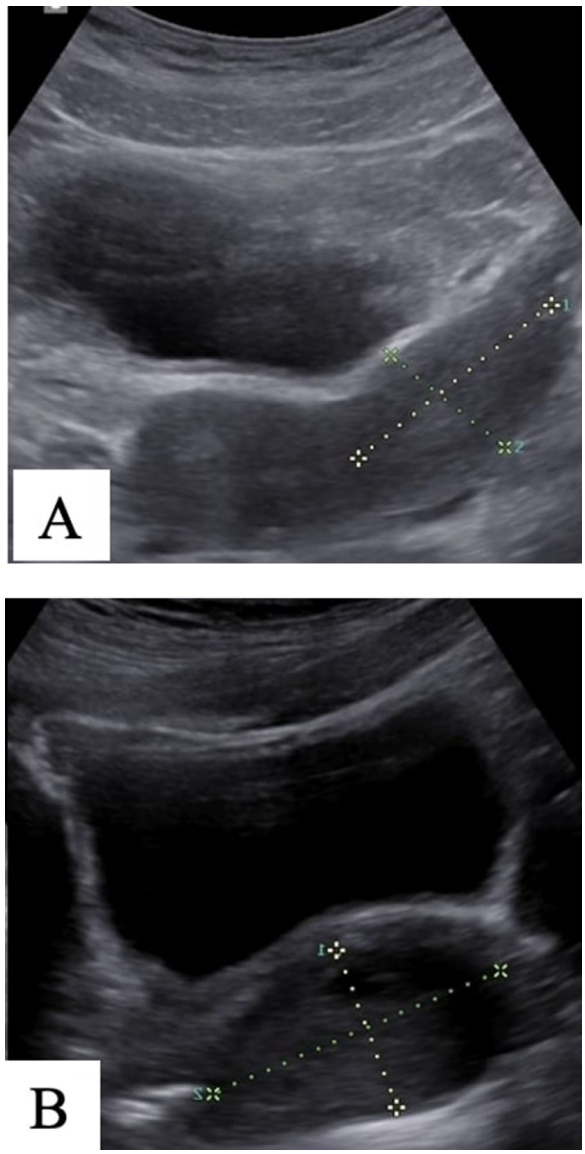

Fig. 4 – Patient 2, a 13-year-old girl. Transabdominal ultrasound showing uterus didelphys and right hematocolpos.

endometriosis. The patient was treated similarly to the first patient.

Discussion

Herlyn-Werner-Wunderlich syndrome (HWWS) was first reported by Purslow in 1922 [10]. It is a very uncommon congenital disorder of Müllerian and mesonephric duct development distinguished by the triad of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis [11]. Renal agenesis on the same side of the obstructed vagina can be explained by embryological arrest at 8 weeks of pregnancy, simultaneously affecting the Müllerian (paramesonephric) and Wolffian (mesonephric) ducts [3,12].

The main cause of congenital Müllerian or paramesonephric duct anomalies is defective fusion (vertical or horizontal direction) or septal resorption failure. The formation of this anomalies is also influenced by multifactorial, polygenic, and familial factors [13]. The embryologic formation of the reproductive and urinary tract systems occurs simultaneously [14]. The Müllerian system forms the uterus, cervix, fallopian tubes, and the upper third of the vagina. The kidneys originate as ureteric buds from the wolffian ducts, and the lower third of the vagina derives from the urogenital sinus (Fig. 7) [15].

The exact incidence of HWW syndrome is yet to be investigated. Patients with HWWS are often asymptomatic until menarche when they present with progressive pain due to hydrometrocolpos and hemivaginal obstruction within the first year of menstruation [16]. The patients with complete hemivaginal obstruction have significantly different presentation when compared to those with incomplete hemivaginal obstruction [3]. The most common clinical presentation

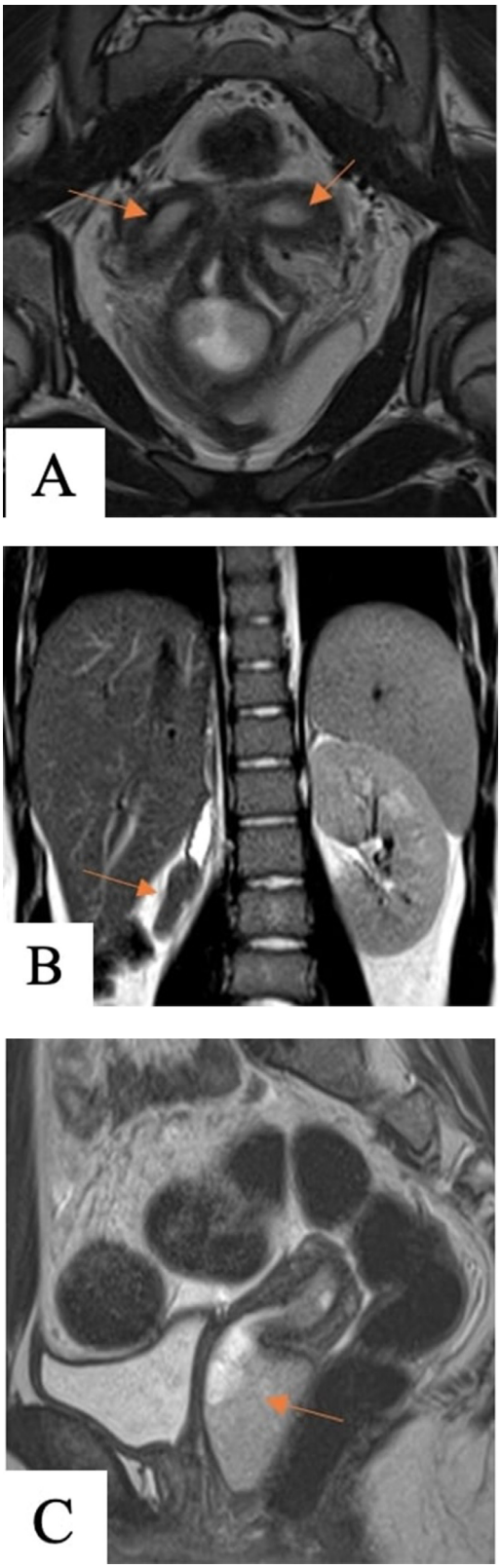

Fig. 5 – Patient 2, a 13-year-old girl. Coronal (A, B) and sagittal (C) T2-weighted magnetic resonance image (A, C). Two separate uterine cavities (A, arrows) with dilatation of right hemivagina. Absent right kidney (B, arrow). High signal intensity fluid in T2W and hyperintense content in T1-weighted fat-suppressed sequence (not shown) in line with blood products.

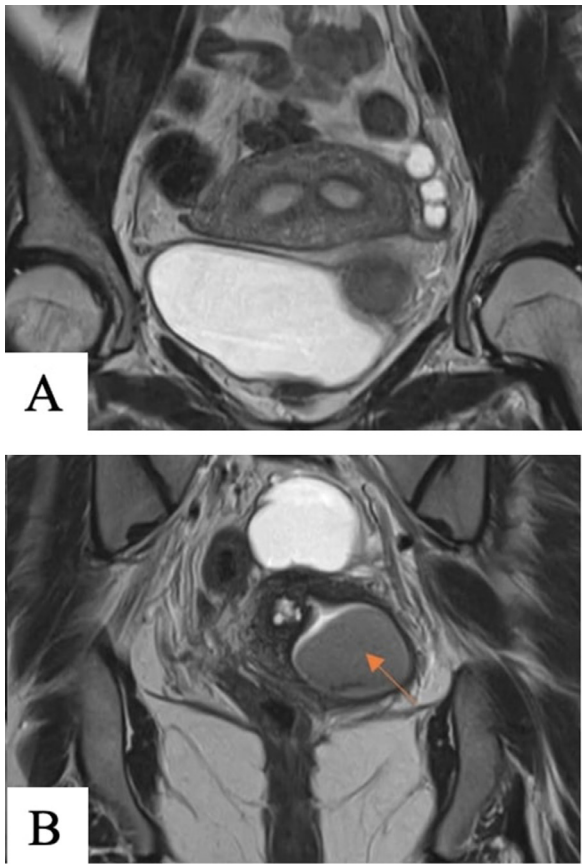

Fig. 6 – Patient 3, a 34-year-old female. Coronal T2-Weighted, (A) didelphys, (B) left hematocolpos.

is cyclical dysmenorrhoea at puberty, abdominal pain, and abdominal mass secondary to hematocolpos, and normal menstrual periods [17].

Rare presentations may include intermenstrual bleeding, other symptoms of primary infertility, urinary obstruction or pyometra, fever, vomiting, and abdominal swelling. Common complications are endometriosis, pyosalpinx or pyocolpos, and pelvic adhesions may present with infertility of miscarriage [18,19]. Children with solitary functioning kidney might be at risk to develop hypertension, proteinuria and chronic kidney disease in long term [20].

Abdominopelvic ultrasound is an initial, and preliminary choice, especially for children and adolescence due to its radiation-free nature to detect genitourinary anomalies [21]. Sonographic findings include uterine anomalies (didelphic/bicornuate uterus), hematometra, hematocolpos, vaginal septum, and ipsilateral renal agenesis with compensatory hypertrophy of the contralateral kidney [22]. Abdominopelvic MRI helps to confirm the diagnosis, especially in cases where the vaginal septum is not clear and requires MRI for better anatomical details, particularly in pediatric patients [23]. Additionally, MRI allows comprehensive evaluation of Mullerian duct abnormality and accurately identifies related complications such as endometriosis, pelvic adhesions [24]. Laparoscopy remains the gold standard for diagnosis and treatment [25,26].

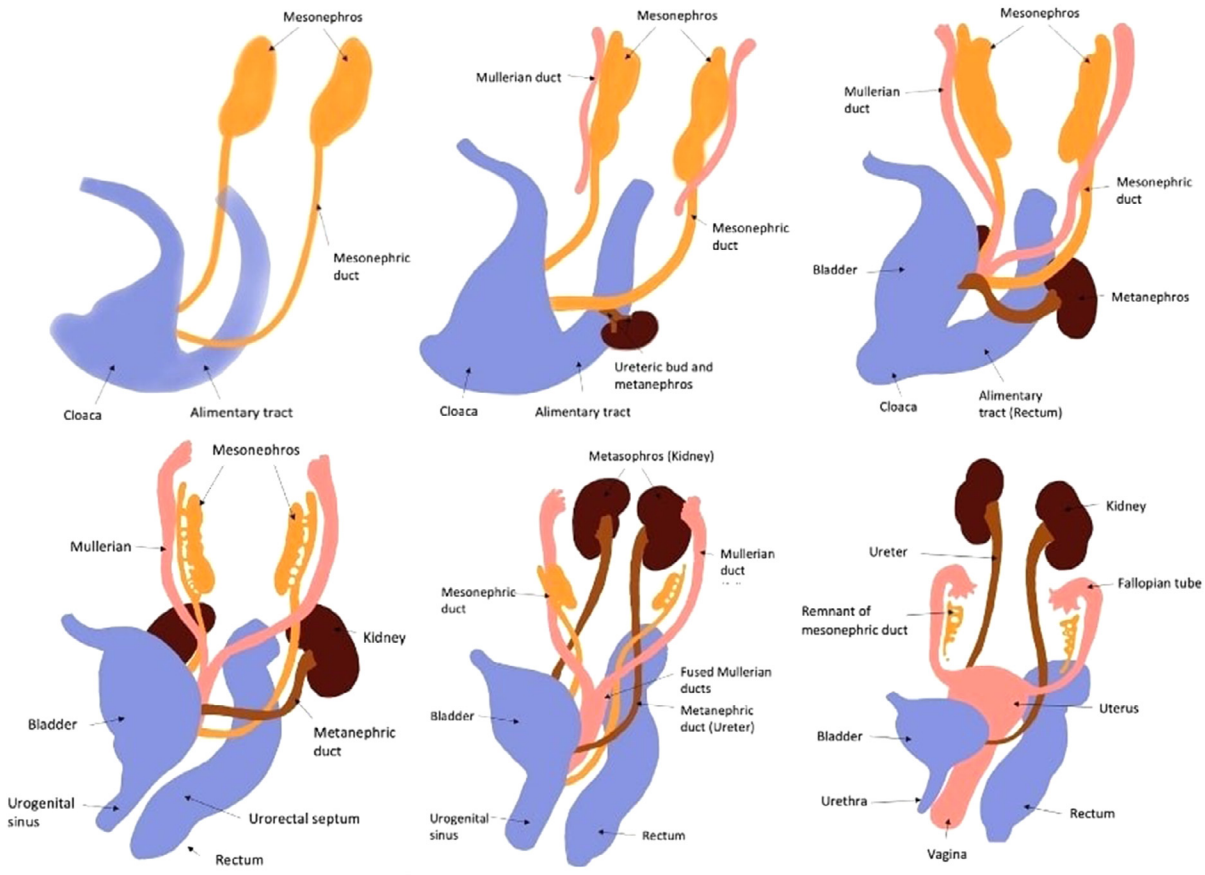

Fig. 7 – The process of formation of the genitourinary system.

Full resection of the vaginal septum has been recommended for those patients with good outcome to relieve the obstruction, prevent the development of further complications, and restore functionality of genital system [27]. Laparoscopic hemihysterectomy may be a simple and effective alternative in treating patients with a didelphic uterus with a hypoplastic cervix [28]. In cases of complication from cervical atresia, ipsilateral hysterectomy is recommended because resection of the septum would not relieve obstructed symptoms.

Conclusion

Herlyn-Werner-Wunderlich syndrome should be suspected in patients presenting with menstrual cramps, vaginal bleeding, dull pain in the hypogastric region, and renal agenesis. Diagnostic imaging techniques, especially ultrasound and MRI, play a crucial role in defining these lesions, identifying related complications and choosing appropriate treatment.

Ethical approval

Institutional Review Board approval was waived due to the nature of the case report. The patients gave consent to publish the case details and any accompanying images.

Author declaration

Conflict of interest

[X] No conflict of interest exists. We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Intellectual property

[X] We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

[X] We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript. [X] IRB approval was obtained (required for studies and series of 3 or more cases) [X] Written consent to publish poten-

tially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

Authorship

The International Committee of Medical Journal Editors (ICMJE) recommends that authorship be based on the following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. [**X**] All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE. [**X**] We confirm that the manuscript has been read and approved by all named authors. [**X**] We confirm that the order of authors listed in the manuscript has been approved by all named authors.

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