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Herlyn-Werner-Wunderlich Syndrome: Challenges in Early Diagnosis

Ayu Natasha[1], Gede Punarbawa[2], Noviyanti[3]
Province Hospital of West Nusa Tenggara, Indonesia
Email: natasha.ayu16@gmail.com

Abstract

Herlyn-Werner-Wunderlich syndrome (HWWS) is a rare *Müllerian* duct anomaly characterized by the triad of uterine didelphys, blocked hemivagina, and ipsilateral renal agenesis. The syndrome often remains asymptomatic until after menarche, when symptoms related to *haematocolpos*, such as severe dysmenorrhea, become apparent. This study presents a case of a 14-year-old female who presented to the Urogynecology Department with complaints of severe dysmenorrhea. Diagnosis was confirmed through CT scan and ultrasound imaging, which revealed the typical triad of HWWS. The treatment involved the surgical incision of the vaginal septum to address the obstructed hemivagina. While HWWS is usually diagnosed after the onset of menstruation due to the development of *haematocolpos*, early detection during infancy could help prevent acute complications. The study emphasizes that gynecologists should consider HWWS in the differential diagnosis when patients present with cyclic pelvic pain, monthly alterations in menstrual flow, pelvic masses, or renal agenesis. Early identification and management of HWWS are crucial to prevent long-term complications.

Keywords: Herlyn-Werner-Wunderlich Syndrome; Dysmenorrhea; Hematocolpos

INTRODUCTION

Herlyn–Werner–Wunderlich syndrome (HWWS) is a rare anomaly of the genitourinary system. HWWS is characterized by uterus didelphys, unilateral blind hemivagina, and ipsilateral renal agenesis—also referred to as obstructed hemivagina and ipsilateral renal agenesis syndrome—which represents a combined anomaly of malformation of the Müllerian duct and mesonephric duct of the female urogenital tract (Zhu et al., 2022). The incidence of HWWS ranges from 0.1% to 3.8% in the female population and from 0.6% to 10% of all Müllerian abnormalities (Batra et al., 2021). This rare condition is often associated with significant clinical symptoms, including menstrual abnormalities, pelvic pain, and infertility (Sullivan et al., 2020). In the diagnosis of HWWS, imaging techniques such as ultrasound and MRI play a critical role in identifying the characteristic features of the syndrome (Patel & Gupta, 2023). Recent studies have indicated that early detection and intervention can lead to better management of reproductive health and prevent complications such as hematometra and pelvic infections (Kaur et al., 2021). Furthermore, surgical treatment options like hemivaginal septum excision or reconstructive surgery may be necessary for symptomatic relief and fertility preservation (Nguyen et al., 2022). HWWS highlights the importance of understanding congenital malformations of the female genital tract for both clinicians and patients (Singh et al., 2021).

The mechanism by which the female reproductive system develops is extremely intricate. Clinicians can diagnose congenital abnormalities of the female reproductive system by having a thorough understanding of its embryology (Nakamura et al., 2021). The genital system is considered undifferentiated during the first six weeks of embryonic development (Zhou et al., 2023). Two pairs of genital ducts, located on either side of the midline, serve as the basis for the sexual differentiation of the female reproductive ducts, which begins early in embryonic development (Lee et al., 2020). These ducts are the Wolffian (mesonephros) and Müllerian (paramesonephros) ducts (Smith & Chang, 2022). Gonadal hormones influence

sexual differentiation, but genetic information governs how embryonic structures differentiate (Huang et al., 2021). The anti-Müllerian hormone (AMH) is a vital hormone that controls sexual differentiation; it halts the development of female genital organs and is produced by Sertoli cells (Kang et al., 2022). The uterus and the round ligaments are produced by the Müllerian ducts, which will continue to expand caudally in the absence of AMH (Shao et al., 2021). At 10 weeks of pregnancy, the caudal portions of the paramesonephros unite before arriving at the urogenital sinus and creating the uterovaginal canal, which then joins the urogenital sinus (Xu et al., 2020). Several signaling molecules and gene expressions control the formation and differentiation of the paramesonephros (Chen et al., 2021). Absence of these transcription factors results in agenesis of the reproductive tract, absence of the kidneys, and agenesis of the Müllerian ducts (Matsuoka et al., 2020). Any interference with this intricate process can result in a variety of congenital abnormalities (Xu et al., 2023).

Because this illness can lead to endometriosis, vaginitis, pelvic inflammation, fallopian tube adhesion, and future fertility problems, it is critical to diagnose and treat it as soon as possible. The symptoms usually start with regular, progressive pelvic pain following menarche. Radiological examination combining magnetic resonance imaging (MRI) and ultrasound is used to diagnose HWWS. *Hematocolpos*, typically identified as a cystic pelvic mass, is caused by the retention of menstrual blood in the obstructed *hemivagina*. The primary therapy is surgery, which involves draining the effusion and removing the vaginal septum.

Prior studies have significantly contributed to the understanding of Herlyn–Werner–Wunderlich syndrome (HWWS), highlighting its pathophysiology and diagnostic methods. Zhuang et al. (2018) provided a comprehensive review of the embryology and anatomical abnormalities associated with HWWS, emphasizing the importance of early diagnosis and the challenges related to its identification in young patients. However, this study focused primarily on the genetic and embryological mechanisms of the syndrome without thoroughly exploring the clinical implications or the specific diagnostic and therapeutic approaches tailored to the age and symptom progression of affected individuals. In contrast, Verma et al. (2020) focused on the clinical manifestations of HWWS in adolescent females, particularly examining how obstructed *hemivagina* presents with progressive pelvic pain following menarche. While the study provides valuable insights into symptoms and surgical treatments, it did not address the long-term outcomes post-surgery or the potential fertility implications for these patients.

The objective of this study is to explore the diagnostic and therapeutic management of Herlyn–Werner–Wunderlich syndrome, focusing on the use of MRI and ultrasound for early detection and the surgical approaches to managing *hematocolpos* and other symptoms. The findings aim to provide clarity on long-term outcomes post-surgery, particularly in relation to fertility and chronic pelvic pain. By offering a comprehensive analysis of the condition's diagnosis, treatment, and follow-up care, this research will help healthcare providers in early intervention, ensuring better patient prognosis and reducing the risk of complications such as endometriosis. The study's benefits extend to improving clinical practices, offering clear guidelines for the treatment of HWWS in adolescent patients, and contributing to the broader understanding of rare reproductive tract anomalies.

Case Presentation

A 14-year-old girl with a history of severe dysmenorrhea was referred from Mataram University Hospital to the Province Hospital West Nusa Tenggara's Urogynecologist Department. Her periods were regular, the menstrual flow typically lasted four to five days, and the menarche had taken place two years prior. She had not yet engaged in sexual activity. Palpable mass on RLQ was the primary physical examination finding. The results of the lab tests were normal. A CT scan at Mataram University Hospital revealed an image suggestive with haematocolpos on the right side and verified the loss of the right kidney. Province Hospital

West Nusa Tenggara conducted a pelvic and abdominal ultrasound, which was verified The sizes of the haematocolpos were 7.1 x 5.4 cm and 5.7 x 4.3 cm. The patient had surgery to remove the vaginal septum, and there were no problems during or after the procedure. She had a smooth recovery and was discharged two days after surgery.

Figure 1. Results of computed tomography scan suggesting Herlyn-Werner-Wunderlich syndrome. Distended left hemivagina with hematocolpos and ipsilateral renal agenesis

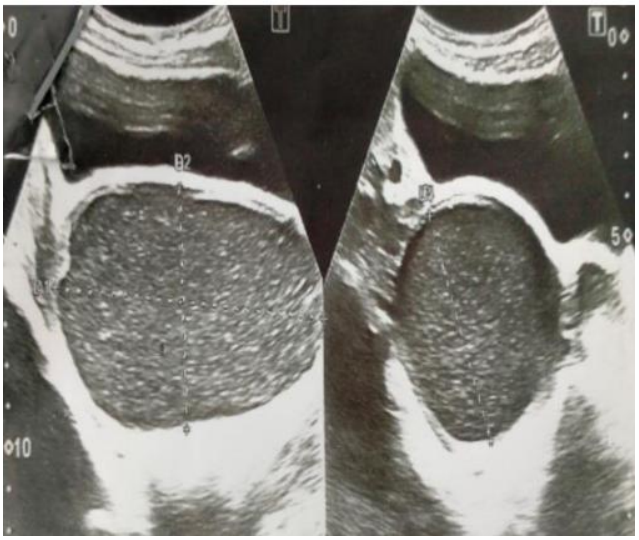

Figure 2. Pelvic ultrasonography revealed hematocolpos

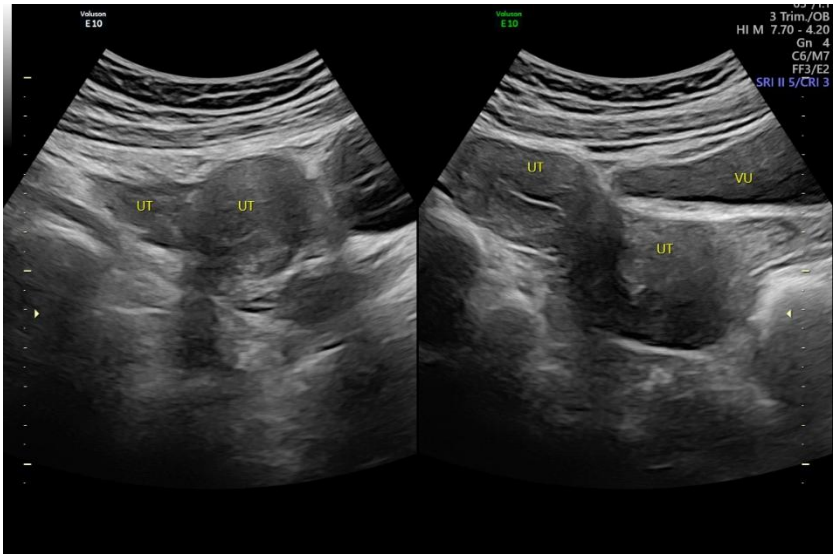

Figure 3. Pelvic ultrasonography post operative revealed not found hematocolpos and there is uterine didelphys

Discussion

HWW syndrome usually manifests as either acute or persistent pelvic discomfort soon after menarche. Other than dismenorrhea, these people may not have any particular symptoms and menstruate regularly (Jeong & Chang, 2009). Additionally, a steadily growing pelvic mass has been reported (Zeng et al., 2023). Delays in therapy can lead to consequences such pelvic adhesions, infections, and endometriosis from retrograde menstruation, which can restrict the genital organs. Therefore, a rapid diagnosis and the avoidance of severe problems depend on clinical suspicion and knowledge of the illness (Jeong & Chang, 2009). It was shown in one study that a number of factors contributed to the diagnosis delay. It is more challenging to diagnose outflow obstruction as the woman frequently gets her period from the unobstructed horn. Second, it is not frequently considered a diagnostic possibility because it is a rare illness. Third, these teenagers are typically prescribed oral contraceptives and anti-inflammatory medications when they visit their pediatrician or family doctor with cyclic dysmenorrhea symptoms. Because these medications reduce or stop menstruation, they unintentionally postpone diagnosis (Zeng et al., 2023). The most popular diagnostic technologies are CT and ultrasonography (Jeong & Chang, 2009). MRI, on the other hand, is thought to be more sensitive for defining minor findings in congenital abnormalities and imaging soft-tissue anatomy. Therefore, it need to be acquired before to any surgical procedure (Kumar et al., 2015). Although it is not required, laparoscopy may be useful in verifying the diagnosis in circumstances where radiologic imaging is not conclusive, particularly when endometriomas need to be removed (Zeng et al., 2023). The preferred method of treating obstructed hemivagina is resection of the vaginal septum (Jeong & Chang, 2009).

All girls with documented kidney problems found antenatally or later, before to the commencement of menstruation, should have their genital tract evaluated by MRI scanning. Due to haematocolpos, haematometra, and retrograde menstruation, this allows us to diagnose some individuals before to menarche and do a surgical repair of the obstruction before any harm has been done (Jeong & Chang, 2009).

CONCLUSION

Herlyn–Werner–Wunderlich (HWW) syndrome, though rare, should be carefully considered in the differential diagnosis of adolescent girls presenting with dysmenorrhea.

Accurate diagnosis relies on close collaboration between radiologists and gynecologists, with ultrasound or MRI serving as the preferred imaging modalities. Management typically involves surgical resection of the vaginal septum and drainage of accumulated blood. Future research should focus on long-term outcomes following surgical intervention, particularly regarding fertility and quality of life, to further optimize care for patients with HWW syndrome.

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