Original Article

New Classification of Herlyn-Werner-Wunderlich Syndrome

Lan Zhu, Na Chen, Jia-Li Tong, Wei Wang, Lei Zhang, Jing-He Lang

Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100730, China

Abstract

Background: Uterus didelphys and blind hemivagina associated with ipsilateral renal agenesis are collectively known as Herlyn-Werner-Wunderlich syndrome (HWWS). In the literature, the syndrome often appears as a single case report or as a small series. In our study, we reviewed the characteristics of all HWWS patients at Peking Union Medical College Hospital (PUMCH) and suggested a new classification for this syndrome because the clinical characteristics differed significantly between the completely and incompletely obstructed vaginal septum. This new classification allows for earlier diagnosis and treatment.

Methods: From January 1986 to March 2013, all diagnosed cases of HWWS at PUMCH were reviewed. A retrospective long-term follow-up study of the clinical presentation, surgical prognosis, and pregnancy outcomes was performed. Statistical analyses were performed using SPSS, version 15.0 (IBM, Armonk, NY, USA). Between-group comparisons were performed using the χ^2 test, Fisher's exact test, and the *t*-test. The significance level for all analyses was set at $P < 0.05$.

Results: The clinical data from 79 patients with HWWS were analyzed until March 31, 2013. According to our newly identified characteristics, we recommend that the syndrome be classified by the complete or incomplete obstruction of the hemivagina as follows: Classification 1, a completely obstructed hemivagina and Classification 2, an incompletely obstructed hemivagina. The clinical details associated with these two types are distinctly different.

Conclusions: HWWS patients should be differentiated according to these two classifications. The two classifications could be generalized by gynecologists world-wide.

Key words: Classification; Diagnosis; Therapy

Introduction

Uterus didelphys and blind hemivagina associated with ipsilateral renal agenesis are collectively known as Herlyn-Werner-Wunderlich syndrome (HWWS), a rare congenital anomaly. The exact etiology of HWWS is still unknown, but it may be caused by the abnormal development of Müllerian and Wolffian ducts.[1,2] Its estimated occurrence is 0.1%–3.8%.[1]

Herlyn-Werner syndrome (i.e., renal agenesis and an ipsilateral blind hemivagina) was initially described in 1971 by Herlyn and Werner.[3] In 1976, Wunderlich described an association of right renal aplasia with a bicornuate uterus and simple vagina in the presence of an isolated hematocervix.[4] Since that time, the anomaly of HWWS has appeared as a single case report or as a small series in the literature. Recent reports regarding uterus didelphys and blind hemivagina associated with ipsilateral renal agenesis have involved eight cases of HWWS and their appropriate interventions in 2004, twelve cases of pediatric HWWS patients in 2006, one case of HWWS and ectopic ureter presenting with vulvodynia and recurrent fever in 2010, and 36 cases of HWWS, with long-term follow-ups, in 1997.[5-8] In 2013, 70 patients with confirmed diagnoses of HWWS who were admitted to the Peking Union Medical College Hospital (PUMCH) between January 1995 and December 2010 were retrospectively reviewed by Tong *et al*.[9] According to the data provided, as well as a literature search, this is the largest case series of HWWS to date.

With a population of 1.4 billion and the largest referral center for complex gynecologic disease in China, at PUMCH, we have diagnosed and treated numerous patients with various female genital malformations over the years. In March 2013, based on Tong' study,[9] we updated relevant information regarding HWWS patients at our hospital.

Methods

From January 1986 to March 2013, 2238 cases of female genital malformations were treated at PUMCH. Of these

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.149208

Address for correspondence: Dr. Lan Zhu, Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China
E-Mail: zhu_julie@vip.sina.com

2238 cases, 79 patients (3.53%) were diagnosed with HWWS. A retrospective long-term follow-up study of the clinical presentation, surgical prognosis, and pregnancy outcomes was performed. All patients were preoperatively diagnosed by ultrasonography and pelvic examination. The anatomical variations among patients were confirmed with intraoperative findings. Data were collected and analyzed. Statistical analyses were performed using SPSS, version 15.0 (IBM, Armonk, NY, USA). Between-group comparisons were performed using the χ^2 test, Fisher's exact test, and the *t*-test. The significance level for all analyses was set at $P < 0.05$. Study approval was provided by the Ethics Committee of PUMCH. All patients provided consent for chart reviews and follow-ups.

Results

From January 1986 to March 31, 2013 the clinical data, long-term follow-up information and pregnancy data were collected from a total of 79 patients with HWWS. An analysis of the medical records from these patients revealed several important clinical characteristics of HWWS that were not previously reported in the literature [Table 1]. According to these newly identified characteristics, we recommend that HWWS be classified according to the complete or incomplete obstruction of the hemivagina as follows: Classification 1, patients with a completely obstructed hemivagina, and Classification 2, patients with an incompletely obstructed hemivagina.

According to our analysis, 24 patients were categorized as Classification 1 and 55 were categorized as Classification 2. The clinical manifestations of patients with complete and those with incomplete obstruction of hemivagina are distinctively different [Table 1]. The mean age at symptoms onset of Classification 1 was significantly younger than the mean age at diagnosis of Classification 2 ($P < 0.05$). The mean age at diagnosis of Classification 1 was also significantly younger than the mean age at diagnosis of Classification 2 ($P < 0.05$). The median time between menarche and the onset of cyclic pelvic pain was 0.3 year for Classification 1 and 3 years for Classification 2. The incidence of dysmenorrhea, intermittent mucopurulent discharge and irregular vaginal hemorrhage for Classification 1 were all significantly lower than Classification 2 ($P < 0.05$). The occurrence of pelvic endometriosis was significantly higher in patients with Classification 1 (38%, 9/24) than in those with Classification 2 (13%, 7/55; $P < 0.05$). Besides, the occurrence of acute pelvic inflammation was significantly lower in patients with Classification 1 (4%, 1/24) than in those with Classification 2 (27%, 15/55; $P < 0.05$).

Table 1: Clinical characteristics of patients with completely or incompletely obstructed hemivagina

Clinical characteristics	Classification 1 (complete obstruction)	Classification 2 (incomplete obstruction)
Age at symptom onset (years)	12.86 ± 1.84	21.68 ± 7.43
Age at time of diagnosis (years)	13.00 ± 2.05	25.74 ± 7.73
Duration between menarche and onset of symptoms (years)	0.3	3
Dysmenorrhea (*n*/*N* (%))	19/24 (79)	27/55 (49)
Intermittent mucopurulent discharge (*n*/*N* (%))	1/24 (4)	28/55 (51)
Irregular vaginal hemorrhage (*n*/*N* (%))	4/24 (17)	14/55 (26)
Endometriosis (*n*/*N* (%))	9/24 (38)	7/55 (13)
Acute pelvic inflammation (*n*/*N* (%))	1/24 (4)	15/55 (27)
Hematometra, hematosalpinx and hemoperitoneum	Common and early	Uncommon
Abdominal pain	Common	Uncommon
Fever and vomiting	Common	Uncommon
Progression to secondary endometriosis, pelvic adhesion, pyosalpinx, pyocolpos	Quick and easy	Gradually

In addition, patients with Classification 1 are more prone to hematometros, hematosalpinx and hemoperitoneum, especially in some more severely affected patients. Acute onset of abdominal pain, fever, and vomiting are common symptoms seveal months after menarche. Endometriosis is common complications, if not treated in time; the condition can progress to secondary endometriosis, pelvic adhesion, pyosalpinx, and even pyocolpos. Although, patients with Classification 2 mainly complaints of purulent or bloody vaginal discharge and ascending genital system infection years after menarche. Most patients with Classification 2 have normal menstrual cycle, but longer menstrual periods, illness attacks years after menarche.

The follow-up period ranged from 1 to 120 months. The median follow-up period was 17 months. The renal agenesis favored the right side in 45 (57%) and the left in 34 (43%) patients. All patients underwent resection of the vaginal septum and drainage of hematocolpos. Eleven (14%) patients underwent abdominal exploration via laparotomy or laparoscopy. In total, 40 women were married and sexually active. There were 52 pregnancies among 28 (85%) of the 33 women who wished to conceive. Pregnancy occurred in the uterus ipsilateral to the hemivaginal septum in 19 (37%) cases, and in the uterus contralateral to the hemivaginal septum in 33 (64%) cases. Eight women experienced separate pregnancies in each of the bilateral uteri. There were no pathologic pregnancies or pregnancy complications. Full resection of the vaginal septum resulted in good outcomes and fertility.

Discussion

Based on our study of HWWS patients at PUMCH, HWWS can be classified into two new types. Below, we describe the characteristics of each classification in detail.

Classification 1, completely obstructed hemivagina

Classification 1.1, with blind hemivagina

In this classification, the hemivagina is completely obstructed; the uterus behind the septum is completely isolated from the contralateral uterus, and no communication is present

between the duplicated uterus and vagina. Hematocolpos may occur only a few months after menarche. Hematometra and hematosalpinx occurred in some more severely affected patients, as well as bleeding in the periadnexal and peritoneal space. Patients with this classification have an earlier age of onset, with a short time from menarche to attack. The presenting symptoms may include the acute onset of abdominal pain, fever, and vomiting. Hemoperitoneum, due to bleeding from the fallopian tube, can be found at surgery.[5,10] Endometriosis can result from blood reflux into the abdominal cavity and may have dire consequences. If not treated in time, the condition can progress to secondary endometriosis, pelvic adhesion, pyosalpinx, and even pyocolpos [Figure 1].[6,7]

Classification 1.2, cervicovaginal atresia without communicating uteri

In this classification, the hemivagina is completely obstructed; the cervix behind the septum is maldeveloped or atresic, and menses from the uterus behind the septum cannot outflow through the atresic cervix. Patients with this classification have similar clinical features as patients with Classification 1.1 [Figure 2].

Classification 2, incompletely obstructed hemivagina

Classification 2.1, partial reabsorption of the vaginal septum

In this classification, a small communication exists between the two vaginas, which make the vaginal cavity behind the septum incompletely obstructed. The uterus behind the septum is completely isolated from the contralateral uterus. The menses can outflow through the small communication, but the drainage is impeded. These patients have a later age of onset. The attack often comes years after menarche. Purulent or bloody vaginal discharge can be the chief complaints. Patients often have ascending genital system infection [Figure 3].

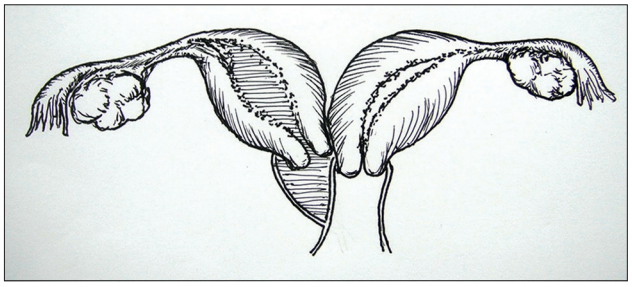

Figure 1: Classification 1.1, with blind hemivagina.

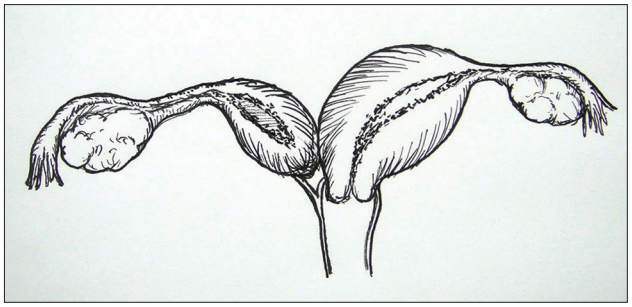

Figure 2: Classification 1.2, cervicovaginal atresia, without communicating uteri.

Classification 2.2, with communicating uteri

In this classification, the hemivagina is completely obstructed, and a small communication exists between the duplicated cervices. Menses from the uterus behind the septum can outflow through the communication to the offside contralateral cervix. Because the communication is small, the drainage is still impeded [Figure 4].

Diagnosis

Sonography and magnetic resonance imaging (MRI) are extremely useful in diagnosing and classifying Müllerian duct anomalies.[10] The ultrasonography features of these conditions include uterine anomalies (didelphic/bicornuate uterus), with or without uterine effusion; an echo-free area below one cervix, sometimes with intensive dot-like hyperechoic regions in the no-echo area; and ipsilateral renal agenesis with compensatory hypertrophy of the contralateral kidney. Centesis of the paravaginal mass indicates accumulated pus or blood. MRI with multiplanar image acquisition provides more detailed information.[11] For patients with Classification 2.2, hysterosalpingography showed that iodine oil passed through the communication between the duplicated cervices to the contralateral uterus and then the cavity behind the septum.

Treatment

To alleviate symptoms and retain fertility in these patients, the most effective treatment is surgery. Resection of as much of the obstructing vaginal septum as possible is the optimal surgery for patients with Classifications 1.1, 2.1, and 2.2. Most patients can recover completely after resection of the

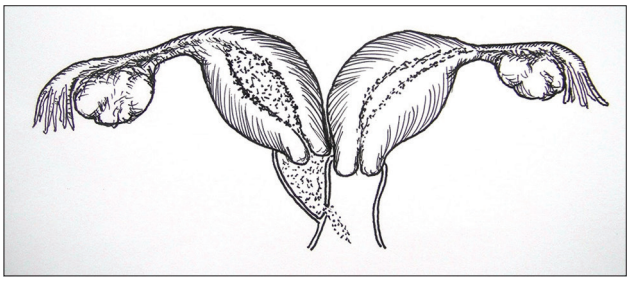

Figure 3: Classification 2.1, partial reabsorption of the vaginal septum.

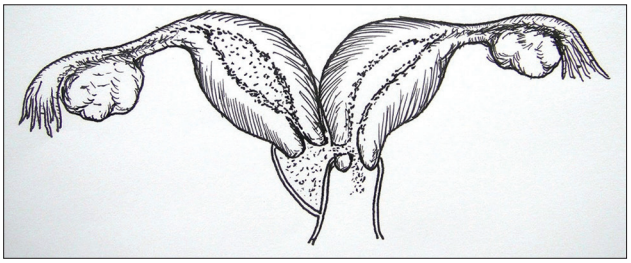

Figure 4: Classification 2.2, incompletely obstructed hemivagina with communicating uteri.

vaginal septum. The best time for surgery in these patients is approximately at the time of menstruation, particularly in patients with Classification 1.1, as a large distended hematocolpos is easy to visualize and palpate, which aids in resection. Hur *et al*. suggested that laparoscopic evaluation should not be omitted in patients who have an obstructed vaginal septum, which may inevitably result in massive menstrual regurgitation or even endometriosis and pelvic adhesions, which cannot be detected by ultrasonography or MRI.[12] Treatment for patients with Classification 1.2 differs from the treatment of patients with other classifications. Cervical agenesis is difficult to correct surgically. After being diagnosed with renal agenesis or renal malformation by imaging studies, laparoscopic or the transabdominal resection of the atresic uterus is suggested.

Prognosis

In conclusion, the prognosis of HWWS is good with early diagnosis and early treatment, except for patients with Classification 1.2. In cases complicated by cervical atresia, ipsilateral hysterectomy is suggested because resection of the septum would not relieve obstructed symptoms. The onset of clinical manifestations was much earlier and more serious in patients with completely obstructed hemivaginal septa compared with those with incomplete obstructions. This new classification of HWWS can help to provide clinicians with earlier diagnoses and treatments to prevent secondary pelvic endometriosis and pelvic inflammation.

References

1. Burgis J. Obstructive Müllerian anomalies: Case report, diagnosis, and management. Am J Obstet Gynecol 2001;185:338-44.
2. Tridenti G, Armanetti M, Flisi M, Benassi L. Uterus didelphys with an obstructed hemivagina and ipsilateral renal agenesis in teenagers: Report of three cases. Am J Obstet Gynecol 1988;159:882-3.
3. Herlyn U, Werner H. Simultaneous occurrence of an open Gartner-duct cyst, a homolateral aplasia of the kidney and a double uterus as a typical syndrome of abnormalities. Geburtshilfe Frauenheilkd 1971;31:340-7.
4. Wunderlich M. Unusual form of genital malformation with aplasia of the right kidney. Zentralbl Gynakol 1976;98:559-62.
5. Zurawin RK, Dietrich JE, Heard MJ, Edwards CL. Didelphic uterus and obstructed hemivagina with renal agenesis: Case report and review of the literature. J Pediatr Adolesc Gynecol 2004;17:137-41.
6. Gholoum S, Puligandla PS, Hui T, Su W, Quiros E, Laberge JM. Management and outcome of patients with combined vaginal septum, bifid uterus, and ipsilateral renal agenesis (Herlyn-Werner-Wunderlich syndrome). J Pediatr Surg 2006;41:987-92.
7. Tong J, Zhu L, Chen N, Lang J. Endometriosis in association with Herlyn-Werner-Wunderlich syndrome. Fertil Steril 2014;102:790-4.
8. Candiani GB, Fedele L, Candiani M. Double uterus, blind hemivagina, and ipsilateral renal agenesis: 36 cases and long-term follow-up. Obstet Gynecol 1997;90:26-32.
9. Tong J, Zhu L, Lang J. Clinical characteristics of 70 patients with Herlyn-Werner-Wunderlich syndrome. Int J Gynaecol Obstet 2013;121:173-5.
10. Prada Arias M, Muguerza Vellibre R, Montero Sánchez M, Vázquez Castelo JL, Arias González M, Rodríguez Costa A. Uterus didelphys with obstructed hemivagina and multicystic dysplastic kidney. Eur J Pediatr Surg 2005;15:441-5.
11. Scarsbrook AF, Moore NR. MRI appearances of Müllerian duct abnormalities. Clin Radiol 2003;58:747-54.
12. Hur JY, Shin JH, Lee JK, Oh MJ, Saw HS, Park YK, *et al.* Septate uterus with double cervices, unilaterally obstructed vaginal septum, and ipsilateral renal agenesis: A rare combination of Müllerian and Wolffian anomalies complicated by severe endometriosis in an adolescent. J Minim Invasive Gynecol 2007;14:128-31.

Received: 13-07-2014 **Edited by:** Yuan-yuan Ji
How to cite this article: Zhu L, Chen N, Tong JL, Wang W, Zhang L, Lang JH. New Classification of Herlyn-Werner-Wunderlich Syndrome. Chin Med J 2015;128:222-5.

Source of Support: Nil. **Conflict of Interest:** None declared.