The New Journal of Urology
*eISSN* 3023-6940
*doi:* https://doi.org/10.33719/nju1421307

*CASE REPORT*

# Zinner Syndrome Versus Herlyn-Werner-Wunderlich Syndrome; Rare Congenital Genitourinary Malformations and Literature Review

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***Submitted:*** *2024-01-17*
***Accepted:*** *2024-04-30*

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**Abstract**
Zinner Syndrome (ZS) and Herlyn-Werner-Wunderlich Syndrome (HWWS) are congenital genitourinary anomalies accompanied by ipsilateral renal agenesis. These syndromes, which can cause symptoms such as infertility, pelvic pain, and bladder irritation, can be diagnosed by digital rectal examination, transrectal and abdominal ultrasonography (US), Computer Tomography (CT) and more ideally Magnetic resonance imaging (MRI). Similar physiopathological processes are observed in both syndromes and urogenital malformations accompany renal agenesis. We aimed to discuss the three cases of ZS in men and two HWWS cases in women, which are rarely observed in the literature.

**Keywords:** Zinner syndrome, Herlyn-Werner-Wunderlich syndrome, Seminal vesicle cysts, renal agenesis, mullerian duct anomaly, blind hemivagina, uterus didelfis

## INTRODUCTION

Zinner syndrome (ZS) is an upper urinary tract malformation first described in 1914. It is characterized by unilateral renal agenesis, ipsilateral seminal vesicle occlusion and ipsilateral ejaculatory duct obstruction (1). Herlyn-Werner-Wunderlich syndrome (HWWS) is a rare variant of mullerian canal anomalies, occurring with blind hemivagina, uterine didelfis and unilateral renal agenesis triad (2).

A developing fetus is constantly under hormonal regulation. In the first phase of development, both XX and XY channels are indistinguishable. In the next stage, depending on whether there are testosterone and Mullerian inhibitory factor, it differs as Wolfian duct or Mullerian duct

Similar physiopathological processes are observed in both syndromes and urogenital malformations accompany renal agenesis. We aimed to discuss the three cases of ZS in men and two HWWS cases in women, which are rarely observed in the literature. Although there is no definitive information about the etiology and pathogenesis of HWWS, it is associated with anomalies formed by the paramesonephric (Müller) and mesonephric (Wolff) ducts (3).

**Cite;** Türkoğlu S, Göya C, Demir M. Zinner Syndrome Versus Herlyn-Werner-Wunderlich Syndrome; Rare Congenital Genitourinary Malformations and Literature Review. New J Urol. 2024;19(2):95-102. **doi:** https://doi.org/10.33719/nju1421307

HWWS is a developmental anomaly that is accompanied by ipsilateral hemivagina obstruction and renal agenesis and is not a genetic disorder. Diagnosis can be made through non-invasive procedures such as physical examination methods and radiological examination. Most patients with HWW syndrome need to be treated surgically. The treatment plan should be made according to the affected anatomical disorder of each patient. Therefore, a detailed and comprehensive evaluation should be made before surgery.

***Case- 1.*** The first case was a 28-year-old male patient who was admitted to the urology outpatient clinic with infertility. After physical examination and medical history, spermiogram was performed with suspicion of testicular dysfunction. Ultrasonography (US) examination was performed due to detection of azoospermia in spermiograms performed at two different times. Furthermore, the semen volume was 0.8 cc, and the pH was 7.2 in both tests. A cystic lesion was detected in the right seminal vesicle, but it could not be detected in the right kidney (agenesis). No significant abnormality was detected in the hormone tests performed.

Computed tomography (CT) revealed right renal agenesis (**Fig. 1.a.b**). The testicular vein calibration draining into the left renal vein was slightly thin and increased vascularity due to pelvic congestion on the left side of the pelvic region were observed **(Fig. 1.c)**. There was also cystic tubular dilatation at the seminal vesicle level **(Fig. 1.d).** In MRI examination; at the seminal vesicle localization, a cystic tubular hyperintense appearance was observed, and the tubular cystic structure on the right was seen extending towards the superior. There was a cystic nodular structure in the central of prostate that caused obstruction at the ductus ejaculatorius level (**Fig. 2**). In addition, these cystic structures were found to be complicated by hemorrhage in T1 Weight images (**Fig. 3**).

***Case- 2.*** In the routine US examination performed in a 36-year-old male patient who was followed up for Acute myeloid leukemia(AML), cystic dilated tubular structures with a maximum diameter of 30 mm were observed in the seminal vesicle localization. Further radiological examinations were performed after the patient described that he had anejaculation and had recurrent pelvic pains. In contrast-enhanced CT examination; right renal agenesis was observed and a cystic lobular lesion was detected at the level of the seminal vesicle (**Fig. 4.a.b).**

***Case-3.*** In another case, dilated seminal vesicles and renal agenesis were observed in MRI examinations performed at the outpatient clinic where he admitted with similar complaints. MRI examination shows dilated seminal vesicles on coronal fat-suppressed T2 and T2-weighted images (**Fig. 5.a.b.c**).

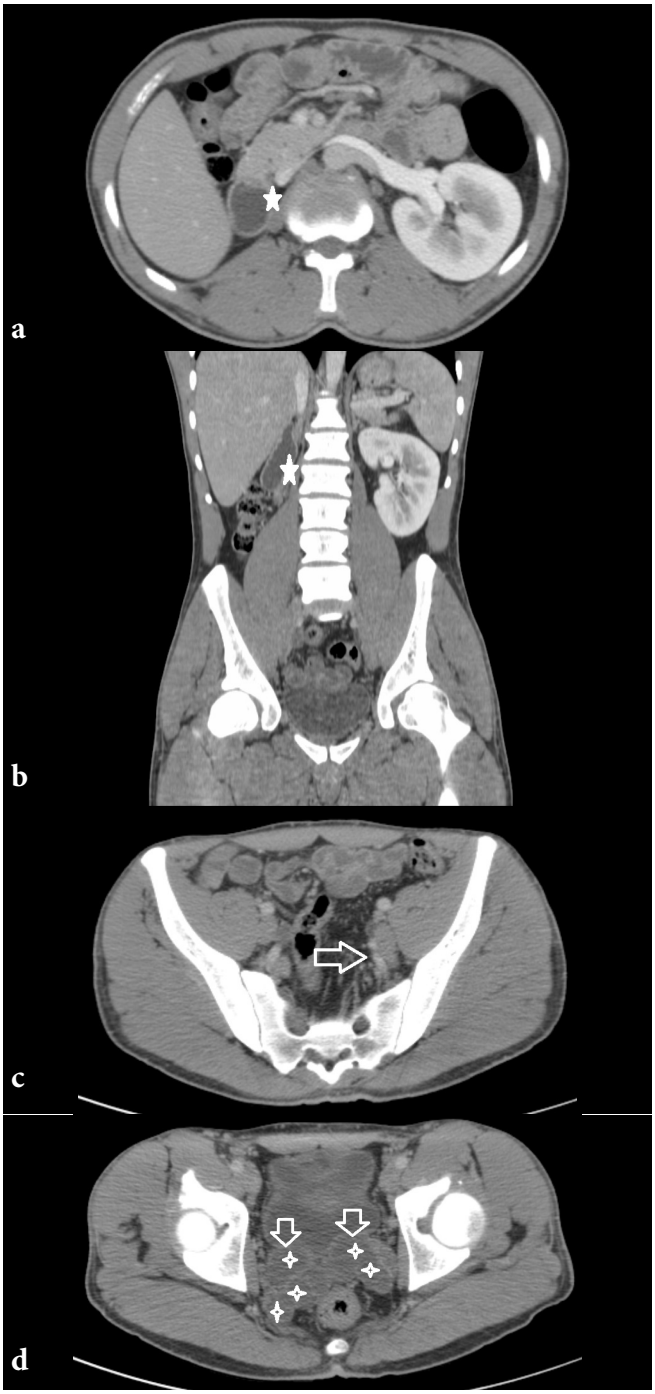


**Fig. 1.** In CT examination; Right kidney agenesis is observed **(a-b).** In the left side of the pelvic region, there is an increase in pelvic vascularity **(c)** and an expansion in the cystic tubular structure at the level of the seminal vesicle **(d).**

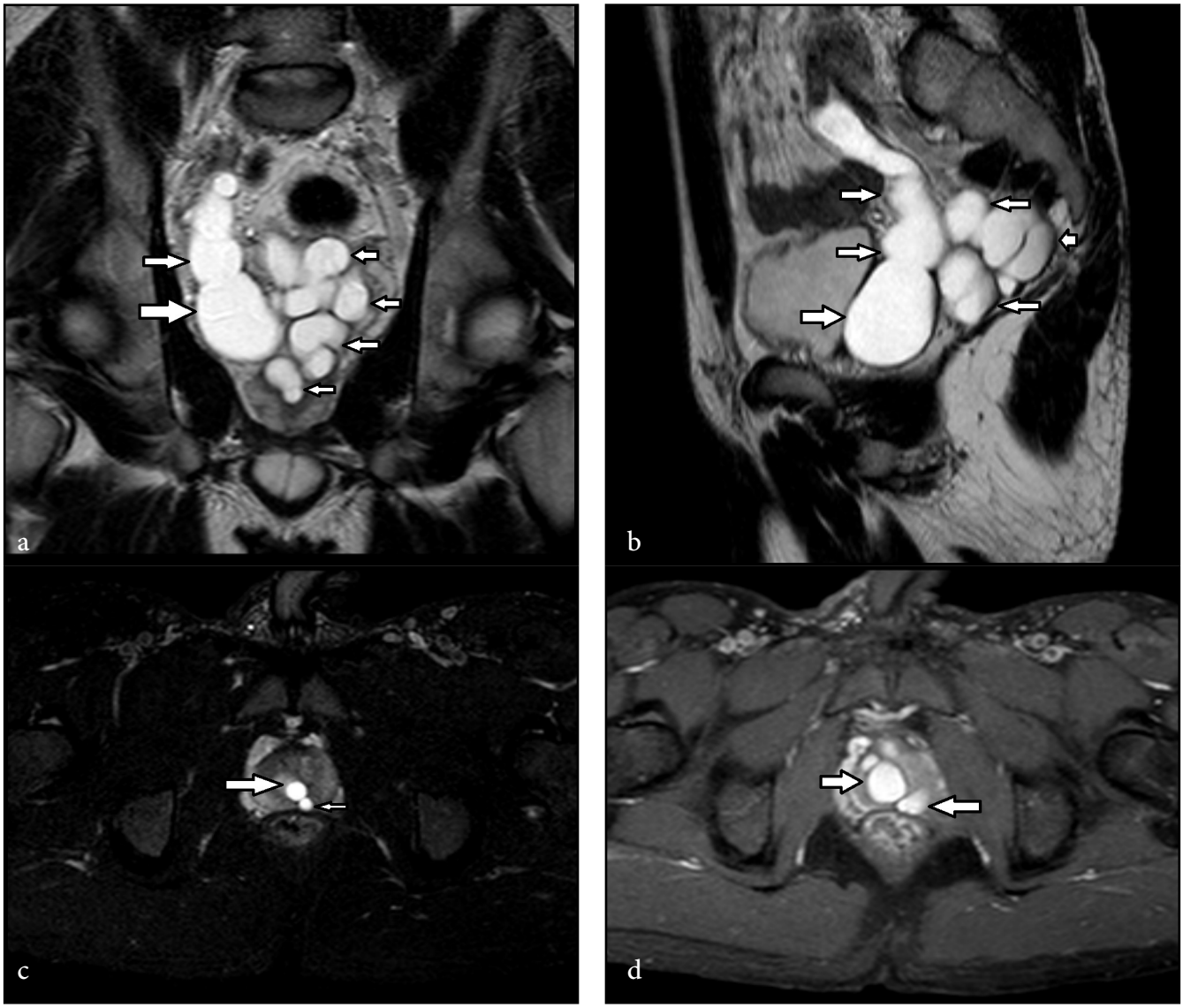


**Fig. 2.** In the seminal vesicle lobe, T2 Weight images show a cystic tubular hyperintense appearance **(a)** and the tubular cystic structure extends towards the superior on the right **(b).** In the prostate central section, a cystic nodular structure that causes obstruction at the level of ductus ejaculatorius is observed **(c-d).**

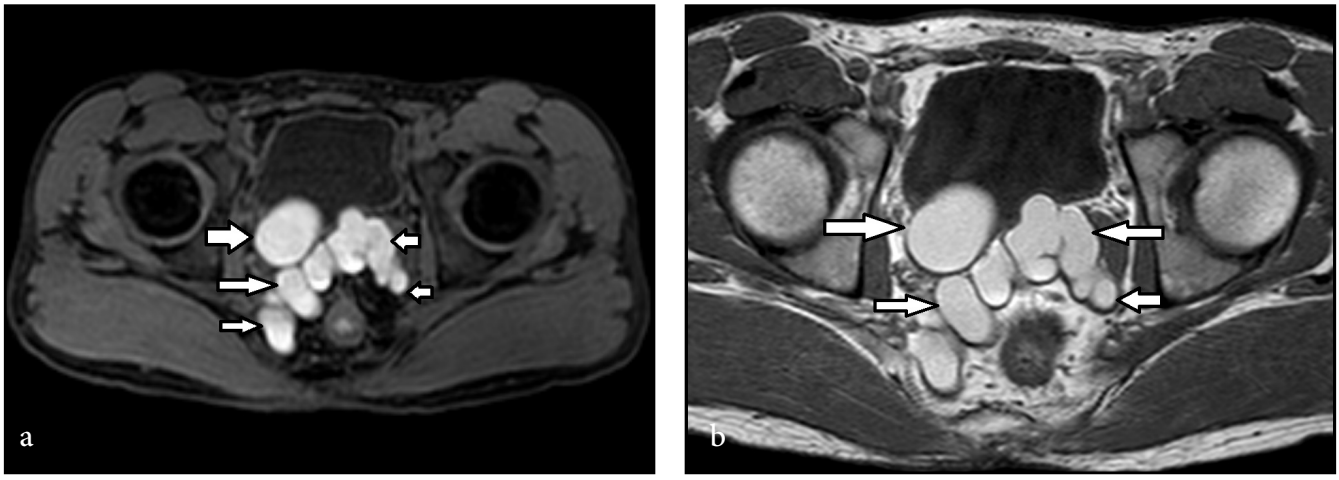


**Fig. 3.** These cystic structures are observed to be complicated by hemorrhage in T1 Weight image **(a)** and fat-sat **(b)** images.

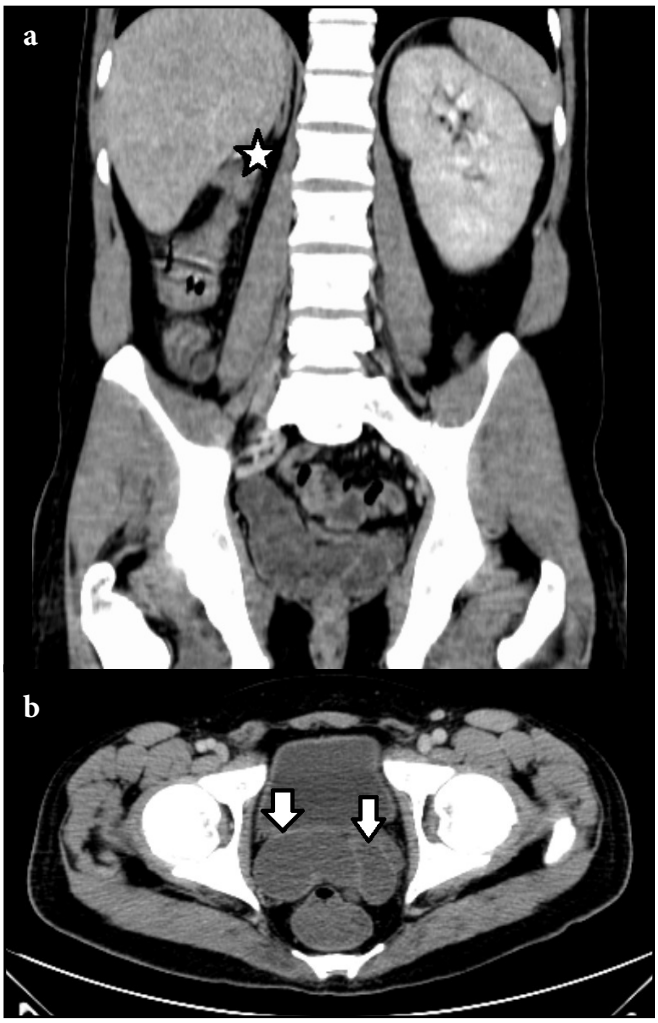


**Fig. 4.** In the CT examination of 36 y.o male patients; On the right, renal agenesis was observed**(a)** and a cystic lobular lesion was observed at the level of the seminal vesicle **(b).**

***Case-4.*** 14 years-old female petient admitted with recurrent abdominal pain and irregular menstrual complaint. Imperforate hymen was detected on physical examination. Thereupon, pelvic US and MRI were examined for further examination.

In ultrasonography examination; the right kidney was not observed in place (right renal agenesis) and endometrial cavity filled with a large hemorrhagic collection extending into the cervix was observed in the pelvic area.

In MRI examination; endometrial cavity showing two separate endometrial bands surrounded by separate muscle layers(uterine didelphys) and the right of this, obstructed blind hemivagina was detected was observed in coronal T2-weighted image (**Fig. 6.a**). In T2-weighted sagittal images; It

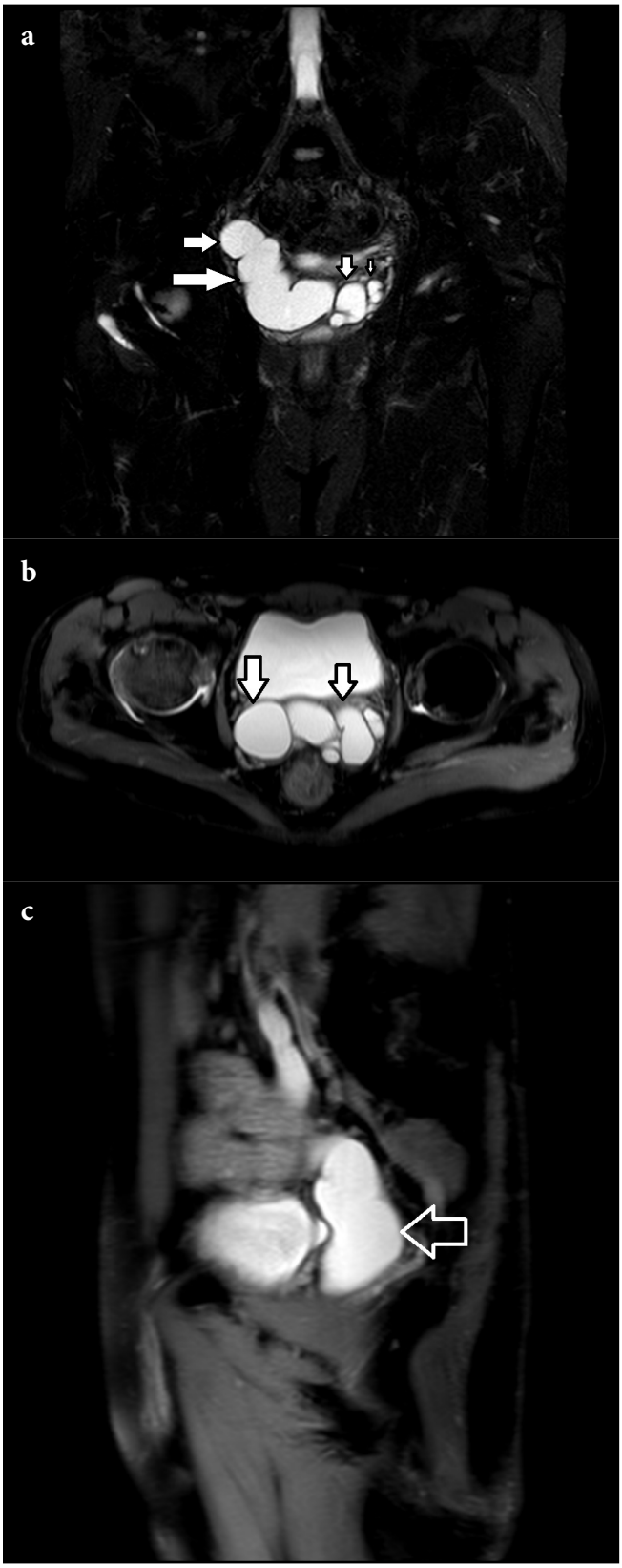


**Fig. 5.** On T2-weighted fat-sat coronal **(a)** and axial **(b)** images; Tubular enlargement was detected in the cystic structure starting from the bilateral prostate central to the lateral and extending from the bladder inferior to the right.

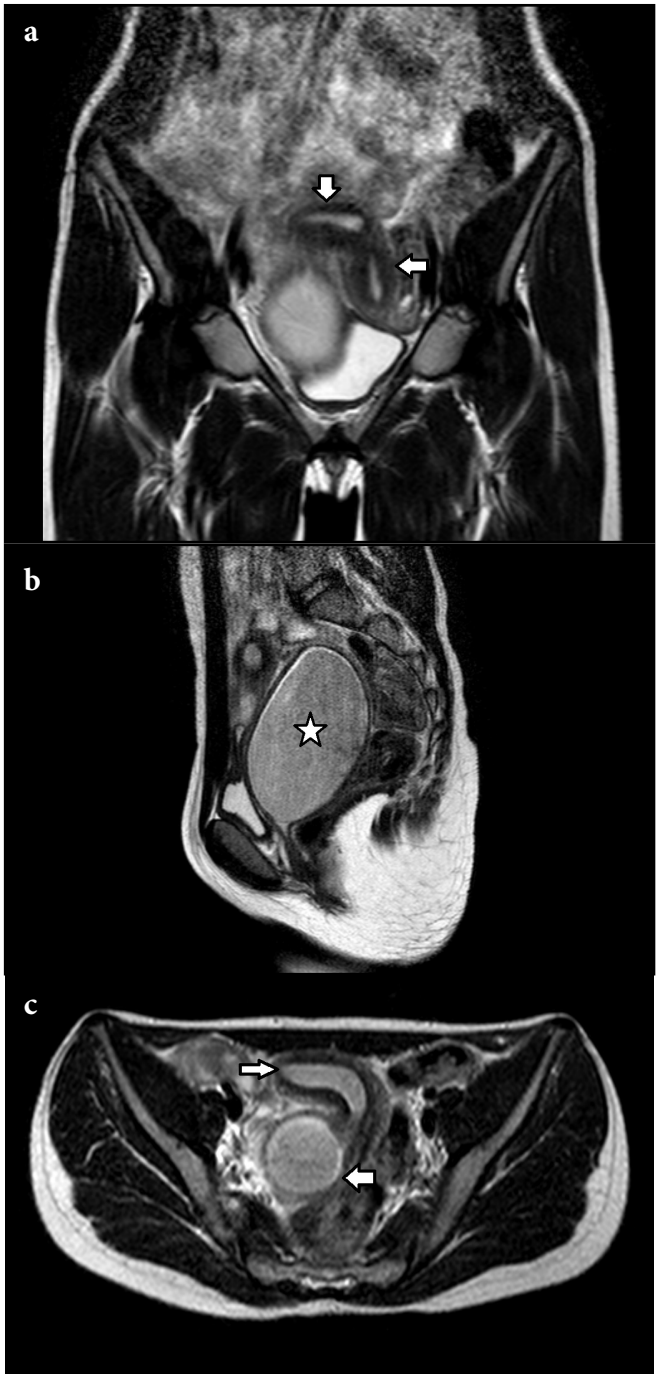


**Fig. 6.** On MRI coronal T2-weighted image **(a)**, an endometrial cavity showing two separate endometrial bands (uterine didelphys) surrounded by separate muscle layers was observed. And to the right of this, there is an obstructed blind hemivagina. Sagittal T2-weighted image **(b)** showing dilation of cervical canal with abrupt termination at vaginal fornix , resulting in obstructed hemivagina. Endometrial cavity was dilated and contained hemorrhagic collection. Axial T2-weighted image **(c)** showing two separate uterine horns and distention of endometrial cavity.

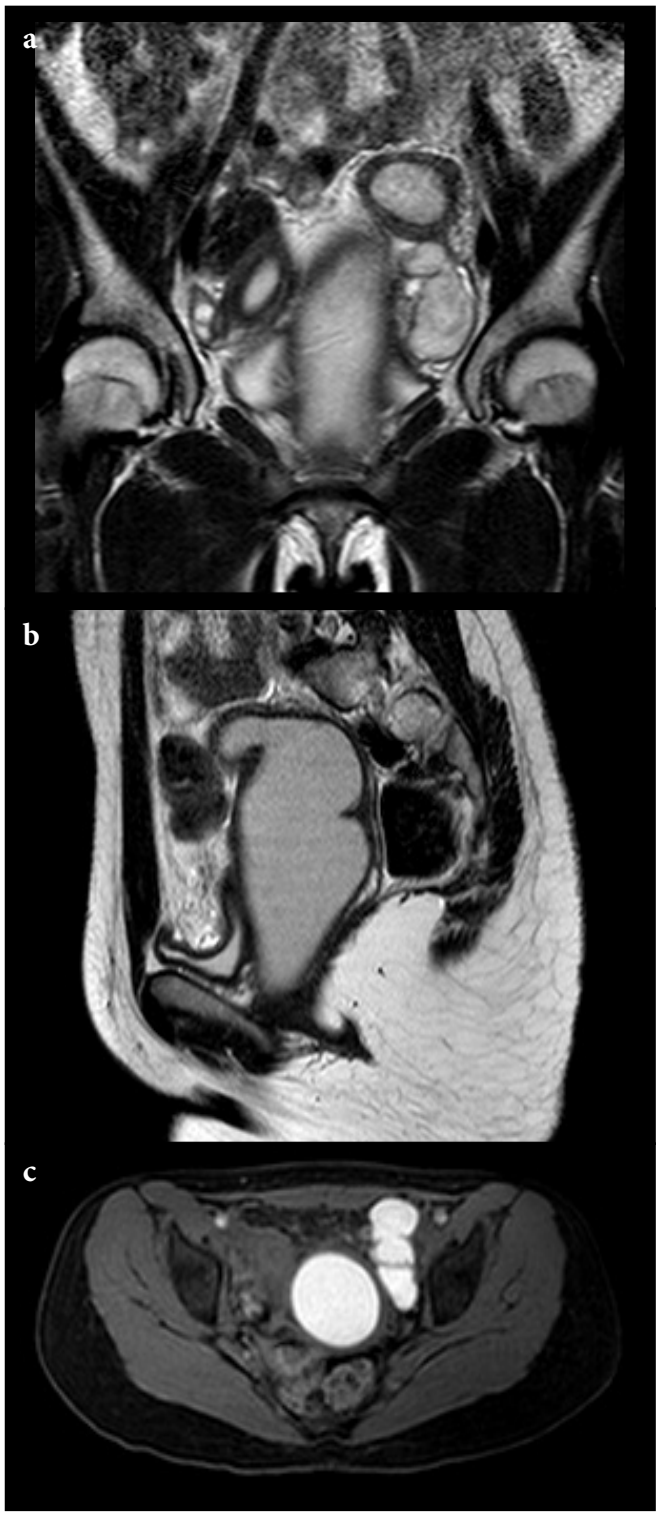


**Fig. 7.** In T2-weighted coronal MRI; Two separate endometrial cavities (a), enlargement of the cervical canal (arrow) with sudden termination of the vaginal fornix in the sagittal image (arrow), hemorrhagic collection in the endometrial cavity with obstructed hemivagina **(b).** In the axial fat-sat image; hematosalpinx image is observed in the left tuba (long arrow) **(c).**

resulted in obstructed hemivagina, which showed the cervical canal dilation with a sudden termination in the vaginal fornix. The endometrial cavity was dilated and contained a hemorrhagic collection. (**Fig. 6.b**). In T2-weighted axial images; Distention of two separate uterine horns and right endometrial cavities was detected (**Fig. 6.c**). The findings were consistent with Herlyn-Werner-Wunderlich syndrome.

***Case-5.*** 19 years-old female patient with previously diagnosed renal agenesis admitted with irregular and painful menstruation, infertility, recurrent cyclic abdominal pain and mass complaints in the pelvic region. On physical examination; there was a palpable, well-defined soft abdominal mass extending towards the superior in the pelvic area. On gynecological examination, imperforated hymen and very enlarged, bulging uterus-cervix were detected. In the MRI examination; there was two separate endometrial cavities, widening of the cervical canal with sudden termination in the vaginal fornix, hemorrhagic collection in the endometrial cavity with obstructed hemivagina on coronal T2 **(Fig. 7.a)**, sagittal **(Fig. 7.b)** and axial T1 weighted images **(Fig. 7.c)**. There was also a hematosalpinx image in the left tuba. Radiological and clinical findings confirmed the diagnosis of Herlyn-Werner-Wunderlich syndrome.

## DISCUSSION

Zinner syndrome is a Wolffian duct abnormality known with unilateral renal agenesis, ipsilateral seminal vesicle cyst and ejaculatory duct obstruction. HWWS is a rare mesonephric duct malformation with mullerian duct anomaly characterized by uterus didelphys, clogged blind hemi-vagina and ipsilateral renal agenesis (OHVIRA) syndrome. It was first reported by Wilson in 1925 (4).

Congenital anomalies of kidney and urinary tract are birth defects that affecting approximately 1% of live births (5). These anomalies include a wide range of malformations such as obstruction of ureteropelvic junction, kidney dysplasia, hydropic or ectopic and short ureters caused by deficiencies in embryonic kidney and lower urinary tract development. Although many gene sequences have been identified, the genetic causes of these malformations are still largely unknown (6). The morphogenesis of the urogenital system is affected by the nephric duct (ND), a common structure also known as the Wolffian duct (7). It is said by the authors that 1-2% of the cause of infertility in men has ND defects (8). Malformations that show a common etiology between the development of the urinary and genital system in the kidneys of patients with hymen impereforation of newborn girls are observed.

Zinner syndrome is based on the common origin of ureter buds and seminal vesicles from the Wolffian duct, associated with upper urinary tract abnormalities and seminal vesicle malformation (9). This syndrome occurs after an inadequate movement in the first trimester of embryogenesis. The ureteral bud originates from the dorsal aspect of the distal mesonephric canal and extends dorsocranially to meet and stimulate the transformation of the metanephric blastema to form the adult kidney. The mesonephric duct is divided into epididymis, paradidim, vas deferens, ejaculatory duct, seminal vesicle and hemitrigon under the influence of testosterone and anti-muller hormone (10). Alternatively, there will be abnormal ureteral budding, which leads to ipsilateral kidney agenesis or dysplasia and atresia of the ejaculatory duct and, consequently, to occlusion and cystic dilatation of the mesonephric duct (11).

HWWS is an anomaly it's etiopathogenesis is not clearly explained and its true incidence is unknown. Development in embryological period is affected by genetic and environmental factors. HWWS also moves towards the paramesonephric system and methanephrosis (12).

The upper two-thirds of the uterus, fallopian tube, cervix, and vagina develop from paired paramesonephric ducts. Then, caudally, it laterally passes into the mesonephric duct, and finally, in the midline, it comes in close contact with the paramesonephric canal from the opposite side and merges to form the upper part of the uterus, cervix and vagina (13). If they do not fuse, two separate hemiuterins and hemicervices occur, resulting in mullerian anomalies associated with OHVIRA syndrome (14).

As in our cases; most patients are asymptomatic from two to four decades until high sexual and reproductive activity periods (15). The clinical picture is related to the size of the seminal vesicle cysts. Cysts smaller than 5 cm are usually diagnosed on abdominal or digital rectal examination. Symptoms occur after progressive dilatation of the seminal vesicles due to the accumulation of secretions after inadequate drainage secondary to the ejaculatory canal atresia (16). In our cases, complicated appearance was observed with hemorrhage due to these drainage disorders. Seminal vesicles are localized in the posterior of the bladder and therefore enlarged cysts may cause different symptoms

due to bladder irritation, such as dysuria, recurrent urinary tract infections, infertility painful ejaculation epididymitis and prostatitis (17-18). Larger cysts (> 12cm) can cause bladder outlet obstruction, colon obstruction, or perianal pain.

Various imaging techniques can be used in the diagnostic study of these congenital malformations. These can be listed as intravenous urography, transrectal, ultrasonography, CT examination, cystoscopy and MRI. Intravenous urography can be used to assess collecting duct system abnormalities or absence and therefore may indicate kidney agenesis. Transrectal USG can be used to determine the size and location of the associated cystic mass and its association with the seminal vesicle or prostate. It may include symptoms suggestive of bleeding or infection but is limited to small field of vision. Pelvic USG can help in the differential diagnosis, to examine whether the kidneys are in normal location, and to accurately identify the relationship of the cystic mass in the pelvic area with adjacent structures.

CT examination can accurately demonstrate pelvic anatomy and atypical kidney structures, the presence of kidney or its association with associated pathology. MR imaging may be preferred due to its relatively better contrast resolution, seminal vesicles, pelvic structures, and collector system imaging. In both of our cases, MRI was performed following CT examination.

Treatment of Zinner syndrome; Surgical resection can be performed for symptomatic seminal vesicle cysts. Also, there is infertility and there is a desire for fertility, testicular sperm extraction can be performed. There are other methods such as transrectal or transurethral interventional procedures or transurethral resection of the seminal coliculus and vas deferens. In HWWS, a therapeutic laparoscopic evaluation or vaginal septum excision can be performed to remove obstruction.

As a result; Zinner syndrome and HWWS are congenital genitourinary anomalies accompanied by ipsilateral renal agenesis. The diagnosis of these patients, which can cause symptoms such as infertility, pelvic pain, and bladder irritation, can be selected as digital rectal examination, transrectal and abdominal USG, CT examination, and the more ideal imaging method MRI. Clinical suspicion and early diagnosis can contribute to directing treatment.

**Compliance with ethical standards:** This article does not contain any studies with human participants or animals performed by any of the authors.

**Funding:** This study , being a case report, did not require any funding.

**Conflict of interest**: The authors declare that they have no conflict of interest.

**Consent of informed:** Written informed consent was obtained from the patients for publication of these reports and accompanying images.

**Authors' contributions:** ST, CG and MD analyzed and interpreted the patient data regarding the clinical and radiological findings of the patient. ST was major contributor in writing the manuscript. All authors read and approved the final manuscript.

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