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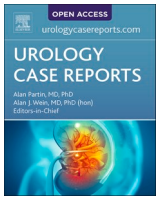

Pediatrics

Zinner syndrome with contralateral hydronephrosis: A rare congenital condition

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ABSTRACT

Zinner Syndrome (ZS) is a rare congenital genitourinary abnormality defined by seminal vesicle cysts, ejaculatory duct obstruction, and unilateral renal dysplasia or agenesis. Patients can be asymptomatic, while others experience pain, urinary or ejaculatory symptoms and infertility. A patient that presented with painless gross hematuria was found to have a large pelvic cystic structure, an absent left kidney, multiple fluid collections in the region of the left seminal vesicle and right hydronephrosis. Hydronephrosis is atypical in ZS. This patient eventually developed right flank and pelvic pain treated with robotic-assisted laparoscopic excision of the pelvic cystic structure and extravesical ureteral reimplantation.

1. Introduction

Zinner syndrome is a rare congenital urological anomaly involving abnormal development of structures derived from the Wolffian duct. The syndrome is characterized by a triad of seminal vesicle cysts, ejaculatory duct obstruction, and unilateral renal dysplasia or agenesis.[1–3] Due to its rarity, the diagnosis of ZS requires a high index of suspicion and multidisciplinary involvement. Symptoms mimic more common lower urinary tract diseases and may include dysuria, hematuria, urinary obstruction, infertility, and pelvic, perineal or scrotal pain. Most commonly, ZS is detected in the 2nd to 4th decade of life as prepubertal patients are generally asymptomatic.[3] The most frequent radiological finding is a retrovesical cyst.[1] With widespread use of ultrasound during pregnancy and infancy, renal agenesis or dysplasia is often discovered early in life. This should prompt consideration of other associated genitourinary malformations.

2. Case presentation

A 5-year-old boy presented to the emergency room with two isolated episodes of painless gross hematuria. There were no other symptoms or signs of infection. His vitals, labs, and physical exam were all normal. A renal and bladder ultrasound showed a large cystic structure in the pelvis, an absent left kidney, and mild to moderate right hydroureteronephrosis. The ultrasound was presumed to represent a left ectopic multicystic dysplastic kidney (MCDK). The initial study at age of presentation was a MAG-3 Nuclear Renogram, which expectedly showed no tracer uptake in the left side and an indeterminate T-1/2 but suggestion of some degree of ureterovesical junction obstruction on the right. Voiding cystourethrogram demonstrated normal bladder distention with no vesicoureteral reflux. During voiding, a rounded contrast-filled out pouching developed from the region of the right inferolateral bladder wall. The bladder completely emptied but the contrast-filled out pouching persisted.

The patient's initial working diagnosis was left ectopic pelvic MCDK. His right flank pain and moderate chronic right hydroureteronephrosis were thought to result from either intermittent external compression from the ectopic MCDK or congenital ureterovesical junction obstruction. A follow up MAG-3 nuclear renogram at age 15 showed a T-1/2 of 7 minutes suggesting no obstruction. The patient's renal function remained normal throughout his follow up visits. Repeat ultrasounds were performed yearly after presentation with stable right hydroureteronephrosis (Fig. 1). MRI Urogram (Fig. 2) obtained at age 20 also showed moderate right hydroureteronephrosis and the reading radiologist attributed the large pelvic cystic structure to be a dysplastic kidney, a theory that was later disproved after histological examination of the surgical specimen. The diagnosis of ZS was ultimately made on the basis of final surgical pathology; the pelvic cyst was confirmed to be consistent with a Wolffian duct cystic malformation.

Over the 15 years after initial presentation, the patient had one

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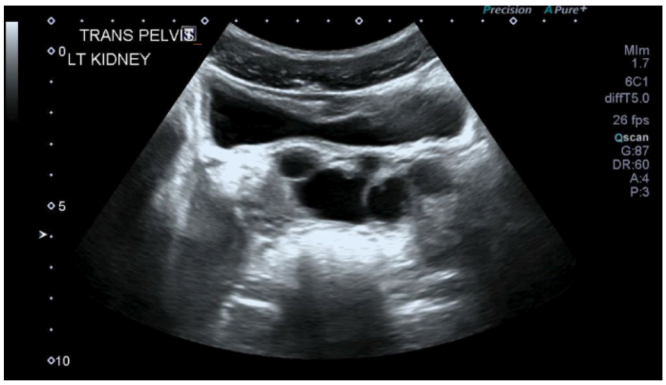

Fig. 1. Renal Ultrasound - Renal ultrasound was repeated annually after presentation. The right hydroureteronephrosis remained stable throughout this time. The size of the pelvic cystic structure increased over time. The most marked increase in size occurred around the patient's pubertal age.

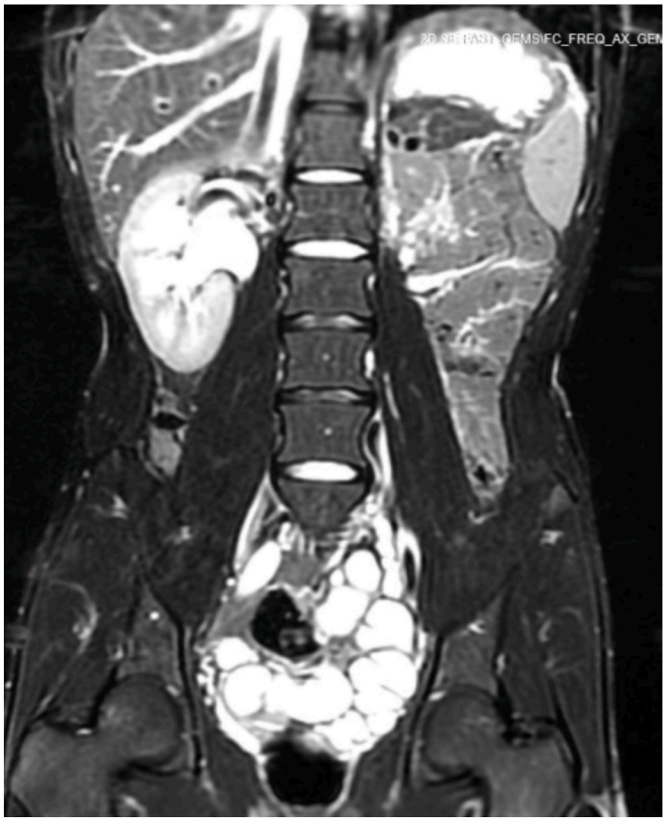

Fig. 2. MRI Urogram- This study was done at about age 20 and showed moderate right hydroureteronephrosis. At the time of the study, the large cystic structure in the pelvis was interpreted by the radiologist to be a dysplastic kidney. The structure was positioned in the left upper pelvis and measured 3.9 cm in length. There was no enhancement following contrast administration. A T1 hyper-intense signal within the cyst was consistent with proteinaceous content. A tubular structure that was thought to be a left ureter appeared to insert ectopically in the expected location of the left seminal vesicle, with associated cystic ectasia of the seminal vesicle projecting across the midline. The right seminal vesicle appeared normal.

urinary tract infection and several intermittent episodes of right flank pain, one of which lasted for a whole week. He also developed left pelvic pain that occurred while running or jogging. The patient had been followed closely by pediatric urology and was referred to adult urology in early adulthood for consideration of surgical excision of his persistent ectopic MCDK given his chronic pelvic pain and failure of involution of the kidney during childhood. A discussion was had about addressing the right hydroureteronephrosis at this time. Patient expressed a strong desire to have both procedures complete concurrently, citing his intermittent right flank pain as the main inciting factor. He ultimately chose to proceed with robotic-assisted laparoscopic excision of the pelvic MCDK and also elected for right ureteral reimplantation. During surgery, a large cystic structure was identified in the posterior pelvis underlying the parietal peritoneum (Fig. 3). The structure was dissected free in its entirety, and no large blood vessels were encountered. Dissection of the posterior and left lateral attachments revealed a tubular structure felt to be consistent with the left vas deferens, which inserted into the cystic structure. The right ureter was not involved with the cystic structure. There was a single attachment that appeared to be traveling into the left seminal vesicle, though the seminal vesicle itself was otherwise uninvolved. Extravesical right ureteral reimplantation was performed uneventfully. The patient did well after surgery and was discharged on postoperative day 1 without any complications. He returned to his normal daily activity after recovering from surgery.

The surgical specimen measured 8.9 cm in length and 6.1 cm in width. It was multicystic and filled with scant tan-brown fluid. There was no grossly identifiable renal parenchyma seen. Two tubular structures were attached to the specimen. Microscopically, the lining epithelium for the cysts and both tubular structures were similar. They were described as pseudostratified, cuboidal to columnar in shape, with focal intracytoplasmic brown pigments (Fig. 4). Surrounding the cysts and both tubular structures were well-organized thick smooth muscle layers. No glomerular or renal tubular structures were seen. The immunoprofile resembled epithelium of Wolffian duct origin, including positive PAX8 marker, consistent with congenital maldevelopment of the Wolffian duct (Fig. 5).

At his 5-month postoperative visit, the patient was symptom-free without right flank or pelvic pain, and his renal ultrasound showed moderate right hydronephrosis that improved to mild after voiding.

3. Discussion

Zinner syndrome was first described in 1914, and since then about 200 cases have been reported in the literature. The constellation of seminal vesicle cysts, ejaculatory duct obstruction, and renal anomalies are caused by maldevelopment of the Wolffian ducts.[10] Ureteric buds are embryological structures that arise from the mesonephric ducts at the 4th week of gestation and their interaction with the metanephric blastema leads to formation of the kidney. At about the 10th-12th week of gestation, the seminal vesicle appears as a diverticulum of the

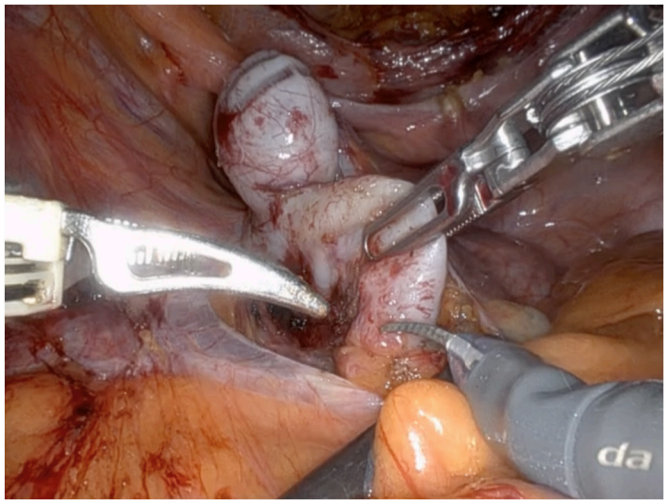

Fig. 3. Intraoperative view of pelvic cyst dissection.

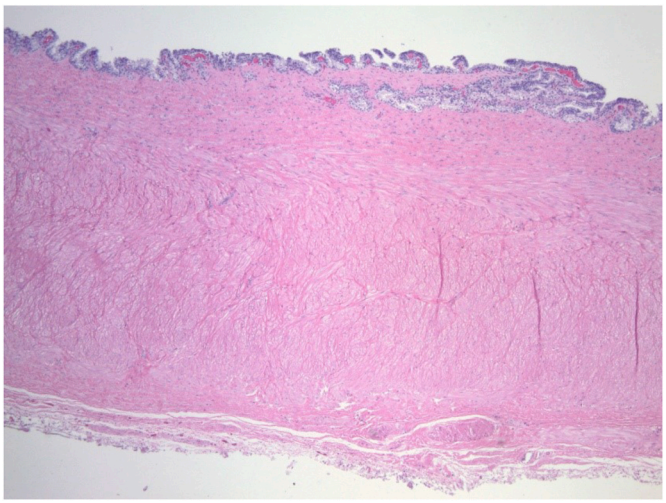

Fig. 4. Cystic wall with epithelial lining and smooth muscle wall, 40x magnification.

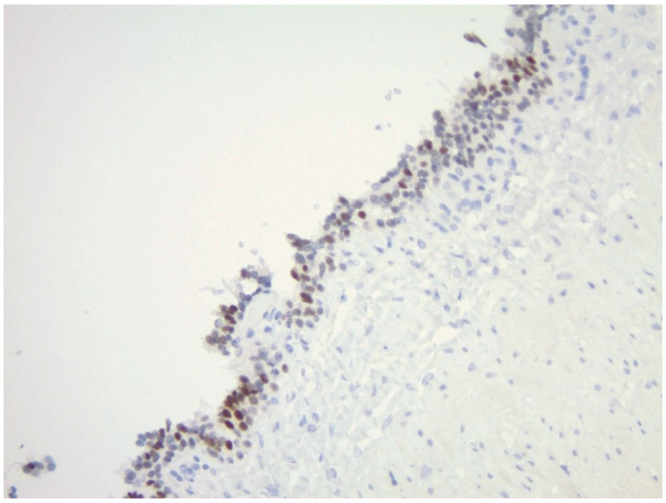

Fig. 5. The immunohistochemical stain of PAX8 shows positivity of lining epithelium, 200x magnification.

mesonephric duct. It subsequently elongates and folds back on itself.[4] The specific events during development that lead to the findings in ZS have not been elucidated.

It is notable our patient was symptomatic from a large cystic structure within the pelvis. Although it was initially thought to represent a MCDK on early imaging, the pathological specimen did not have the histologic appearance of renal architecture. In our review of the literature, there were no reports of similar findings that describe a non-renal cystic structure in the pelvis with an immunoprofile consistent with epithelium of Wolffian duct origin.

An additional interesting finding in our patient was associated symptomatic contralateral hydroureteronephrosis. Besides initially presenting with asymptomatic gross hematuria, the patient in this report mainly experienced recurrent right flank and pelvic pain. Ultimately, surgical intervention was successful in treating his pain. Patients with ZS often remain asymptomatic until between puberty and the 4th decade of life with the onset of sexual activity. Accumulation of seminal fluid within the seminal vesicles is thought to be a contributing factor.[1,3] Patients have reported pain in the abdomen, pelvis, scrotum, or perineum. Lower urinary tract symptoms can occur because of mass effect on the urethra or bladder. Recurrent urinary tract infection, epididymitis, and prostatitis have also been reported.[1] Contralateral renal and genitourinary anomalies are less common in patients with Zinner syndrome; one case of contralateral vesicoureteral reflux was described by Lin et al.[2] and another case reported by Almuhana et al. escribed contralateral ejaculatory duct obstruction.[5]

Early diagnosis of ZS is a challenge for several reasons. ZS may present rarely on prenatal ultrasound with findings such as MCDK with pelvic cysts.[6] Alternatively, pelvic cysts may appear on postnatal imaging for renal anomalies.[7] It should remain on the differential for boys with unilateral renal agenesis/dysplasia as they are followed sonographically.[8] Symptoms are more pronounced after patients reach puberty, which may delay diagnostic imaging. Limited clinical experience due to the rarity of the condition is also a factor. The most commonly used imaging modalities are MRI, ultrasound, and CT scan; in a study by Liu et al., these were used 67.8 %, 65 %, and 60.7 % of the time respectively.[9] Other imaging modalities may also be helpful. Voiding cystourethrogram may show a seminal vesicle cyst (SVC) filling with contrast, which is suggestive of ejaculatory duct obstruction. Reflux of contrast into the SVC was seen in 25 % of the 16 patients published in a recent case series.[2] In one study that included findings on digital rectal examination (DRE), all 14 patients had a palpable bulging mass superior to the prostate.[10] However, others have reported that DRE was only performed in 18.7 % of patients.[7] Cystoscopy has also been used to evaluate the urethra and bladder for any other urological abnormalities. There have been reports of concomitant posterior urethral valves, membranous obstruction of the ejaculatory duct, contralateral hutch diverticulum, and an absent ipsilateral hemitrigone.[1,3]

4. Conclusion

Zinner Syndrome is a rare congenital abnormality and requires a high index of suspicion along with adequate radiological studies. A pelvic cystic structure and ipsilateral renal agenesis or dysplasia should prompt consideration. Although uncommon, our case demonstrates contralateral genitourinary abnormalities may be present in patients with Zinner Syndrome. Furthermore, robotic-assisted laparoscopic excision of pelvic cysts is feasible, safe and effective.

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CRediT authorship contribution statement

Andrew Shanholtzer: Writing – review & editing, Writing – original draft. **Daniel A. Sidhom:** Writing – review & editing, Writing – original draft, Conceptualization. **Kristina D. Suson:** Writing – review & editing, Writing – original draft, Conceptualization. **Barrett G. Anderson:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of competing interest

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