The Endless Differential Diagnosis of Acute Obstructive Renal Failure: Unusual Challenges for the Sharp-Sighted Clinician

Hemda Rosenblum MD[1], Yaron Bar-Dayan MD MHA[1,2], Zamir Dovrish MD[1], Sylvia Lew MD[1], Noemi Weisenberg MD[1], Avivit Neumann MD[1], Tzvi Klein MD[1] and Howard Amital MD MHA[1]

[1]Department of Medicine D, Meir Medical Center, Kfar Saba, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel
[2]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

ABSTRACT: Obstruction of urine outflow can result from mechanical blockade as well as from functional defects. In adults, urinary tract obstruction is due mainly to acquired defects, such as pelvic tumors, calculi, and urethral stricture. In childhood it is mostly due to congenital malformations. In this article we present two rare cases of acute obstructive renal failure that presented with hydronephrosis. These cases underline the wide range of causes that may lead to this clinical feature.

IMAJ 2010; 12: 280–282

KEY WORDS: obstructive renal failure, bladder metastasis, gastric signet-ring cell carcinoma, CHARGE syndrome, genitourinary abnormalities

Urinary flow obstruction can occur anywhere from the renal pelvis to the urethra. The development of renal insufficiency in patients without intrinsic renal disease requires bilateral obstruction (or unilateral obstruction with a single functioning kidney). We often encounter this clinical entity in patients with prostatic disease, which causes mechanical obstruction to the urinary outflow; however, there are numerous other causes such as calculi, blood clots, infections and tumors.

In this report we will elaborate on two rare causes of obstructive uropathy; the first is a rare case of a patient with gastric signet-ring cell adenocarcinoma who presented initially with hydronephrosis and acute renal failure as a result of metastases to the bladder. The second is the first reported case of a woman with CHARGE syndrome, a rare congenital syndrome that includes multiple congenital anomalies of the genitourinary system and other systems. She was diagnosed in adulthood after an episode of acute obstructive renal failure. These two cases represent the wide range in the differential diagnosis of obstructive uropathy, including pathologic conditions of all disciplines in medicine.

PATIENT DESCRIPTIONS

PATIENT 1

This 83 year old woman had a history of hypothyroidism, essential hypertension and ischemic heart disease. She was cured from left breast cancer 7 years previously. She was admitted because of acute renal failure, with an elevated creatinine level of 8 mg/dl. Sonography of the kidneys demonstrated severe left renal hydronephrosis. A nephrostome was inserted and the creatinine level decreased, stabilizing at 1.2 mg/dl. Gross hematuria later appeared. After withdrawing antiplatelet aggregation therapy and ensuring kidney function, the nephrostome was removed.

A computed tomography scan showed ascites and infiltration of the omentum. Retroperitoneal lymph nodes were observed, as well as uniform thickening of the bladder. Pelvic and abdominal organs, including the gastrointestinal wall, appeared normal. Gynecological examination and transvaginal ultrasound did not reveal any masses in the ovaries or uterus. Urinary bladder biopsy showed tissue infiltrated by a signet-ring cell adenocarcinoma, but no evidence of carcinoma *in situ* was found. Immunohistochemical study of the bladder biopsy was positive for cytokeratin 20 and negative for estrogen receptor [Figure 1]. Ascitic fluid and pleural effusion were examined: Periodic acid-Schiff stain of the cytologic material was positive for neoplastic cells, indicating possible gastrointestinal origin of the tumor.

Metastasis of gastric origin to the bladder was the first probable diagnosis. The final diagnosis was based on upper gastrointestinal endoscopy and biopsy that revealed primary signet-ring cell carcinoma of the stomach. The patient developed urinary tract infection and sepsis, with subsequent multiorgan failure. She succumbed to her disease 2 months following her initial admission.

PATIENT 2

The patient was a 46 year old Arab woman who had been diagnosed in childhood with total left eye and partial right eye blindness, bilateral coloboma, complete right ear deafness and anosmia. She was mentally retarded, and her height was 1.5 meters. She had bilateral facial paralysis. The gynecological history of the patient was unclear: she had occasional urinary bleeding, but had primary amenorrhea. She had never had a proper medical examination, including gynecological.

She presented with abdominal and right flank pain, nausea and vomiting. Creatinine level was 1.5 mg/dl. Ultrasonography of the kidneys revealed right hydronephrosis. An abdominal and pelvic CT scan showed a dysplastic, small, non-functioning left kidney, and a cystic pelvic mass that was interpreted as a bladder diverticulum containing a stone. A gynecological examination was not possible because of the absence of a vaginal orifice. A pelvic laparoscopy revealed pus in the pelvis and a right unicornate uterus, ovary and fallopian tube. The left ovary and fallopian tube were absent. A CT scan demonstrated malrotation of the right colon, without volvulus [Figure 2]. A right nephrostome was inserted, with a subsequent daily urine output of > 6 L. After several days of follow-up, both the urine output and creatinine level decreased gradually until the creatinine stabilized at normal ranges.

Ten days later, the patient was again hospitalized because of recurrent abdominal and right flank pain. Urine output was normal, and she did not urinate through the urethra. Both CT scan and rectal examination suggested hematocolpos. Urinalysis and cultures revealed urinary tract infection.

Treatment with fluids and antibiotics was initiated. The patient refused any further gynecological examination. Her medical condition was stable, and she was released. Based on her medical history and the present findings, the patient was discharged with a diagnosis of CHARGE syndrome.

Figure 1. Bladder biopsy: metastatic gastric signet-ring cells showing positive reaction for immunohistochemical stain with cytokeratin 20

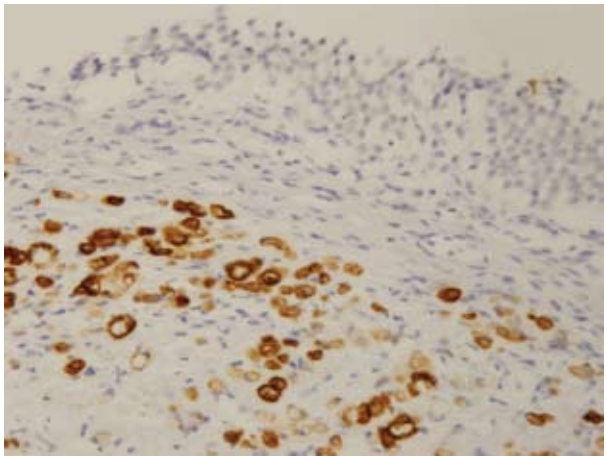
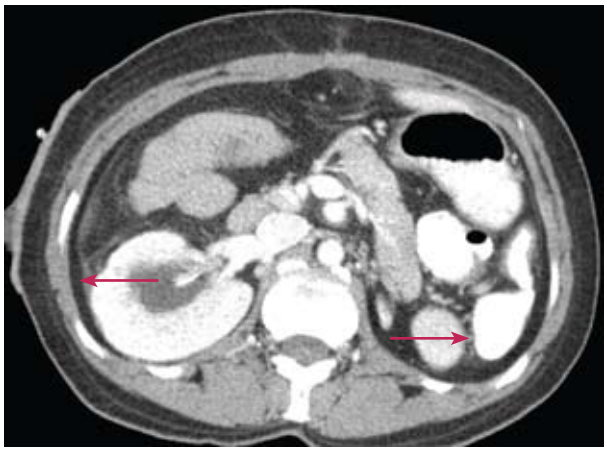


Figure 2. CT scan showing right hydronephrosis, nephrostome in the right kidney (red arrow) and malrotation of the right colon, without volvulus



DISCUSSION

Urinary tract obstruction accounts for fewer than 5% of cases of acute renal failure. It can be classified on the basis of location in the urinary tract, either in the upper urinary tract (above the ureterovesical junction) or in the lower urinary tract [1].

In the upper urinary tract an obstruction can result from intrinsic or extrinsic mechanical blockade. Extrinsic lesions that lead to obstructive uropathy originate from the vascular system, reproductive system, gastrointestinal tract and the retroperitoneum. In the lower urinary tract the lesions can originate from the meatus, urethra, prostate and bladder. In both our cases the presenting symptom was hydronephrosis. Hydronephrosis has been found in 3.5–3.8% of all postmortem examinations, with an equal male-female distribution. At autopsy, the frequency in children is 2% and is primarily due to congenital anomalies of the urinary tract. Obstruction related to renal calculi is three times more common in men than in women. Between the ages of 20 and 60 years, urinary obstruction is more common in women and is due to pregnancy and pelvic cancer. After the age of 60 most cases are seen in men and are related to prostatic hypertrophy or malignancy [2,3].

The first patient described here developed obstructive renal failure as a result of bladder metastases originating from gastric signet-ring cell adenocarcinoma. Secondary bladder neoplasms represent no more than 3% of all malignant tumors in surgical specimens, of which distant metastases from the stomach account for about 4% [4]. Adenocarcinoma of the bladder comprises fewer than 2% of all bladder tumors,

in most cases as a result of direct invasion from the surrounding organs [5,6].

Adenocarcinomas originating from different organs have a similar histologic appearance. Immunohistochemical staining profile may be helpful in determining the primary origin of the neoplasm. Breast and gastric cancer are the most common primary sites of signet-ring cell carcinoma. By combining the results of cytokeratin 20 and estrogen receptor staining, all metastases can be properly classified. The cytokeratin 20+/ER- pattern is characteristic of gastrointestinal tumors [6,7].

Only five cases of gastric signet-cell adenocarcinoma with metastases to the urinary bladder have been described in the literature: in four cases, the patients were already diagnosed with gastric signet-ring cell adenocarcinoma and underwent a gastrectomy prior to the uorologic presentation. In one of these four cases the disease recurred as hydronephrosis. The previously reported patients were between the ages of 52 and 59, whereas our patient was much older [4,5,8,9].

We present the sixth case of gastric signet-ring cell adenocarcinoma with metastases to the bladder. In contrast to the other cases, in our patient the initial presentation of the primary gastric tumor was urologic with left hydronephrosis and acute renal failure. Our second case was a woman with CHARGE syndrome that was diagnosed in adulthood after an episode of acute obstructive renal failure due to congenital genitourinary malformations.

The acronym CHARGE summarizes six cardinal features: **c**oloboma, **h**eart defect, **a**tresia of the choanae, **r**etarded growth and development, **g**enitourinary anomalies, and **e**ar anomalies/deafness. CHARGE syndrome is often associated with dysfunction of multiple cranial nerves, particularly the first (anosmia), the seventh (facial palsy) and the eighth (sensorineural hearing loss). The syndrome has an estimated incidence of 0.1–1.2:10,000. It affects both genders equally and occurs in many races. About 60% of patients have mutations in the *CHD7* gene [10,11].

CHARGE syndrome is one of several conditions characterized by multiple congenital anomalies that should be considered in a patient with both auricular and renal anomalies. Neurosensory hearing loss was found to be associated with renal agenesis, and its incidence among patients with chronic renal failure is considerably higher than in the general population. A close connection seems to exist between renal diseases and hearing disorders. According to Abbasi et al. [12] this link might be explained by the fact that similar proteins exist in both renal and ear tissues. When auricular anomalies are present, a careful assessment for accompanying dysmorphic features should be performed, and when present a renal ultrasound is mandatory [13,14].

According to Ragan and colleagues [15] there is a high incidence of genitourinary anomalies in CHARGE syndrome. They reviewed 32 patients who were diagnosed with CHARGE syndrome and found that 69% had genitourinary abnormalities, including atresia of uterus, unicornate uterus, cervix and vagina, and hypoplastic female labia and clitoris. Renal anomalies have also been reported, including solitary kidney, hydronephrosis, renal hypoplasia and nephrolithiasis. Therefore, patients with this condition should undergo a careful genitourinary evaluation, including renal and bladder ultrasound, and voiding cystourethrography screening [10,11,15].

In this article we presented two rare cases of obstructive renal failure apparently caused by a common simple mechanism: compression of the lower urinary tract. Based on these two cases we conclude that a high index of suspicion is needed to enable early and accurate diagnosis and concomitant treatment and follow-up of patients with obstructive renal failure.

Correspondence:
Dr. H. Amital
Chair, Dept. of Medicine D, Meir Medical Center, Kfar Saba 44281, Israel
Phone: (972-9) 747-2598
Fax: (972-9) 747-1313
email: howard.amital@clalit.org.il, hamital@netvision.net.il

References

1. Smith AD. Update on endourology. *Urol Clin North Am* 1988; 15: 295-354.
2. Vidt DG. Recognition and management of reversible renal failure. *South Med J* 1994; 87: 1018-27.
3. Klahr S. Obstructive Uropathy. Principles and Practice of Nephrology. Philadelphia: BC Decker, 1991: 432-41.
4. Farhat MH, Moumneh G, Jalloul R, et al. Secondary adenocarcinoma of the urinary bladder from a primary gastric cancer. *J Med Liban* 2007; 55(3): 162-4.
5. Valero Puerta JA, Medina Perez M, Garcia Carriazo M, et al. Bladder metastases of signet-ring cell adenocarcinoma from the stomach. *Arch Esp Urol* 2000; 53(9): 839-41.
6. Raz O, Stav K, Mendlovic S, Bar I, Zisman A. Exceptional site of metastatic adenocarcinoma of the lung. *IMAJ Isr Med Assoc J* 2007; 9: 119-20.
7. Tot T. The role of cytokeratins 20 and 7 and estrogen receptor analysis in separation of metastatic lobular carcinoma of the breast and metastatic signet-cell carcinoma of the gastrointestinal tract. *APMIS* 2000; 108: 467-72.
8. Uemura M, Inoue H, Nishimura K, et al. Metastatic bladder disseminated lymphogenously from gastric cancer: a case report. *Hinyokika kiyo* 2000; 46(10): 723-5.
9. Nakamura K, Hihara T, Nishiumi T, et al. A case of metastatic urinary bladder tumor from gastric carcinoma. *Hinyokika kiyo* 1992; 38(7): 845-7.
10. Klingenberg C, Andersen WH. The CHARGE syndrome. *Tidsskr Nor Laegeforen* 2008; 12: 1401-5.
11. Wincent J, Holmberg E, Stromland K, et al. CHD7 mutation spectrum in 28 Swedish patients diagnosed with CHARGE syndrome. *Clin Genet* 2008; 74(1): 31-8.
12. Abbasi AH, Ramadan R, Hoffman A, Abassi Z. Kidney-ear axis. *IMAJ Isr Med Assoc J* 2007; 9: 814-18.
13. Wang RY, Earl DL, Ruder RO, et al. Syndromic ear anomalies and renal ultrasounds. *Pediatrics* 2001; 108(2): E32.
14. Haung HM, Yeh RM, Tan CT, et al. Auditory abnormalities associated with unilateral renal agenesis. *Int J Pediatr Otorhinolaryngol* 2001; 60(2): 113-18.
15. Ragan DC, Casale AJ, Rink RC, et al. Genitourinary anomalies in the CHARGE association. *J Urol* 1999; 161(12): 622-5.