A case of acute kidney injury due to secondary retroperitoneal fibrosis caused by direct invasion of esophageal squamous cell carcinoma

Tatsuhiko Mori · Saeko Nabeshima · Sawaka Fujino ·
Akira Imoto · Hideaki Shima · Kazuhiro Yamamoto ·
Motomu Tsuji · Nobukazu Ishizaka

Received: 29 September 2014 / Accepted: 23 December 2014 / Published online: 15 January 2015
© Japanese Society of Nephrology 2015

Abstract A 71-year-old man who developed renal failure was admitted to our hospital. Computed tomography without contrast enhancement showed bilateral hydronephrosis together with a soft tissue mass around the abdominal aorta, leading to the diagnosis of retroperitoneal fibrosis. Serum levels of immunoglobulin G4 were within the normal range. The patient was then evaluated for the presence of undiagnosed malignancy as a possible cause of secondary retroperitoneal fibrosis. Upper gastrointestinal tract endoscopy demonstrated esophageal cancer. Histology of the esophageal lesion and the retroperitoneal mass showed squamous cell carcinoma (SCC). Therefore, the retroperitoneal fibrosis was considered to be due to the invasion of SCC of the esophagus, and chemotherapy was chosen as the treatment. This is the first case report of postrenal failure due to secondary

retroperitoneal fibrosis caused by the direct invasion of esophageal SCC. Physicians should be aware of occult malignancy as the cause of unexplained retroperitoneal fibrosis, even clinically silent, to avoid inappropriate management or delay in the treatment of potentially life-threatening co-morbidities.

Keywords Retroperitoneal fibrosis · Esophageal cancer · Hydronephrosis · Acute kidney injury (AKI)

Introduction

Acute kidney injury (AKI) is defined by an abrupt decrease in kidney function indicated by increased serum creatinine level or decreased urine volume (KDIGO) [1]. Although the renal impairment is most frequently due to tubular and vascular factors, AKI can be due to a broad range of causes, and the differential diagnosis must be considered in a systematic fashion to avoid missing multiple factors that may be contributing to the condition [2]. The traditional paradigm divides AKI into prerenal, renal, and postrenal causes. We have sometimes had patients referred with AKI due to postrenal causes. Postrenal obstructive renal failure is usually diagnosed by urinary tract dilatation on renal ultrasound or computed tomography scanning.

Retroperitoneal fibrosis is a rare disease, one of the causes of postrenal obstructive renal failure, characterized by the presence of retroperitoneal tissue, consisting of chronic inflammation and marked fibrosis, which often entraps the ureters or other abdominal organs. The idiopathic form of the disease accounts for more than two-thirds of cases, with the rest being secondary to other factors, such as neoplasms, infections, trauma, radiotherapy, surgery, and use of certain drugs [3].

T. Mori (✉) · S. Nabeshima · S. Fujino · H. Shima
Division of Nephrology, Department of Internal Medicine,
Osaka Medical College, 2-7 Daigaku-machi, Takatsuki,
Osaka 569-8686, Japan
e-mail: tatmori@poh.osaka-med.ac.jp

A. Imoto
Second Department of Internal Medicine, Osaka Medical
College, Takatsuki, Japan

K. Yamamoto
Department of Radiology, Osaka Medical College, Takatsuki,
Japan

M. Tsuji
Department of Pathology, Osaka Medical College, Takatsuki,
Japan

N. Ishizaka
Department of Cardiology, Osaka Medical College, Takatsuki,
Japan

There have been several reported cases of retroperitoneal fibrosis associated with gastric cancer [4], while there have been only a few reports associated with esophageal cancer [4].

Case report

A 71-year-old man developed a loss of appetite 2 months prior to admission, lost 2 kg in 2 weeks, had difficulty in swallowing, developed general malaise a week prior, and noticed a decreased amount of urine since 3 days prior. He was referred to our division because blood examinations done by a primary care physician showed a significantly increased serum creatinine level of 4.06 mg/dL, in contrast to the level of only 0.74 mg/dL 6 months earlier. The patient had a history of hypertension and hyperuricemia, as well as a 27-pack-year history of tobacco smoking.

Physical examination on admission did not show any abnormalities except for high blood pressure (172/100 mmHg). Laboratory findings were as follows: white blood cell (WBC) count 7,520/ μ L, hemoglobin 15.1 g/dL, platelet count 16.3×10^4 / μ L, and C-reactive protein concentration 2.25 mg/dL. The serum creatinine level was increased to 4.66 mg/dL, with an increased blood urea nitrogen level of 37 mg/dL and a uric acid level of 10.2 mg/dL. The serum creatinine level was further increased 2 days after admission to 8.24 mg/dL, and then it decreased to 2.06 mg/dL with placement of a ureteral stent.

Antinuclear antibody was negative, and serum levels of IgG (1,368 mg/dL), IgG4 (47.6 mg/dL), and soluble interleukin receptor (407 U/mL) were within the normal ranges. In addition, carcinoembryonic antigen (1.9 ng/mL), CA19-9 (2.8 ng/mL), and α -fetoprotein (24.7 U/mL) were within the normal ranges. On the other hand, squamous cell

carcinoma (SCC)-related antigen was increased (23.3 ng/mL).

The urinary protein to creatinine ratio was 0.03 g/gCr. The red blood cell count in the urine sediment was 5/ μ L. Fractional excretion of sodium (FENa) was 1.45 %, the urine sodium concentration was 42 mEq/L, and urinary osmolality was 222 mOsm/kg. Plain abdominal computed tomography (CT) showed bilateral soft tissue masses surrounding the abdominal aorta and hydronephrosis of both kidneys caused by ureteral strictures due to the mass (Fig. 1). These findings collectively indicated the tentative diagnosis of retroperitoneal fibrosis and accompanying hydronephrosis.

The patient was then evaluated for the presence of occult malignancy. Upper gastrointestinal fiberscopy showed ulcerative regions with an irregular border in the middle esophagus (Fig. 2), and a diagnosis of SCC was made histologically (Fig. 3). Endoscopic ultrasound-guided fine-needle aspiration of the retroperitoneal mass through the lesser curvature of the esophagogastric junction using a 22-G needle was performed, and atypical cells with thick cytoplasm and densely stained nuclei that suggested SCC were obtained (Fig. 4).

A contrast CT performed after the placement of intra-ureteral stents showed a continuous soft tissue mass from the esophagogastric junction through the around abdominal aorta (Fig. 5), suggesting a diffusely infiltrative SCC of the esophagus. These findings collectively indicated that hydronephrosis was induced by direct invasion of the esophageal cancer into the retroperitoneal fibrosis.

In this case, chemotherapy was chosen as the treatment for diffusely infiltrative SCC of the esophagus. The chemotherapy was not effective and he developed ileus supposed to be due to invasion of tumor to ileum. This patient

Fig. 1 Computed tomography (CT). **a, b** Plain CT image on the day of referral to our division. There is fibrous tissue around the abdominal aorta at the level of the left renal hilum, resulting in left

hydronephrosis. In addition, a stenosis in the right upper ureter causing right hydronephrosis is seen

Fig. 2 Findings of upper endoscopy. Ulcerative regions in the middle esophagus are observed

did not want further invasive therapy and chose the best supportive care. He was discharged from the hospital and died 1 month later.

Discussion

Acute kidney injury due to hydronephrosis

In the hospital setting, prerenal uremia and acute tubular necrosis account for the majority of cases of AKI. Although not as likely, obstructive causes must be

excluded first, because prompt intervention can result in improvement or complete recovery of renal function. In the present case, abdominal CT was performed at the first visit, and AKI due to hydronephrosis was diagnosed. We have had several patients with a postrenal etiology of AKI found on CT or abdominal ultrasonography.

As causes of postrenal forms of AKI with hydronephrosis, bladder outlet obstruction, tumors, renal calculi, and retroperitoneal fibrosis must be considered. Most causes of obstructive uropathy are amenable to therapy, and the prognosis is generally good, depending on the underlying disease. Indeed, in the present case, the increased level of serum creatinine was significantly decreased by ureteral stent placement.

Diagnosis of retroperitoneal fibrosis, especially secondary retroperitoneal fibrosis

There are no standardized diagnostic criteria for retroperitoneal fibrosis. However, CT or MRI scans, or both, are the modalities of choice for its diagnosis and follow-up. The finding of a soft tissue mass surrounding the abdominal aorta and the iliac artery, and with the possible encasement of neighboring structures such as the ureters and inferior vena cava, usually suggests a diagnosis of retroperitoneal fibrosis [3].

The differential diagnosis of retroperitoneal fibrosis between the idiopathic form and secondary forms should be addressed. The idiopathic form of the disease accounts for more than two-thirds of cases, with the rest being secondary to other factors [3]. Vaglio et al. mentioned that idiopathic retroperitoneal fibrosis is a manifestation of a

Fig. 3 The biopsy specimen of the ulcerative regions in the middle esophagus (a, b). Infiltrative growth of SCC is observed

Fig. 4 Cytological examination of the endoscopic ultrasound-guided fine-needle aspiration of the retroperitoneal mass through the lesser curvature of the esophagogastric junction using a 22-G needle. **a**,

b Clusters of atypical cells with thick cytoplasm and densely-stained nuclei suggest that they are cells of SCC

Fig. 5 **a–h** Subsequent slices of contrast CT. **i** Vertical CT image reconstructed from each horizontal slice. The contrast CT clearly shows that the soft tissue mass has spread from the esophagogastric

junction to the abdominal aorta. In the left kidney, the mass seems to invade the renal pelvis and induce hydronephrosis. The right kidney shows hydronephrosis

systemic autoimmune disease. Secondary retroperitoneal fibrosis is caused by a broad range of factors, such as neoplasms, infections, trauma, radiotherapy, surgery, and use of certain drugs. In the present case, the laboratory findings did not show immune system abnormalities, with normal IgG and IgG4 levels. From the history of difficulty in swallowing and very fast weight loss, the presence of malignancy was suspected. On plain CT performed on the day of referral to our division, no findings suspicious of malignancy were obtained. Subsequently, upper gastrointestinal tract endoscopy showed ulcerative regions with an irregular border in the esophagus, and histologic examination of biopsy specimens showed SCC. The esophageal cancer may have promoted the formation of retroperitoneal fibrosis.

In most cases of retroperitoneal fibrosis secondary to malignant disease, abnormal collagen deposition in the retroperitoneum results from an increased desmoplastic reaction to retroperitoneal metastases [3]. A fibrotic reaction due to cancer invading the periureteral and retroperitoneal area without direct invasion of the ureters that may result in gradual ureteral obstruction has been reported. Furthermore, it is believed to be an immune-mediated process, in which macrophages release cytokines that stimulate fibroblast proliferation with subsequent fibrosis [4].

Peritoneal fibrosis due to esophageal cancer

This is the first case report of hydronephrosis caused by direct invasion of esophageal SCC into retroperitoneal fibrosis. CT showed retroperitoneal fibrosis, and an endoscopic ultrasound-guided fine-needle aspiration of the retroperitoneal mass showed SCC, suggesting the direct involvement of the carcinoma in the formation of the retroperitoneal mass.

There have been few reports related to retroperitoneal fibrosis due to esophageal cancer. Peixoto et al. [4]

reported one case of retroperitoneal fibrosis associated with esophageal cancer. The biopsy finding was poorly differentiated adenocarcinoma consistent with metastasis from the previous esophageal cancer.

In Japan, Nagata et al. [5] reported a case of diffusely infiltrative SCC of the esophagus with hydronephrosis. They did not mention retroperitoneal fibrosis and speculated that extensive lymphatic infiltration and dissemination to the surrounding tissues induced hydronephrosis. Diffusely infiltrative SCC of the esophagus is rare [5].

In brief, it is important to consider postrenal obstructive renal failure as one cause of acute kidney injury. In addition, the presence of malignancy as a cause of retroperitoneal fibrosis should be considered. In the present case, a very rare case of retroperitoneal fibrosis, AKI was caused by hydronephrosis induced by direct invasion of esophageal SCC to the retroperitoneal fibrosis.

Conflict of interest The authors have declared that no conflict of interest exists.

References

1. KDIGO AKI Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012;2:1–138.
2. Jefferson JA, Thurman JM, Shrier RW. *Comprehensive clinical nephrology*, Chapter 66. 4th ed. St Louis: Elsevier; 2010. p. 797–812.
3. Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. *Lancet.* 2006;367:241–51.
4. Peixoto RD, Al-Barrak J, Lim H, Renouf D. Gastroesophageal cancer and retroperitoneal fibrosis: two case reports and review of the literature. *World J Gastrointest Oncol.* 2013;5:68–70.
5. Nagata MTY, Miihara M. A case of diffusely infiltrative squamous cell carcinoma of the esophagus with hydronephrosis and rapid progression after neoadjuvant chemotherapy. *J Japan Surg Assoc.* 2013;74:1842–9.