



Case report

Gastric cancer recognized by metastasis to the ureter

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Abstract

Although ureteral obstruction is rarely noted in patients with gastric cancer at an advanced stage or at autopsy, the condition caused by authentic ureteral metastasis of gastric cancer is extremely rare. We experienced a case of gastric cancer in a 51-year-old woman who showed bilateral ureteral metastasis. The patient initially complained of right flank pain, caused by right ureteral obstruction, and was referred to our hospital, where she underwent a right nephroureterectomy, with suspicion of primary ureteral neoplasm. Histopathological examination of the resected specimen showed that metastatic growth of adenocarcinoma in the ureteral wall had caused the obstruction, and the subsequent extensive search for the primary lesion revealed asymptomatic gastric cancer. Soon after the nephroureterectomy, the patient developed left hydronephrosis, possibly caused by left ureteral metastasis, and a left percutaneous nephrostomy was performed. She then received chemotherapeutic reagents. However, she finally developed peritoneal carcinomatosis, and died of the disease about 1 year after the onset of the disease. In this report, we also review true ureteral metastasis from the stomach, and discuss the clinicopathologic features.

Key words Gastric cancer · Ureteral metastasis · Hydronephrosis · Hydroureter

Introduction

Ureteral obstruction caused by gastric cancer may be classified into the following three conditions, although there have been a considerable number of indistinguishable cases. (1) Direct extension from the primary site, peritoneal deposit, or lymph node metastasis of gastric cancer may involve the ureter. These cases are usually seen in very advanced cancers [1–4] and also in

autopsies [5], and they are not considered to be very rare. (2) A sclerotic reaction induced by cancer cells invading the periureteral region, but not a direct invasion into the ureter, may constrict the ureter, and result in ureteral obstruction [6–9]. This condition is known as secondary or malignant retroperitoneal fibrosis. (3) Distant metastases, so-called true metastases, may occur to the ureter from the primary site of gastric cancers through lymphatic and/or blood vessels [10,11], and these are considered to be quite rare. We report here a patient with gastric cancer who developed hydronephrosis caused by ureteral metastasis, without any symptoms of the primary lesion. We also briefly review true ureteral metastasis secondary to gastric cancer in Japan.

Case report

A 51-year-old Japanese woman was referred and admitted to the Department of Urology, National Okura Hospital, on February 2, 1999, with a 5-day history of right colic flank pain. Routine blood test results on admission were normal, except for slightly elevated serum levels of C-reactive protein (CRP) (1.44 mg/dl; normal range, less than 0.3 mg/dl). Serum levels of creatinine and BUN were 0.97 mg/dl (normal range, 0.4–1.2 mg/dl) and 11.8 mg/dl (normal range, 6–20 mg/dl), respectively. Urinalysis also showed no abnormal findings. Ultrasonography, drip infusion pyelography, and computed tomography (CT) performed after admission disclosed right hydronephrosis and hydroureter, but no evidence of a ureteral stone or tumor. Cystoscopy did not indicate any abnormalities in the bladder. Right retrograde pyelography (RP) was then tried. A catheter could be passed up 20 cm from the right ureterovesical junction, and RP was successfully performed. The RP revealed an obstruction of the right ureter at a 5-cm proximal level from the right

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Fig. 1. Right retrograde pyelography. The obstruction site is indicated by an *arrow*

ureterovesical junction (Fig. 1), but we could not make any definitive diagnosis. Urine cytology was repeatedly performed, but we failed to detect malignant cells. Results of a gynecological examination and barium enema were normal.

A primary ureteral neoplasm was suspected, so a right nephroureterectomy with partial cystectomy was performed, by the transabdominal approach, on February 26. Macroscopic observation did not reveal any particular findings in the abdominal cavity, including the peritoneum covering the retroperitoneal space. Retroperitoneal and paraaortic node swelling were not found. A tumorous lesion of approximately 3-cm length was identified in the lower ureter, and it was removed without difficulty. The macroscopic appearance of the resected specimen is shown in Fig. 2. The ureteral wall was indurated in the right lower ureter, where the ureter was obstructed, and the mucosa in that part showed a whitish appearance. Histopathological examination of the resected specimen revealed poorly differentiated adenocarcinoma with signet-ring cells infiltrating all layers of the right lower ureter (Fig. 3A), strongly suggesting that the tumor had metastasized from another organ, although extensive examination failed to reveal evidence of cancer cells in lymphatic or blood vessels in the ureteral wall. Microscopic metastasis (about 1-mm diameter) was also found in the paren-

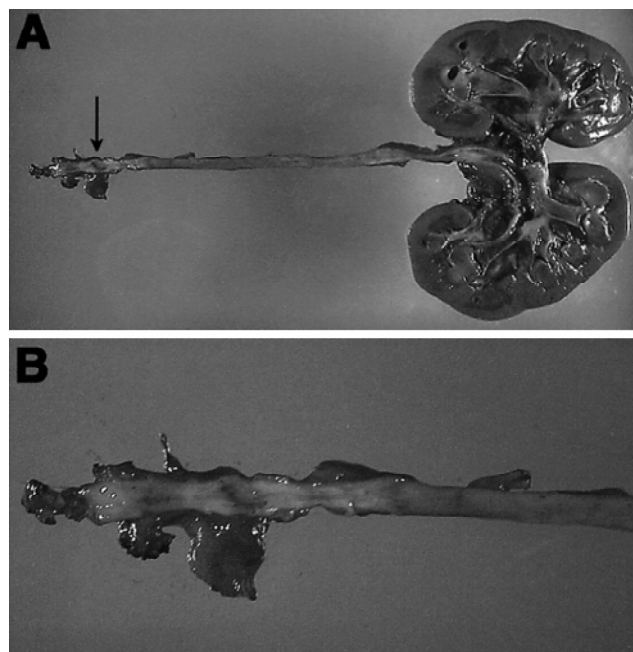


Fig. 2A,B. Macroscopic appearance of resected specimen. **A** The obstruction site in the right ureter is indicated by an *arrow*. **B** Close-up view of the right ureter

chyma of the right kidney. The cancer cells were positive for carcinoembryonic antigen by immunohistochemistry (data not shown). According to the above findings, further close examinations were performed, and a type 3 gastric tumor was finally identified in the posterior wall in the upper part of the stomach on gastrofiberscopy (Fig. 4). Histopathological examination of the biopsy specimens revealed poorly differentiated adenocarcinoma with signet-ring cells identical to those of the ureteral tumor (Fig. 3B). Other examinations targeting the whole body, including thyroid gland, breast, lung, and pancreas, did not indicate any lesions. Thus, it was concluded that the right ureteral and renal tumors were metastases from the gastric cancer.

The patient was then transferred to the Surgical Department for systemic chemotherapy. On April 15, the day after the first day of chemotherapy, she experienced sudden left colic back pain. Emergent ultrasonography and CT scan disclosed left hydronephrosis and hydroureter, without any evidence of a neoplasm, and the chemotherapy was immediately stopped. This episode was quite similar to the first manifestation of the right tumor. A left percutaneous nephrostomy was performed, and pyelography revealed severe stenosis of the left middle ureter, strongly suggesting left ureteral metastasis of the gastric cancer. She then received two courses of cisplatin and 5-fluorouracil (20mg/day and 500mg/day for 5 days, respectively/course), and then two courses of a novel oral anticancer drug composed of

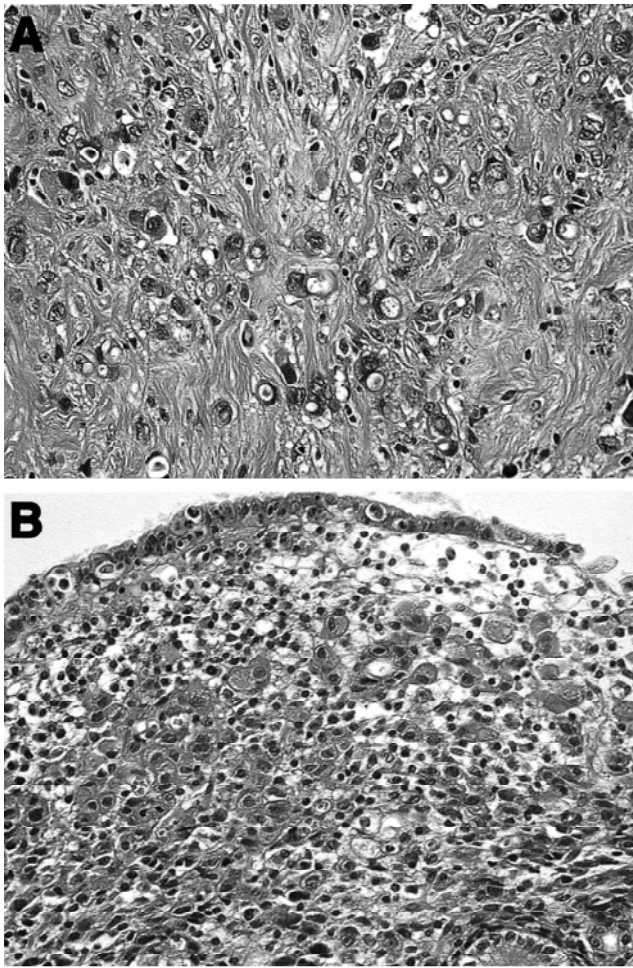


Fig. 3A, B. Microscopic appearance of tumors of **A** right lower ureter and **B** stomach. Scattered cancer cells infiltrating **A** the muscular layer of the ureter and **B** the mucosal layer of the stomach are shown. H&E. *scale bar at the bottom represents 50µm*

tegafur, gimestat, and otostat potassium (TS-1; Taiho Pharmaceutical; 100mg/day for 4 weeks/course) [12]. Although she had been in a stable condition with the left nephrostomy for about 7 months, peritoneal carcinomatosis and subsequent bowel obstruction developed. Her condition gradually deteriorated, and she died of the disease on January 31, 2000, about 1 year after the onset of the disease. An autopsy was not performed. The primary lesion did not show detectable changes on gastrofiberscopy during the entire clinical course.

Discussion

Distant ureteral metastasis first appeared in the literature in 1909 [13], and Schlagintweit reported the

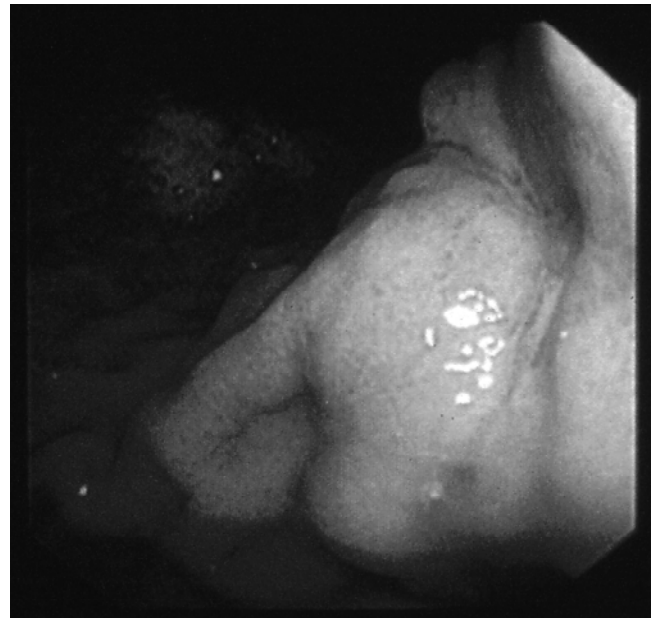


Fig. 4. Endoscopic appearance of gastric tumor. A type 3 tumor is located in the posterior wall of the upper part of the stomach

first case of gastric cancer metastasizing to the ureter in 1911 [14]. Since then, reports describing ureteral metastasis from distant organs, including the stomach, have occasionally been published. However, whether a secondary ureteral tumor is a true distant metastasis or develops by direct extension from the adjacent tissues has always been an important question. MacKenzie and Ratner [10] first proposed a rigid criterion for true ureteral metastasis, stating that “in metastatic growths of ureters malignant cells can always be demonstrated in the perivascular lymphatic spaces or in the blood vessels about the ureter”; later, Presman and Ehrlich [11] modified the criterion. The criterion of Presman and Ehrlich has been widely accepted to date, and is as follows: “the demonstration of malignant cells in a portion of the ureteral wall together with the absence of any neoplasm in adjacent tissues”. Our patient showed no tumorous lesions around the right ureter or in the retroperitoneal space during surgery, indicating that the disease was true ureteral metastasis from the stomach, according to the criterion of Presman and Ehrlich, although it remains unclear whether the later left hydronephrosis and hydroureter were caused by true metastasis or by direct extension from peritoneal deposit or lymph node metastasis to the left ureter. However, the latter possibility is unlikely, because it was 7 months later when her peritoneal carcinomatosis was detected, and CT scan did not disclose any evidence of neoplasm around the left ureter. Thus, we conclude that our patient represented a rare case of gastric cancer showing bilateral ureteral metastases.

In Japan, Jibiki et al. [15] reviewed 23 cases of gastric cancers with ureteral metastasis that were thought to agree with the criterion of Presman and Ehrlich. Since then, to our knowledge, 3 additional cases have been reported in Japan. Thus, including our case, there have been 27 cases of true ureteral metastasis of gastric cancer described in Japan. An analysis of the 27 cases revealed the following features. The age of the patients ranged from 34 to 74 years, with a median age of 52 years, and the condition occurred in 13 men and 14 women. The unilateral ureter was involved in 15 patients (56%), equally on each side (right, in 7 patients; left, in 8 patients), and in the other 12 instances (44%), ureteral involvement occurred bilaterally, as in our patient, indicating that both ureters were frequently involved in this condition. The most common symptom was back, lumbar, flank, or abdominal pain that seemed to be caused by hydronephrosis, and such pain was noted in 22 patients (81%). Oligouria or anuria was found in 4 patients, and macroscopic hematuria was never observed. One patient showed microscopic hematuria. Eleven patients (41%) had previously undergone gastrectomy for gastric cancers that metastasized to the ureter 6 months to 10 years before the onset of the symptoms. The final diagnosis of ureteral metastasis from the stomach was made after histopathological examinations of the resected ureters in 13 patients (48%), including the present patient, after autopsy in 8 patients (30%), and before any surgical procedure or death in only 2 patients (7%), indicating that it is quite difficult to make a correct diagnosis early for this condition. In the remaining 4 patients (15%), it was noted that the ureteral metastasis from the stomach was considered to be one of the differential diagnoses at surgery. According to the reports describing detailed histopathological findings, poorly differentiated adenocarcinoma and signet-ring cell carcinoma were the most common type, and lymphatic and venous invasion in the ureteral wall was noted in 7 patients and 1 patient, respectively, suggesting that most of the metastasis was established via lymphatic vessels. The prognosis is poor. The majority of the patients died of the disease within 1 year from the onset of their first symptoms, and survival for more than 2 years has not been reported.

There has been no report describing any effective therapy for this condition. In the present patient, we used chemotherapeutic agents, including cisplatin, 5-

fluorouracil, and TS-1, but these failed to even retard the disease progression. Although future studies will be necessary to develop an effective therapy, one must be aware of this condition that indicates a very advanced stage of gastric cancer, even if the primary lesion appears to be in its early stage and/or other organs appear to be free of the disease, as occurred in the present patient.

References

1. Bartels EC. Carcinoma of the stomach with bilateral ureteral metastasis. *Minn Med* 1933;16:578-9.
2. Niimoto M, Matsuki K, Hirono M, Hattori T. Management of rectal and ureteral obstruction following gastrointestinal cancer (in Japanese with English abstract). *Jpn J Cancer Chemother* 1983;10:194-7.
3. Saida Y, Tsunoda H, Matsueda K, Kurosaki Y, Kuramoto K. Gastric cancer and obstructive uropathy (in Japanese with English abstract). *Nippon Acta Radiol* 1990;50:390-7.
4. Liaw C-C, Chuang C-K, Chen J-S, Chang H-K. Gastric cancer with obstructive uropathy: clinical experience with 17 cases. *Chang Gung Med J* 1997;20:286-92.
5. Cohen WM, Freed SZ, Hasson J. Metastatic cancer to the ureter: a review of the literature and case presentations. *J Urol* 1974; 112:188-9.
6. Jönsson G, Lindstedt E, Rubin S-O. Two cases of metastasizing scirrhous gastric carcinoma simulating idiopathic retroperitoneal fibrosis. *Scand J Urol Nephrol* 1967;1:299-302.
7. Thomas MH, Chisholm GD. Retroperitoneal fibrosis associated with malignant disease. *Br J Cancer* 1973;28:453-8.
8. Usher SM, Brendler H, Ciavarrá VA. Retroperitoneal fibrosis secondary to metastatic neoplasm. *Urology* 1977;9:191-4.
9. Dohmen K, Mizukami Y, Tanaka K, Nakamura H, Arase K, Yokogawa Y, et al. Retroperitoneal fibrosis associated with scirrhous gastric cancer. *Gastroenterol Jpn* 1993;28:699-705.
10. MacKenzie DW, Ratner M. Metastatic growths in the ureter. A report of three cases and a brief review of the literature. *Can Med Assoc J* 1931;25:265-70.
11. Presman D, Ehrlich L. Metastatic tumors of the ureter. *J Urol* 1948;59:312-25.
12. Sakata Y, Ohtsu A, Horikoshi N, Sugimachi K, Mitachi Y, Taguchi T. Late phase II study of novel oral fluoropyrimidine anticancer drug S-1 (1M tegafur-0.4M gimestat-1M otastat potassium) in advanced gastric cancer patients. *Eur J Cancer* 1998;34:1715-20.
13. Stow B. Fibrolymphosarcomata of both ureters metastatic to a primary lymphosarcoma of the anterior mediastinum of thymus origin. *Ann Surg* 1909;50:901-6.
14. Schlagintweit F. Metastatische Karzinose der Ureteren mit Anurie bei gleichzeitiger Nephritis. *Z Urologie* 1911;5:665-71.
15. Jibiki M, Kawasaki T, Dobashi Y, Kikuchi M. A case of metastasis of gastric cancer to the right ureter (in Japanese with English abstract). *Prog Dig Endosc* 1995;46:160-1.