A 66-year-old man, with a history of gastric signet ring cell carcinoma, was admitted due to intermittent dull pain in the left lower abdomen for 3 months. Left ureteral obstruction with suspicious tumor encasement and hydronephrosis was found on imaging studies. Endoscopic ureteral biopsy revealed infiltrating high-grade urothelial carcinoma. As a result, he underwent left nephroureterectomy and bladder cuff excision. Unexpectedly, metastatic carcinoma of the left ureter from the stomach was the final diagnosis after comparison of the permanent sections of the two specimens. Unfortunately, acute disseminated intravascular coagulation developed and the patient died of disease complications 16 days after the operation, even with intensive care. The details of this rare condition are reported herein with a review of the medical literature.

Key Words: disseminated intravascular coagulation, gastric signet ring cell carcinoma, ureteral metastasis

revealed left hydronephrosis. Retrograde pyelography failed due to the sharp angle of the distal ureter. Antegrade pyelography showed left ureteral obstruction. Percutaneous nephrostomy and double J stent were then placed successfully by a radiologist.

However, gross hematuria developed and urine cytology raised a high degree of suspicion of carcinoma. Subsequent ureterscopy showed persistent left ureteral obstruction after ureteral stenting for 1.5 months. Biopsy of the obstructive site was performed, and the section showed highly pleomorphic cancer cells infiltrating the desmoplastic ureteral muscle wall. The pathologist interpreted the specimen as showing high-grade infiltrating urothelial carcinoma.

As a result, the patient underwent left nephroureterectomy and bladder cuff excision. Severe periureteral adhesion and diffuse wall thickening were found in the ureter. The clinical course of the first 5 days after operation was smooth, as anticipated, except for mild thrombocytopenia postoperatively (121,000 cells/mm³). However, gross hematuria occurred on the 6th postoperative day and the platelet count dropped to 17,000 cells/mm³. Laboratory data, including decreased serum fibrinogen level, positive 3P test and increased D-dimer level, led to a diagnosis of DIC. Low urine output, progressive shortness of breath, orthopnea, and lower leg edema developed shortly thereafter. Metabolic acidosis, electrolyte imbalance, pulmonary congestion, and acute renal failure followed, and emergent hemodialysis was performed. He was transferred to an intensive care unit, where a heparin drip was used and intubation was performed due to respiratory distress. Massive gastrointestinal bleeding started on the 15th day after surgery and we were unable to reverse the bleeding tendency, even with continuous administration of platelet concentrates and fresh-frozen plasma. The patient passed away the following day due to hypovolemic shock and subsequent pulseless electrical activity. Unexpectedly, histopathologic examination of the specimen revealed infiltrating cancer cells exhibiting undifferentiated signet-ring cell features (Figure), and the final pathology report was high-grade metastatic carcinoma.

**DISCUSSION**

Hemostatic abnormalities are rather common in cancer patients. They are recognizable in about 50% of patients with localized tumors and in more than 90% of patients with metastatic disease [7]. The cancers that are most frequently associated with an increased risk of clotting include acute leukemia [8] and solid tumors such as carcinomas of the lung, breast, stomach, pancreas, prostate, ovary, and colon [9–14]. A variable percentage of cancer patients, ranging from 9% to 15%, may develop DIC during the course of their disease [12]. Most of these develop chronic DIC, characterized by few laboratory abnormalities and no hemorrhagic symptoms, whereas a minority of patients with DIC have an acute course with evident laboratory alterations and bleeding [15].

The syndrome of DIC results from injury to the vascular endothelium. Platelets and clotting factors are activated and consumed, leading to thrombosis and bleeding. An unidentified procoagulant substance from adenocarcinomas directly stimulates the coagulation mechanism [16]. Surgery causes tissue injury, exposes transmembrane glycoproteins that bind with coagulation factors, and further enhances the development of DIC. Recognizing DIC in the early phase can be difficult. There is no one test or scan that can conclusively diagnose acute DIC in a patient with cancer [16]. Bleeding is the most obvious sign of DIC, such as the gross hematuria in our patient.

Acute DIC as a complication of solid tumors appears to be rather rare. Pasquini et al reported that 1.6% of the patients with solid cancers diagnosed and followed in their institution developed acute DIC and
that 0.68% of them had gastric cancers [6]. As DIC is mainly associated with a large tumor burden or with metastatic disease, it is difficult to manage because effective therapy for solid tumors is lacking. Pasquini et al [6] reported that acute DIC occurred in four patients with gastric cancer and three with breast cancer. All patients died rapidly because of major hemorrhagic complications, except for one patient who initially responded to blood component transfusion and heparin therapies.

Treatment for DIC in cancer patients is essentially based on the administration of platelets and coagulation factors, but it is often not sufficient to ameliorate the complication of acute DIC [5,6]. The basic principle of treating cancer-associated acute DIC involves treating the underlying stimulus, that is, gaining control of the cancer [16]. However, the critical clinical condition, severe thrombocytopenia, and the associated bleeding tendency limit the use of myelosuppressive chemotherapy. Nevertheless, Yeh and Cheng reported that high-dose 5-fluorouracil and leucovorin were effective treatment for acute DIC in gastric cancer patients [17].

Metastases from distant primary tumors to the ureter are rare. The primary sites of distant tumors with ureteral metastasis are mostly the breast, colon, prostate, and cervix [1,2]. The criterion of true ureteral metastasis 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”.

Metastasis of gastric carcinoma to the ureter is very rare [1–4]. In most published cases, the diagnosis is only made at postmortem examination. There are three types of presentation [2]. It can appear as transmural/perireteral adventitial involvement with resultant compression of the ureteral wall or local mucosal metastasis. The first two types manifest as stricture formation with or without an associated mass, and the third type is seen radiographically as one or more filling defects within the lumen [18]. The present case fits the transmural pattern of metastasis.

In the past, pathologists have supposed that, although histologic examination is helpful in diagnosis of metastatic ureteral neoplasm, often the lesion may be extremely pleomorphic, so that histologic examination is of little value in determining whether the lesion is primary or secondary. In the present case, the primary tumor was a gastric signet ring cell carcinoma, and it is known that the urothelium has potential for metaplastic change to primary signet ring cell carcinoma, a phenotypic variant of transitional cell carcinoma [19,20]. This further increases the difficulty in making an accurate diagnosis. We retrospectively reviewed the previous biopsy section from our patient and found that the cancerous cells were mainly located in the deeper layers, with a relatively intact mucosa. Although this provides indirect support for the existence of a secondary lesion, it could be a result of extensive disease caused by the primary tumor.

The largest series of gastric cancer patients was reported in the Japanese literature. Shimoyama et al reviewed 27 cases of gastric cancer with true ureteral metastasis [4]. The most common symptom was back, lumbar, flank, or abdominal pain that seemed to be caused by hydronephrosis (81%). Poorly differentiated adenocarcinoma and signet ring cell carcinoma were the most common tumor types, and, in the majority, metastasis was established via lymphatic vessels. The diagnosis of ureteral metastasis from the stomach was made before any surgical procedure or death in only two patients (7%), suggesting that it is quite difficult to make a correct diagnosis early on. Most of the patients died of the disease within 1 year, and survival for more than 2 years has never been documented. Notably, although acute DIC is a known complication of gastric cancer, none of their patients who received surgery (13/27, 48%) developed this severe complication. To our knowledge, the patient reported here may be the first patient to develop acute DIC immediately after resection of metastatic ureter lesions from gastric cancer.

The treatment for solitary ureteral metastasis from gastric carcinoma is indefinite. There has been no report describing an effective therapy for this condition. Although the prognosis of patients with metastasized gastric carcinoma is poor, nephroureterectomy for treatment and diagnosis seems to be adequate [3,4]. However, surgical resection can run counter to our desire due to the possible development of fatal complications. Chemotherapeutic agents fail to even delay disease progression. Therefore, palliative treatment, such as adequate drainage of the involved kidney, is usually advocated [1]. Percutaneous nephrostomy has been reported to be a better procedure to preserve renal function owing to the high failure rate of double J stents [21].
When facing an unusual presentation of a ureteral tumor, we should consider the probability of metastasis carefully if a malignancy has been previously diagnosed. A biopsy ought to be obtained if feasible and the surgeon must discuss the interpretation with the pathologist in detail. When the metastatic nature is confirmed, the necessity of an operation has to be deliberated over. To prevent the development of acute DIC, the best policy is adequate drainage by percutaneous nephrostomy. Once acute DIC has occurred, high-dose 5-fluorouracil and leucovorin treatment is the best option.

REFERENCES

胃癌輸尿管轉移患者術後產生瀰漫性血管內凝集

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一位三年前因胃癌細胞阻塞接受手術治療的 66 歲男性患者，在最近三個月因間歇性的左下腹悶痛而入院。影像學的檢查發現左側輸尿管阻塞併腫隆水腫，疑似為腫瘤包覆所引起。經內視鏡的輸尿管切片所取得的組織顯示為浸潤性的泌尿上皮癌，因此為病人施行左側腎輸尿管及膀胱體口切除手術。但在比較前後兩次手術的組織切片後，最終的病理診斷為源自胃的左側輸尿管轉移癌。病人在術後產生急性瀰漫性血管內凝集，雖然轉入加護病房密集照護，仍不幸於術後第十六天死亡。我們在此報告此罕見病例的細節並回顧相關的醫學文獻。

關鍵詞：瀰漫性血管內凝集，胃癌細胞阻塞，輸尿管轉移

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