Oncology

Granulocyte-Colony Stimulating Factor Producing Infiltrating Urothelial Carcinoma of the Left Renal Pelvis: A Case Report

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A B S T R A C T

We report a case of granulocyte-colony stimulating factor (G-CSF) producing infiltrating urothelial carcinoma of the left renal pelvis. The patient was referred to our hospital for fever and anorexia. Blood tests showed elevated level of leukocytosis without any infectious diseases. The serum concentration of G-CSF was remarkably elevated. Abdominal computed tomography (CT) revealed a huge mass in the left renal pelvis and para-aortic lymph node enlargement. He was underwent left nephroureterectomy and para-aortic lymphadenectomy. The histological examination revealed infiltrating urothelial carcinoma with positive staining for G-CSF antibody. The postoperative course was smooth and the leukocyte count became normalized within a week postoperatively. However, multiple lung metastasis and leukocytosis were revealed about 2 months after the operation. G-CSF producing infiltrating urothelial carcinoma of the renal pelvis is reported to have a significantly poor prognosis, so it is very important to monitor closely after the operation.

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Introduction

Carcinomas producing granulocyte-colony stimulating factor (G-CSF) is known to occur in multiple cancers. It is reported that about half of them are found in lung cancers. In urological field, we reveal most of them in urinary bladder cancers. G-CSF producing renal pelvic carcinoma is rare, especially infiltrating urothelial carcinoma is very rare. It is known to be extremely malignant and a poor prognosis. Herein, we report a case of G-CSF producing infiltrating urothelial carcinoma of the left renal pelvis.

Case presentation

A 67-year-old man visited our hospital due to fever and anorexia. He was admitted to our hospital and underwent serial examinations. Physical examination revealed a large mass in the left abdominal region. Blood tests showed severe inflammation. The leukocyte count was 22,900/mm³ with 74% segmented form. The C-reactive protein level was 11.0 mg/dL. The serum concentration of G-CSF was 77.8 pg/mL (Quantikine Human G-CSF Immunoassay; normal range < 39 pg/mL).

There was no evidence of infectious diseases. Cystoscopy revealed no abnormal findings.

Abdominal computed tomography (CT) revealed a huge mass measuring 12 × 17 cm in the left renal pelvis and para-aortic lymph node enlargement (Fig. 1). Urinary cytology of the left renal pelvis was positive for malignant cells.

He was underwent left nephroureterectomy and para-aortic lymphadenectomy. The histological examination revealed infiltrating urothelial carcinoma of the left renal pelvis with squamous differentiation and para-aortic lymph node metastasis (pT3N1M0) (Fig. 2A). Immunohistochemical staining using anti-G-CSF antibody demonstrated G-CSF secreting cells (Fig. 2B). After the operation, the leukocyte count became normalized within a week. The postoperative course was smooth and he was discharged on the 28th postoperative day. Two months after the operation, we revealed multiple lung metastasis and leukocytosis (Fig. 3).

Discussion

Granulocyte-colony stimulating factor (G-CSF) is produced by endothelium, macrophages, and a number of other immune cells. G-CSF is a glycoprotein that stimulates the bone marrow to produce
granulocytes and stem cells and release them into the bloodstream. Functionally, it is a cytokine and hormone, a type of colony-stimulating factor, and it also stimulates the survival, proliferation, differentiation, and function of neutrophil precursors and mature neutrophils.

In 1967, Robinson et al first reported that elevated level of G-CSF production with malignant tumors showed marked neutrocytosis. Asano et al detected that mice transplanted human lung carcinoma tissue had remarkable degree of G-CSF and leukocytosis in serum in 1977.

It is reported that G-CSF producing carcinomas occur in many organs such as lung, stomach, liver, thyroid gland, urinary bladder and so on. It is very important to consider about G-CSF producing tumors, if we see a patient with severe degree of leukocytosis with no obvious infections or hematologic diseases. Actually, in our case, we first thought leukocytosis was caused by infection. We performed antibiotic treatment.

Diagnostic criterions for G-CSF producing tumors are as follows: i) remarkable degree of leukocytosis and G-CSF in serum, ii) decrease of elevated leukocytosis and G-CSF along with the treatment, and iii) detection of G-CSF activation in tumors. Recently, it is getting easier to diagnose with the advent of immunohistochemical staining using anti-granulocyte-colony stimulating factor antibody.

One of the reasons why the prognosis is significantly poor is considered to be due to the existence of VEGF which is a proangiogenic factor. Overexpression of proangiogenic factors produced by the tumors can promote neovascularity. Hyper-vascularity in urothelial carcinomas of renal pelvis is rare characteristic. It is reported that VEGF was also shown to promote invasion and metastasis of urothelial tumors. According to recent reports, VEGF protects tumor cells from chemotherapy-induced apoptosis.

Among G-CSF producing urothelial carcinomas of the renal pelvis, infiltrating urothelial carcinomas have worse prognosis. Because, when we reveal the tumors, about half of them already have lymph node metastasis or invasions to the surroundings.

Higaki et al reported that the most effective treatment for G-CSF producing renal pelvic tumors was surgical resection. Others reported chemotherapy was also effective, but the regimen of chemotherapy still has not been decided. It depends on the individual pathological findings of the tumor. Recent studies demonstrate that G-CSF receptor autocrine activates the proliferation or invasion in several cancers. Tachibana et al demonstrated that anti-G-CSF antibody suppressed the proliferation of the G-CSF producing tumors. Therefore, anti-G-CSF antibody therapy can be an effective and alternative therapy in the case of G-CSF producing tumors.

In conclusion, when we see a patient with remarkably degree of leukocytosis, we should consider G-CSF producing carcinomas and examine the patients carefully.

Herein, we reported a case of G-CSF producing infiltrating urothelial carcinoma of the renal pelvis. To our knowledge, this case is the second case of G-CSF producing infiltrating urothelial carcinoma of the renal pelvis in the English literature.

Figure 1. Abdominal computed tomography showed a huge mass measuring 12 × 17 cm in the left renal pelvic, and para-aortic lymph node enlargement. Red arrow heads indicate the location of the tumor.

Figure 2. A: Histological examination showed high grade urothelial carcinoma with squamous differentiation (HE ×400). B: Immunohistochemical stain showed the tumor cells were positive for G-CSF, stained brown (anti G-CSF antibody staining ×400).
Conflict of interest
None.

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Figure 3. CT showed multiple lung metastasis 2 months after the operation. Red arrow heads show the metastasis of lungs.