

A Case of Synchronous Renal Cell Carcinoma Producing Granulocyte Colony Stimulating Factor (G-CSF) and Abdominal Aortic Aneurysm

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Abstract: A 73-year-old man consulted our cardiology department for hypertension and post-myocardial infarction angina pectoris. After the examination, early gastric cancer was discovered at the lower gastric confines. Preoperative examination (abdominal CT scan) revealed an abdominal aortic aneurysm 7 cm in diameter and a left renal tumor. Simultaneous nephrectomy and repair of the abdominal aortic aneurysm were performed with a median retroperitoneal approach. Immediately after the operation, the white blood cell count increased transiently. At that time, the level of granulocyte colony stimulating factor (G-CSF) in the blood was high (81 pg/ml). The histopathological diagnosis of the tumor was renal cell carcinoma and immunohistochemical staining with an anti G-CSF antibody demonstrated cancer cells producing G-CSF. The postoperative course was uneventful. The patient underwent endoscopic resection of the gastric cancer 38 days after the first operation. (Jpn. J. Vasc. Surg., 15: 521-524, 2006)

Key words: Abdominal aortic aneurysm, Renal cell carcinoma, Single stage operation

Introduction

Abdominal aortic aneurysms are often discovered unexpectedly by computed tomography (CT) or ultrasonography for other purposes. Furthermore, many renal tumors exhibit few symptoms or signs, such as hematuria and fever. This report describes a case in which preoperative abdominal CT scan for gastric cancer revealed an abdominal aortic aneurysm and left renal tumor.

Case

A 73-year-old man consulted the cardiology department for

hypertension and post myocardial infarction angina pectoris. The patient had undergone catheter intervention twice before (September 22, 1999 and February 9, 2000). Hypertension was controlled with a calcium antagonist. The patient was admitted to our institute for examination of the upper digestive tract, because he had a gastroduodenal polyp. Endoscopy revealed early gastric cancer was discovered in the lower gastric confines. The biopsy specimen strongly suggested well differentiated tubular adenocarcinoma of the stomach. The gastric cancer lesion was within the mucosa, however, the general surgeon planned to resect it because of previous catheter intervention for angina pectoris (dilatation and stenting in the stenotic coronary artery). Preoperative abdominal CT scan revealed an abdominal aortic aneurysm 7 cm in diameter with thick mural thrombi and also a left renal tumor (**Fig. 1**). Prior to treatment for the gastric lesion, simultaneous nephrectomy and repair of the abdominal aortic aneurysm were performed, with no blood transfusion, through a median retroperitoneal approach. Immediately after the operation, transient remarkable leukocytosis appeared. The white blood cells count

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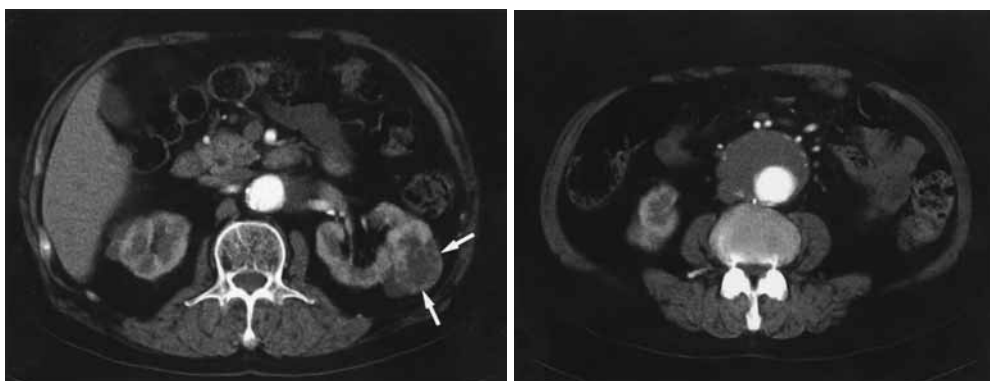
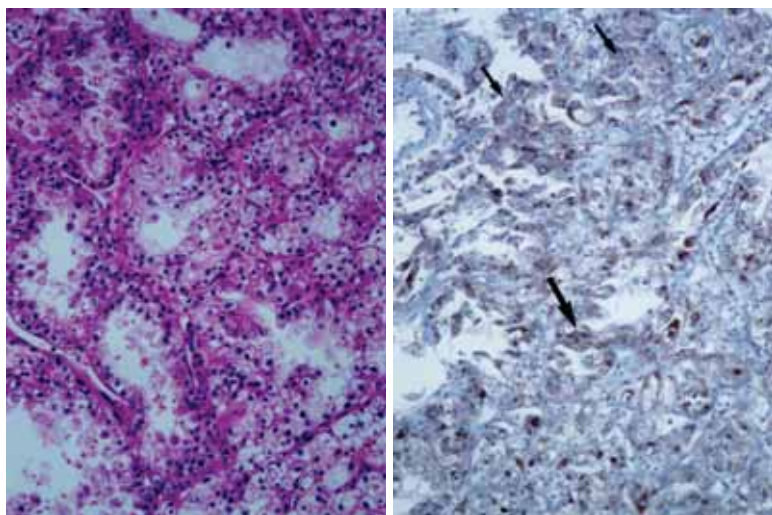


Fig. 1 Preoperative abdominal computed tomography scan shows the left renal tumor (A) and the abdominal aortic aneurysm 7 cm in diameter (B). The white arrow indicates the renal cell carcinoma.

A | B



A | B

Fig. 2 The resected specimen exhibited renal cell carcinoma (clear cell>> granular subtype, G1>2) histopathologically (A; H-E stained) and demonstrated cancer cells producing granulocyte colony stimulating factor (G-CSF) immunohistochemically by staining with an anti-G-CSF antibody (B). Cells producing G-CSF were colored brown (black arrow).

was 6,830/ μ l (neutro: 40.4%) before the operation, and it increased to 33,290/ μ l (neutro: 88.3%) just after the operation. Four days after the operation, the leukocyte count decreased to 8,117/ μ l (neutro: 65.4%) without any treatment for leukocytosis. At that time, the level of granulocyte colony stimulating factor (G-CSF) in blood elevated to 81 pg/ml (normal range: 4.7 to 18.1). The histopathological diagnosis was renal cell carcinoma (clear cell>> granular subtype, G1>2) (**Fig. 2A**) and immunohistochemical staining with anti-G-CSF antibody demonstrated that the cancer cells produced G-CSF (**Fig. 2B**). Renal function did not deteriorate after the nephrectomy.

Eighteen days after the operation, the patient was transferred to the department of general surgery for treatment of the gastric cancer. Thirty days after the nephrectomy and abdominal aortic replacement, the level of G-CSF reduced to almost the normal range. Endoscopic resection of the cancer was performed 38 days after the first operation. The post-operative course of the patient was uneventful and the patient left our hospital 44 days after the first operation.

Discussion

From 1983 to 2005, there have been 7,147 reports on the Internet dealing with G-CSF in Japan. Of course not all of

these reports dealt with only G-CSF producing tumors. Among all of the cancer reports referring to G-CSF, lung cancer is the most frequent (586), ovarian cancer is the second most frequent (186), while there are 131 gastric cancer reports, 82 bladder cancer reports, 63 esophageal cancer reports, 37 hepatocellular carcinoma reports, 33 renal cell carcinoma reports, and 26 pancreatic cancer reports. The number of reports does not necessarily mean the number of patients. However, these proportions are almost the same as reported by Saeki¹⁾ in 1990. In almost all of the reports of G-CSF producing tumors, white blood cell counts were extremely high before the treatment and the cell counts decreased in level dramatically to a normal range. Morikawa²⁾ reported 8 cases of renal cell carcinoma among 37 cases of malignant urinary neoplasms producing G-CSF. The present case exhibited a normal white blood cell count before the operation, but it increased transiently and then returned to the normal range after the operation.

At first, the transient leukocytosis was considered to be due to the surgical or inflammatory response, but no obvious infection or inflammation was detected. It was considered unlikely that G-CSF was responsible for the transient leukocytosis. Laboratory data of the patient's blood just after the operation were re-examined and the resected specimen was stained immunohistochemically using an anti-G-CSF antibody. The level of G-CSF in blood was high (81 pg/ml) and immunohistochemical staining using the anti-G-CSF antibody demonstrated that the cancer cells produced G-CSF. Since 1977, when Asano³⁾ first reported a G-CSF-producing tumor (lung cancer), malignant tumors complicated by leukocytosis have become considered due to the increased G-CSF production. Thus, the following four criteria of G-CSF producing tumors have been adopted: i) Leukocytosis coincident with tumor, ii) Increase in blood G-CSF levels, iii) Improvement of leukocytosis by tumor resection, iv) Evidence of G-CSF production by the tumor.

This case completely satisfied these criteria. Generally, G-CSF-producing tumors have a very poor prognosis: almost all of the reported renal cell carcinoma cases that produced G-CSF died within a year.⁴⁻⁷⁾ This poor prognosis might also be related to the fact that the production of G-CSF itself can be related to cancer proliferation.⁷⁾ Breakdown of leukocytes

can cause high concentrations of uric acid and renal dysfunction that cause the condition to rapidly deteriorate.⁸⁾ Abdominal aortic aneurysm complicated by renal cell carcinoma is not an extremely rare condition. Oyama⁹⁾ reported a two-stage surgical treatment in which renal cell carcinoma revealed an abdominal aortic aneurysm at the time of the rupture. Kazuno¹⁰⁾ also reported a two-stage surgical treatment case for synchronous abdominal aortic aneurysm and renal carcinoma invading the inferior vena cava. Furthermore, Orita¹¹⁾ also reported a case of a two-stage operation for synchronous renal carcinoma and chronic aortic dissecting aneurysm (DeBakey's classification type IIIb). However, there have been very few reports of two-stage surgical treatment for synchronous renal cell carcinoma and abdominal aortic aneurysm. Most cases of synchronous renal cell carcinoma and aortic disease were treated surgically at the same time in Western countries¹²⁻¹⁵⁾ and also in Japan.^{16, 17)}

Conclusion

Synchronous renal cell carcinoma and abdominal aortic aneurysm were treated in a single-stage operation. Immediately after the operation, leukocytosis appeared transiently. Abnormal change in white blood cell counts suggested that G-CSF was involved in the leukocytosis. Plasma G-CSF level and immunohistochemical staining using anti G-CSF antibody demonstrated renal cell carcinoma cells producing G-CSF. It is important to pay attention to remarkable changes in blood cells during the surgical treatment of neoplasms.

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