A case of primary renal angiosarcoma

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Abstract

A 78-year old man was diagnosed with a left bleeding renal cyst from CT scan results. Serial CT scans revealed the left kidney mass to be increasing in size and a new lesion in the liver. Renal cell carcinoma with liver metastasis was diagnosed and a radical nephrectomy performed. The initial pathological diagnosis was a benign chronic hematoma. However, the liver mass increased in size and multiplied, while another mass emerged in the twelfth thoracic vertebra with spinal paralysis and was immediately removed. Pathological findings for that specimen showed malignancy of stromal cell origin but low atypia. The renal specimen was re-evaluated using whole cross-section analysis and immunohistochemistry, and diagnosed as a primary renal angiosarcoma. Recombinant interleukin-2 therapy was started immediately; however, the patient died of metastatic disease 13 months after the initial operation. Although contrast imaging depicted the primary lesion as a non-specific hematoma with little focal pooling, and low-grade cytological atypia was shown pathologically, the angiosarcoma was extremely aggressive.

Introduction

Angiosarcomas comprise only two percent of all soft tissue sarcomas.[1] The large majority originate from the skin of the scalp and face, while those with a visceral origin including the kidneys are extremely rare.[2] Recently we treated a case of primary renal angiosarcoma, in which a prompt and exact diagnosis was difficult to obtain. We report here a brief review of the literature and the clinical course of this malignancy.

Case Report

The patient was a 78-year old Japanese man, who was treated previously for a peptic ulcer, an abdominal aortic aneurysm, and angina pectoris. He had been employed until the age of 60 years old in the production of plastic auto parts, such as those made from polyethylene and acrylonitrile-butadiene-styrene copolymer.

In May 2006, the patient noticed a bruise on his back after falling and become aware of persistent pain in his left flank. He consulted a family doctor, who diagnosed the condition as a hemorrhage from a left renal cyst and prescribed conservative treatment. However, the symptoms remained and the patient was referred to our hospital three months later.

Routine blood tests showed the presence of anemia and an IAP value that increased to 1060, while other parameters were within the normal range and a urine test showed no abnormal findings including hematuria. An abdominal CT scan demonstrated a distinctly bordered mass located on the upper pole of the left kidney that measured approximately 14 cm in maximum diameter. The images also showed that the distribution of contrast material was limited to the margin of the mass without focal pooling, which suggested that the central part was hemorrhagic or necrotized, while the periphery had no obvious tumor formation (Figure 1). Additionally, CT scanning depicted a newly developed low density area with poor contrast in the sixth segment of the liver (Figure 1). Therefore, we considered that the lesions located in the left kidney and liver corresponded, respectively, to primary renal and metastatic hepatic lesions of renal cell carcinoma. We performed a radical nephrectomy in August 2006 in order to achieve tumor cytoreduction. The excised kidney was 960 g in weight, while the tumorous lesion was approximately 18x11x7 cm in size, and composed of a non-specific hematoma and surrounding fibrous capsule (Figure 2). The initial pathological diagnosis was a chronic hematoma with no evidence of malignancy.

Two months after the operation, follow-up CT scans showed the hepatic lesion to be increasing in size and multiplying; however, we were not able to perform a liver biopsy because of the high risk of bleeding or rupture. Four months after the operation, spinal paralysis developed suddenly, and MR imaging revealed a new tumor that had destroyed the twelfth thoracic vertebra and compressed the adjacent spinal cord. The tumor was removed immediately by orthopedic surgeons. According to the pathological report, the tumor in the thoracic vertebra was composed of spindle cells with mildly atypical nuclei and a sheet-like appearance, and which were proliferating and infiltrating the surrounding area. Following the second surgery, cross-sections of the total kidney specimen were prepared and subjected to re-evaluation, which demonstrated spindle-shaped tumor cells, the same as those seen in the thoracic vertebra (Figure 3).

Immunohistochemistry findings showed

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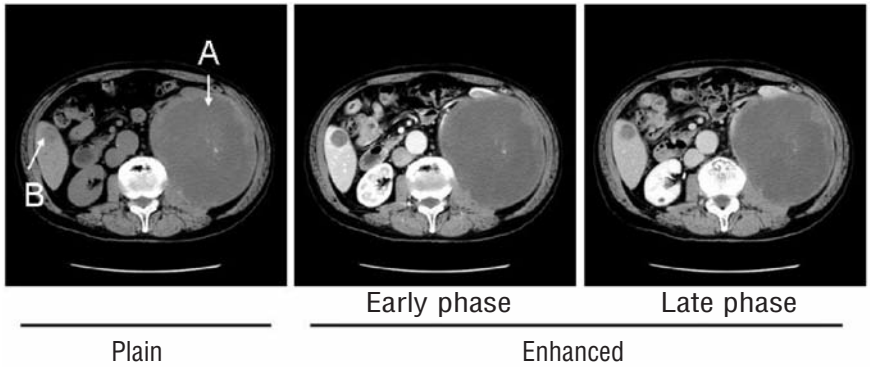

Figure 1. Abdominal CT scan findings obtained before the initial operation. An approximately 14 cm-sized mass with a distinct border was found located on the upper pole of the left kidney (A). The distribution of contrast material was limited to its margin without pooling. A new lesion that later developed in the sixth segment of the liver was shown as a low density area with poor enhancement (B).

that the neoplastic cells were not positive for cytokeratin, a marker of epithelial cells, but rather for vimentin, a marker of mesenchymal cells. The neoplastic cells were positive also for factor VIII-related antigen, CD31, and CD34, which are markers of endothelial cells, and for VEGF and its receptor, Flk-1. These immunohistochemical findings supported a final diagnosis of angiosarcoma. Immediately after the final diagnosis, recombinant interleukin-2 monotherapy (35~70 C x 10^4 IU three times a week for a total dose of $22x10^6$ IU) was started for the liver metastases in February 2007. However, the patient died of metastatic disease 13 months after the initial operation.

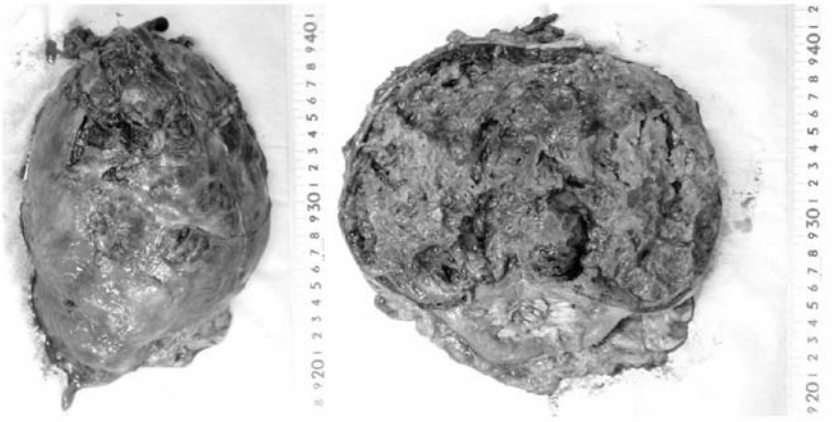

Figure 2. Macroscopic appearance of affected kidney. The mass was located on the upper pole of the left kidney. The majority of the lesion was occupied by a non-specific hematoma and its periphery was composed of fibrous tissue. No neoplastic lesions were observed in macroscopic observations.

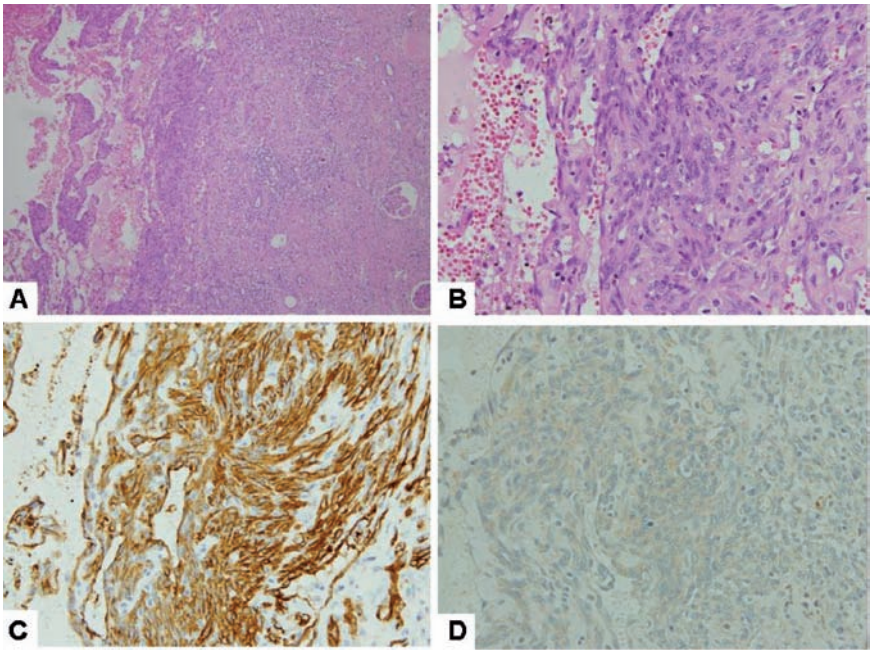

Figure 3. Microscopic findings of the primary renal lesion. Most areas of the specimens were occupied by the non-specific hematoma, whereas the tumor was located in the periphery of the hematoma (A). Spindle-shaped tumor cells with low-grade atypia had proliferated and invaded the adjacent parenchyma, which exhibited a sheet-like formation with no vascular architecture (B). The tumor cells were positive for CD31 (C), and VEGF (D).

Discussion

Angiosarcomas comprise only two percent of all soft tissue sarcomas,[1] while those deeply located including a primary renal angiosarcoma are extremely rare.[2] To the best of our knowledge, 25 cases of primary renal angiosarcoma have been reported in the English literature until the end of 2007, and the outcome for nearly all of the affected patients has been extremely poor.[3-6] The main cause for poor prognosis is the difficulty of prompt and accurate diagnosis, especially for angiosarcomas in deep organs such as the kidneys. In the present case, because the actual tumor size was extremely small, CT scanning failed to exhibit the exact tumor shape with abnormal contrast pooling, while a pathological examination also failed to provide an accurate diagnosis without cross-sections from the entire specimen. In addition, a precise pathological diagnosis required immunohistochemistry analysis,[7] as the tumor cells lacked some particular features, such as a vascular architecture. In patients with an angiosarcoma of the kidney, a prompt and exact diagnosis is not easy to obtain in the early stage, because clinical symptoms generally do not develop at that point, and the disease often shows rapid growth and metastasis. Therefore, effective systemic treatments as standard therapies are needed, although they have yet to be established. In recent years, new treatments such as immunotherapy, including recombinant interleukin-2 (rIl-2) administration,[8] and molecular targeting therapies using bevacizumab[9] and sorafenib[10] have been utilized increasingly. However, the long-term and large-scale effectiveness of these therapies remains to be assessed. We applied rIl-2 therapy to the liver metastasis in our patient via intravenous administration. The patient showed good tolerance for the drug; however, the metastatic lesions did not show a response, possibly because the drug was given as monotherapy and in a low dose, and also because the disease was well advanced at the time of the initial administration.

In conclusion, the present case confirmed the aggressive biological behavior of a primary angiosarcoma of the kidney, regardless of its relatively gentle features in imaging and pathological examinations. It is important to be aware of the possibility of angiosarcoma as well as more well-known malignancies such as renal cell carcinoma when treating a patient with an unusual hematoma of the kidney.

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