# Primary Osteogenic Sarcoma of the Kidney

## *A Case Report and Review of the Literature*

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Primary osteogenic sarcoma of the kidney is an extremely rare tumor. The original description of the disease by Haingin & Poole (1) was based entirely on autopsy evidence and since then only 25 cases have been reported in the international literature (2–24). Extraskeletal osteogenic sarcomas are uncommon tumors and can originate either from soft tissues or from parenchymatous organs such as the lung, breast or kidney (25). They represent approximately 4% of all osteogenic sarcomas and are frequently located on the proximal lower extremities and buttocks and their onset has been associated with radiation or trauma (26). In contradistinction to skeletal osteosarcomas, extraskeletal osteosarcomas are found mainly in elderly people with a median age of 51 years (26). Primary sarcomas of the kidney are rare, accounting for approximately 1% of malignant renal parenchymal tumors, with leiomyosarcoma being the most common type (27). Primary osteosarcomas of the kidney are exceedingly rare tumors. Their origin is not known but it is postulated to be derived from reversion of connective tissue to embryonic mesenchyma, which then differentiates to osteoblast. This theory has neither been confirmed nor ruled out (9, 24).

In this paper we report a new case of primary renal osteosarcoma studied with immunohistochemistry. We describe treatment, response to chemotherapy and survival in comparison with previously reported cases.

A 67 year-old male patient was admitted to our hospital presenting an 8-month history of intermittent gross hematuria and dull left-flank pain. Past medical history was negative and the patient had never at any time been given radiation therapy. On physical examination a hard palpable left-sided abdominal mass was revealed. Laboratory findings were insignificant, except for mild anemia (hematocrit 34.5%) and elevated ESR of 105 mm. Renal ultrasound presented a calcified solid mass originating from the left kidney, while on IVU the left kidney was distorted in shape and contour, calcified and no excretion was noted. CT scan and MRI also revealed a calcified left renal tumor with evidence of thrombus in the ipsilateral renal vein and regional lymphadenopathy (Figs. 1 and 2). Chest x-ray was negative. Radical nephrectomy and regional lymphadenectomy through a left thoracoabdominal incision was performed. The patient had an uneventful postoperative recovery and was discharged from hospital on the tenth postoperative day.

Macroscopically, the left kidney measured $28 \times 14 \times 10$ cm, weighed 1600 g and was almost completely occupied by the tumor. The tumor infiltrated the renal capsule, perinephric fat, and the ipsilateral adrenal gland, extending into the left renal vein. Microscopically, the tumor consisted of bundles of neoplastic spindle cells producing osteoid and neoplastic bone. A three-step immunoperoxidase staining technique was used on paraffin-embedded 4 $\mu$m-thick sections. On immunohistochemical examination the tumor was found to be negative for epithelial markers, and negative for mutated p53. The tumor stained negative for the mesenchymal markers, neuron specific enolase, lysozyme, myoglobin and desmin and positive for vimentin and smooth-muscle actin in rare cells. These findings confirmed the diagnosis of osteogenic sarcoma.

Postoperatively, the patient was re-evaluated using a chest CT-scan and bone scan. Disease was detected only in the lungs, where several small deposits were found. Pulmonary metastases were not obvious in the preoperative chest x-ray. Chemotherapy started 6 weeks postoperatively and at that time lung metastases were obvious. A combination of Cis-platinum 90 mg/m$^2$, doxorubicin 40 mg/m$^2$ and cyclophosphamide 500 mg/m$^2$ were administered once every 3 weeks for 3 courses. No response was noted but there was measurable progress of the disease on the basis of the chest CT-scan. By the end of the second month metastatic disease

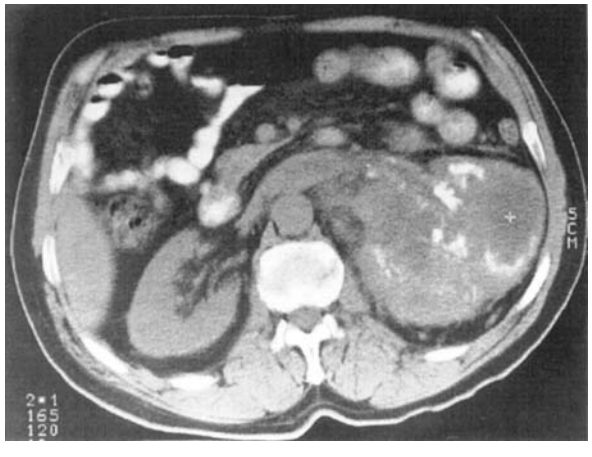


*Fig. 1.* Abdomen CT scan displaying regional lymphadenopathy and evidence of left renal vein tumor thrombus.

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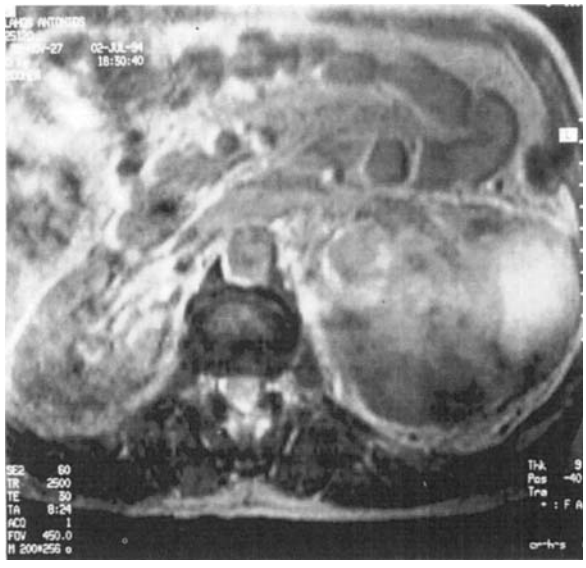

*Fig. 2.* MRI demonstrating calcified left renal tumor.

had increased in size. Following the third course, the patient presented mucositis and pleural effusion. His general condition was aggravated and paracentesis of the pleural effusion was performed. Cytology of the fluid was negative for malignant cells and a culture showed Gram-negative bacteria. Despite appropriate antibiotic treatment, the patient's condition continued to deteriorate and he died 4 months following surgery. A post-mortem examination was not performed, in accordance with the wishes of the patient's relatives.

The findings of our case and data from 26 other cases reported in the literature, are discussed.

Most of the already reported primary renal osteosarcomas tend to affect middle-aged to elderly patients. Their clinical presentation frequently includes abdominal or flank pain, weight loss and gross hematuria. Physical examination usually reveals a palpable abdominal mass with a hard consistency. A typical 'sun-burst' calcification pattern of the involved kidney has been described (11), but semilunar or circular calcification may also be present (2, 16). Elevated serum alkaline phosphatase, in the absence of liver and bone disease may be noted (11, 17, 22, 24) and is thought to be indicative of hyperactive bone metabolism. Alkaline phosphatase seems to be important in the follow-up of patients with extraossseous osteogenic sarcomas as a potential tumor marker, monitoring response to treatment (25). Radiotherapy has not been associated with the cause of any of the reported cases.

Differential diagnosis of primary renal osteosarcoma metastatic sarcoma should include adult Wilms' tumor and sarcomatoid renal cell carcinoma. Metastases of osteosarcomas to the kidney have been described, but the primary site can be identified (28) from past medical history and physical examination. Primary renal osteosarcoma has been reported to metastasize to bone and this may cause a problem in identifying primary tumor (9, 22, 29). Of all reported cases, immunohistochemical studies were carried out in two cases. Vimentin positivity was noted in one case (20) while no reactions for desmin and cytokeratin have been reported (19, 20). In our case, positivity was noted for vimentin and in rare cells for smooth-muscle actin and mutant p53 expression was negative on tumor cells. Negative staining for epithelial markers excludes sarcomatoid renal cell carcinoma and lack of blastemal component excludes adult Wilms' tumor. Negative staining for different specific mesenchymal markers excludes other types of sarcomas. Concerning age, and the histological and immunohistochemical findings, our case is strongly consistent with the diagnosis of renal osteosarcoma.

In most cases including the present one, the tumor rapidly metastasized usually to lungs and abdominal cavity, showing that the disease has the potential to progress. Six cases including our own were treated with chemotherapy, mainly with adriamycin combined regimens, but no response was observed (30). Two patients were treated with radiotherapy plus chemotherapy, also without response. Prognosis of the disease is bleak, reflecting the prognosis of primary renal sarcomas in general. The poor prognosis and short survival of our patient as well as the lack of response to chemotherapy are compatible with the prognostic profile described in previous cases. The majority of patients died within 18 months (24) and only one patient has been reported to be free of disease at a three-year follow-up (15). This patient received adjuvant chemotherapy with a single course of doxorubicin. It seems that the prognosis is based on the aggressiveness of the disease, advanced stage at time of diagnosis, and lack of response to chemotherapy. The absence of mutant p53 gene should be associated with a rather good prognosis, but this was not confirmed in our case. There are no data regarding p53 expression on previously reported cases. There is a slight predominance in male subjects.

In conclusion, primary osteogenic sarcoma of the kidney, an extremely rare entity with a poor prognosis, affects mainly the middle- and old-age groups, is often not diagnosed until the advanced stage, and shows no response to chemotherapy.

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