Osteosarcoma Metastatic to the Kidneys Without Lung Involvement

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Symptomatic renal metastasis is very rare in osteosarcoma. A few reported cases had pulmonary metastases before renal involvement. We present a case of metastatic renal osteosarcoma without pulmonary involvement. The patient presented with hematuria 8 years after initial treatment of osteosarcoma of the left distal femur. Computed tomography revealed a bilateral calcified renal mass. The patient died of disease 4 months after detection of the metastases. At autopsy, metastatic osteosarcoma was discovered in the bilateral kidney, both renal veins, inferior vena cava and right atrium. There was no pulmonary involvement. We emphasize the need for renal evaluation for the follow-up of patients with osteosarcoma.

Key words: osteosarcoma – kidney metastasis – cardiac metastasis

INTRODUCTION

Although intensive multimodality therapy has prolonged the survival of patients with osteosarcoma, the prognosis of patients with metastatic diseases is still poor. Early detection of the metastases may affect the outcome. In autopsy cases, over 90% have pulmonary metastases and 10–12% have renal metastases (1,2). However, pre-mortem diagnosis of renal metastasis is very rare. Some reports have described such cases and those patients usually had pulmonary metastases before renal involvement (3–11). We describe a case of metastatic osteosarcoma in the kidneys without lung metastasis and present a review of the literature.

CASE REPORT

In April 1986, a 19-year-old female underwent marginal excision of a bone tumor of the left femur at another hospital. The tumor was located on the posterior surface of the distal femur. The pathological diagnosis was osteochondroma. In March 1991, the tumor reoccurred with a large soft tissue nodule and heavily osteoplastic lesion in the medullary cavity and the patient was referred to our hospital (Fig. 1). A biopsy proved parosteal osteosarcoma with intramedullary dedifferentiated element. Histologically, the tumor contained well differentiated osseous trabeculae and spindle to oval tumor cells with minimal atypia (Fig. 2). There were areas of conventional high-grade osteosarcoma in the medullary cavity (dedifferentiation) (Fig. 3). The serum alkaline phosphatase (ALP) level was 428 IU/l (normal, 77–244 IU/l).

Preoperatively, four cycles of chemotherapy with a high dose of methotrexate were performed. Plain radiographs after chemotherapy did not show remarkable changes, but the serum ALP level was decreased to 228 IU/l. The patient underwent wide resection and prosthetic replacement in September, 1991. Histologically, all surgical margins were free from the tumor. In high-grade tumor (dedifferentiation), over 90% of areas showed tumor necrosis, whereas in low-grade tumor, no tumor necrosis was observed. Two weeks after the surgery, acute renal failure developed, possibly as a result of hemolytic jaundice due to blood transfusion. Hemodialysis was performed for 15 days and her renal function recovered. A further six cycles of adjuvant chemotherapy with doxorubicin were performed. In April 1992, the patient underwent thigh amputation because of late infection of the endoprosthesis.

Although routine follow-up chest radiography had revealed no metastatic nodules, the patient presented with a 1-month history of hematuria in November 1993. The serum ALP level was elevated to 764 IU/l. Plain abdominal radiography revealed multiple mineralized nodules in the renal regions (Fig. 4). Computed tomography confirmed a heavily mineralized mass in the bilateral kidneys and tumor thrombus in the inferior vena cava (Fig. 5). A Tc-99m bone scan showed marked uptake in the kidneys without any bone involvement (Fig. 6).

The patient continued to deteriorate and died of disease in April 1994. At autopsy, there were an 8 x 13 x 11 cm firm osteosarcoma in the left kidney and numerous small metastatic nodules in the right kidney (Fig. 7). The tumors extended into the bilateral renal veins, inferior vena cava and right atrium. There were no metastatic lesions in other organs including the bilateral lungs.
Parosteal osteosarcoma often develops at the posterior surface of the distal femur. This low-grade malignant tumor can show features mimicking osteochondroma in both radiographic and histological respects. Incomplete resection is often associated with local recurrence and high-grade change (dedifferentiation).
and this dedifferentiation markedly increases the risk of metastasis as conventional osteosarcoma (12). Retrospectively, the clinical course of this case indicates that this tumor was initially a parosteal osteosarcoma and developed dedifferentiation.

The reported incidence of renal metastasis of extrarenal neoplasms varies from 2 to 20% (13). In osteosarcomas, 10–12% of patient autopsies showed renal involvement (1,2). Renal metastasis of osteosarcoma is usually detected after death as part of widespread disease. Pre-mortem diagnosis of renal metastasis is very rare. Jeffree et al. (2) reported no cases of clinical renal metastasis in 91 osteosarcomas. In our series, only one of 110 patients had a pre-mortem diagnosis of renal metastases. Although the true incidence of pre-mortem diagnosis of renal metastasis is unknown, we found 10 such cases, including the present case, in the literature (Table 1) (3–11). There were eight females and two males. The age at diagnosis of metastatic renal tumor ranged from 15 to 27 years (mean, 23 years). Primary tumors were located in seven femurs, one ulna, one tibia and one fibula. Three patients had bilateral kidney metastases, four had left metastases and three had right metastases. The time from treatment of primary tumor to diagnosis of renal metastases was long (4–168 months; mean, 62 months). The reason for the long duration is probably that patients with rapidly progressive osteosarcomas do not usually undergo renal evaluation before their death and only long-term survivors receive renal evaluation. Five patients had no symptoms, three had pain and two had hematuria. Five of eight abdominal radiographies showed calcification and four of four bone scans showed abnormally increased uptake in the kidneys. Even in the patients whose abdominal radiography showed no calcification, bone scans showed abnormality. Advanced osteosarcoma often develops bone metastasis (1). Therefore, bone scan for routine follow-up of patients of osteosarcoma is recommended for the detection of metastases of not only the bone but also the kidney. We consider that patients with advanced osteosarcoma should undergo a bone scan every 6 months.
Metastatic osteosarcoma of the kidney

Table 1. Literature review of metastatic osteosarcoma of the kidney

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age/gender</th>
<th>Primary site</th>
<th>Interval to renal metastasis (months)</th>
<th>Metastasis of other lesions</th>
<th>Symptom</th>
<th>Calcification on abdominal radiography</th>
<th>Uptake on bone scan</th>
<th>Urinalysis</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marshall and Drake (3)</td>
<td>33/f</td>
<td>R. femur</td>
<td>128</td>
<td>Lung</td>
<td>Pain</td>
<td>+</td>
<td>UK</td>
<td>Hematuria</td>
<td>Alive at least 20 months</td>
</tr>
<tr>
<td>Nelson et al. (4)</td>
<td>23/m</td>
<td>L. femur</td>
<td>4</td>
<td>Lung</td>
<td>None</td>
<td>+</td>
<td>UK</td>
<td>Normal</td>
<td>DOD 4 months</td>
</tr>
<tr>
<td>Watson and Cubilla (5)</td>
<td>15/f</td>
<td>R. femur</td>
<td>30</td>
<td>Lung</td>
<td>Flank pain</td>
<td>–</td>
<td>UK</td>
<td>UK</td>
<td>UK</td>
</tr>
<tr>
<td>Goldstein et al. (6)</td>
<td>25/f</td>
<td>R. femur</td>
<td>36</td>
<td>Lung, bone</td>
<td>None</td>
<td>+</td>
<td>UK</td>
<td>Normal</td>
<td>DOD 3 months</td>
</tr>
<tr>
<td>Hallet et al. (7)</td>
<td>27/f</td>
<td>L. ulna</td>
<td>168</td>
<td>Lung</td>
<td>None</td>
<td>UK</td>
<td>+</td>
<td>UK</td>
<td>Alive at least 24 months</td>
</tr>
<tr>
<td>Ayres et al. (8)</td>
<td>16/f</td>
<td>L. femur</td>
<td>24</td>
<td>Lung, bone</td>
<td>None</td>
<td>+</td>
<td>+</td>
<td>Normal</td>
<td>DOD 6 months</td>
</tr>
<tr>
<td>Lockhart et al. (9)</td>
<td>17/f</td>
<td>R. tibia</td>
<td>29</td>
<td>Lung</td>
<td>None</td>
<td>–</td>
<td>+</td>
<td>UK</td>
<td>Alive at least 20 months</td>
</tr>
<tr>
<td>Barnes et al. (10)</td>
<td>21/m</td>
<td>L. fibula</td>
<td>46</td>
<td>Lung</td>
<td>Hematuria</td>
<td>+</td>
<td>UK</td>
<td>Hematuria</td>
<td>UK</td>
</tr>
<tr>
<td>Raby et al. (11)</td>
<td>21/f</td>
<td>R. femur</td>
<td>60</td>
<td>Lung</td>
<td>Flank pain</td>
<td>UK</td>
<td>UK</td>
<td>UK</td>
<td>UK</td>
</tr>
<tr>
<td>Present case</td>
<td>27/f</td>
<td>L. femur</td>
<td>90</td>
<td>Atrium</td>
<td>Hematuria</td>
<td>+</td>
<td>+</td>
<td>Hematuria</td>
<td>DOD 6 months</td>
</tr>
</tbody>
</table>

UK, unknown; DOD, dead of disease.

The level of serum ALP is frequently elevated in patients with osteosarcoma and elevation of ALP after surgery indicates, persistent, recurrent or metastatic disease (14). In the present case, ALP was elevated after the renal metastases.

Although the prognosis of these patients was poor, three patients survived at least 20 months after complete removal of the renal tumors. Early detection and complete surgical removal of the renal lesion may provide worthwhile palliation and long-term survival.

All previously reported cases had pulmonary metastases before the detection of renal lesions. However, the present patient had no history of lung metastasis. Autopsy also showed no pulmonary involvement. The reason for the unusual metastatic pattern in this case is not clear. Animal experiments demonstrated that tissue regeneration influenced tumor metastases and the inflammatory reaction promoted tumor metastasis at the site of regenerating tissues (15). Acute renal failure caused by hemolytic jaundice and recovery by hemodialysis in this case may be a reason for this unique metastatic pattern.

In conclusion, osteosarcoma can develop renal metastasis long after initial treatment. For early detection of this unusual metastasis, bone scan is an appropriate routine follow-up examination for patients with osteosarcoma.

References