Telangiectatic osteosarcoma

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ABSTRACT

Purpose. To review records of 8 patients with telangiectatic osteosarcoma (TOS) and determine whether pathologic fractures correlate with recurrence and survival.

Methods. Records of 4 men and 4 women aged 17 to 44 (mean, 28) years treated for TOS were reviewed.

Results. Of the 8 patients, 4 developed a pathologic fracture and 4 did not. In each group, 2 patients underwent limb salvage surgery and 2 underwent amputation. All patients received neoadjuvant and adjuvant chemotherapy with a combination of at least 2 of the following drugs: doxorubicin, methotrexate, cisplatin, and vincristin. After a mean follow-up of 5.6 (range, 2–16) years, all 4 patients with a pathologic fracture and 2 of the 4 patients without a pathologic fracture were still alive and disease-free. For the remaining patients, one died after 31 months from progression of a lung metastasis, and the other was alive with the disease and had had 2 recurrences, a lung metastasis, and an infection with Klebsiella oxytoca that eventually led to an amputation.

Conclusion. The presence of a pathologic fracture in patients with TOS was not associated with worse outcome in terms of recurrence and survival.

Key words: disease-free survival; fractures, spontaneous; neoplasm metastasis; neoplasm recurrence, local; osteosarcoma; prognosis

INTRODUCTION

Osteosarcoma is the most common primary malignant bone tumour. Telangiectatic osteosarcoma (TOS) is its subtype and accounts for 2 to 12% of all osteosarcomas.1–4 TOS is characterised by multiple aneurysmally dilated blood-filled cavities with high-grade sarcomatous cells on the peripheral rim and septae.5 The survival rate of TOS patients is similar to that of other osteosarcoma subtype patients.1,3,6–7 TOS is especially sensitive to chemotherapy, owing to its high cell turnover potential.4,8–10 Age, gender, tumour size and location are not predictors of non-metastatic TOS.4,6,10 Osteosarcoma patients with a pathologic fracture have a higher risk of local recurrence, decreased survival, and
the need for amputation than those without such a fracture. Patients with TOS are at higher risk of pathologic fractures than those with conventional osteosarcoma. We reviewed records of 8 patients with TOS and determined whether pathologic fractures correlated with recurrence and survival.

MATERIALS AND METHODS

Of 155 patients treated for osteosarcoma between 1991 and 2008, 4 men and 4 women aged 17 to 44 (mean, 28) years were identified as having TOS and their records were reviewed (Table). According to classification by the World Health Organization, the histological and radiographic diagnostic criteria for TOS were (1) numerous large spaces filled with blood and separated by fibrous septa, (2) areas of conspicuous cellular anaplasia frequently associated with giant cells of the osteoclast type or with atypical multinucleated giant cells and presence of osteoid that may be difficult to find, (3) radiological appearance as a moth-eaten or permeative radiolucent lesion, most commonly located in the metaphysodiaphyseal region, and (4) on gross examination, appearance as a haemorrhagic multiloculated mass.

Pathology, radiography, computed tomography (CT), and magnetic resonance imaging (MRI) records were reviewed by experienced pathologists and radiologists. The presence of a pathologic fracture was based on radiological findings (radiography, CT, or MRI).

RESULTS

The most common site involved was the distal femur (n=5), followed by the proximal tibia (n=2) and proximal humerus (n=1, Fig. 1). One of the patients had a lung metastasis at presentation. The diagnosis was confirmed after the first biopsy in 4 patients. In one patient, it was misdiagnosed as an aneurismal bone cyst and required 2 biopsies to confirm. In 3 patients, it was diagnosed as a high-grade osteosarcoma until pathological and radiological findings confirmed it as a TOS. Of the 8 patients, 4 developed a pathologic fracture and 4 did not. In each group, 2 patients underwent limb salvage surgery and 2 underwent amputation.

The mean time from diagnosis to surgery was 3.5 (range, 2–5) months. Four patients underwent limb salvage surgery and reconstruction with a modular arthroplasty (n=3, Fig. 2) or an arthroplasty-allograft composite (n=1). The other 4 underwent amputation.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex/age (years)</th>
<th>Tumour site</th>
<th>Follow-up (years)</th>
<th>Pathologic fracture</th>
<th>Disease stage</th>
<th>Surgical treatment</th>
<th>Adjuvant chemotherapy</th>
<th>Recurrence/metastasis</th>
<th>Complications</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/19</td>
<td>Distal femur</td>
<td>2</td>
<td>Yes, 2 days after biopsy</td>
<td>Localised Coxofemoral disarticulation</td>
<td>No</td>
<td>-</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F/17</td>
<td>Distal femur</td>
<td>13</td>
<td>Yes, during chemotherapy</td>
<td>Localised Limb salvage surgery + arthroplasty-allograft composite</td>
<td>No</td>
<td>12-cm dismetry</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M/44</td>
<td>Distal femur</td>
<td>16</td>
<td>No</td>
<td>Localised Limb salvage surgery + arthroplasty</td>
<td>No</td>
<td>Femoral stem breakage</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F/27</td>
<td>Proximal tibia</td>
<td>3</td>
<td>No</td>
<td>Localised Supracondylar amputation</td>
<td>No</td>
<td>-</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M/16</td>
<td>Proximal tibia</td>
<td>4</td>
<td>No</td>
<td>Metastatic Supracondylar amputation + thoracic surgery</td>
<td>No</td>
<td>Lung metastasis</td>
<td>Dead</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F/44</td>
<td>Distal femur</td>
<td>2</td>
<td>Yes, during chemotherapy</td>
<td>Localised Limb salvage surgery + arthroplasty</td>
<td>No</td>
<td>-</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>F/26</td>
<td>Distal femur</td>
<td>3</td>
<td>No</td>
<td>Localised Limb salvage surgery + arthroplasty</td>
<td>No</td>
<td>2 recurrences Klebsiella oxytoca infection</td>
<td>Alive, with disease Alive, disease-free</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M/28</td>
<td>Proximal Humerus</td>
<td>2</td>
<td>Yes, at diagnosis</td>
<td>Localised Scapulothoracic amputation</td>
<td>No</td>
<td>-</td>
<td>Alive, disease-free</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
in terms of coxofemoral disarticulation (n=1), supracondylar amputation (n=2) and scapulothoracic amputation (n=1).

All patients received neoadjuvant and adjuvant chemotherapy, with a combination of at least 2 of the following drugs: doxorubicin, methotrexate, cisplatin, and vincristin. For adjuvant chemotherapy, 2 to 6 cycles of the same drugs were used. Necrosis of 90 to 95% of the tumour is considered a good response to chemotherapy. The chemotherapy regimen was changed when necrosis was <90%. Echocardiography and blood tests were routinely performed to evaluate cardiac and renal function, before beginning potentially toxic treatment. No patient underwent radiotherapy.

After a mean follow-up of 5.6 (range, 2–16) years, all 4 patients with a pathologic fracture and 2 of the 4 patients without a pathologic fracture were still alive and disease-free. For the remaining patients, patient 5 died after 31 months from progression of a lung metastasis. He had undergone supracondylar amputation and resection of the lung metastasis. Patient 7 was alive with the disease and had 2 recurrences, a lung metastasis, and an infection with *Klebsiella oxytoca* that eventually led to an amputation. She had undergone wide resection and reconstruction with a modular arthroplasty. The first recurrence was treated with resection and a skin flap. The patient developed a lung metastasis and was lost to follow-up for 2 months. The second recurrence and infection with *Klebsiella oxytoca* eventually led to an amputation (Fig. 3). The 5-year survival rate was 88% for these TOS patients and 67% for all other osteosarcoma patients. Despite the small sample size, the presence of a pathologic fracture in patients with TOS was not associated with worse outcome in terms of recurrence and survival.

Other complications included a fracture of the prosthetic femoral stem (in patient 3), which was treated with revision arthroplasty, and a 12-cm dismetry (in patient 2), which was treated with a 10-cm tibial enlargement with external fixation.

**DISCUSSION**

Using both pathologic and radiological criteria to diagnose TOS is important. Although TOS has well-defined characteristics, misdiagnosis has been...
reported. Delay in diagnosis and treatment may have a negative effect on survival.\textsuperscript{3,13} An aneurysmal bone cyst can be indistinguishable from TOS on radiographs, but microscopic examination can establish the diagnosis.\textsuperscript{24} The diagnostic criteria by the World Health Organization are appropriate and commonly used.\textsuperscript{3,5,12}

Multi-agent chemotherapy that was active against osteosarcoma improved survival rates in patients with TOS.\textsuperscript{2,9,13} The increased vascularity of TOS may enhance drug delivery to the tumour site,\textsuperscript{4,9} and high cell turnover makes TOS more chemoresponsive than other osteosarcoma subtypes.\textsuperscript{4,8–10}

The rates of pathologic fractures are higher in TOS patients than those with conventional osteosarcomas (17–43\% vs. 6–13\%).\textsuperscript{2,4,8,11} This may be due to the lytic and cystic nature of TOS that makes the bone weaker and more prone to fracture.\textsuperscript{3,4,15} Osteosarcoma patients with a pathologic fracture are at higher risk of recurrence and decreased survival.\textsuperscript{11,15} In the current study, the 4 patients with a pathologic fracture did not develop a recurrence. The negative prognosis associated with pathologic fractures may be compensated by the extreme chemosensitivity of TOS.\textsuperscript{4}

Conventional treatment for patients with TOS was amputation, particularly in those with pathologic fractures.\textsuperscript{16} In the current study, the presence of a pathologic fracture did not predispose to recurrence or worse outcome. All 4 patients with pathologic fractures were alive and disease-free. Thus, limb salvage surgery may be a good option.\textsuperscript{3} Improved outcome was associated with the use of ≥3 chemotherapeutic agents and radical surgery (limb salvage surgery when feasible). Limitations of the current study were its retrospective nature and the small sample size. Moreover, the heterogeneity of chemotherapy protocols over the years may have introduced biases.

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**DISCLOSURE**

No conflicts of interest were declared by the authors.

REFERENCES