Telangiectatic osteosarcoma arising in osteogenesis imperfecta

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ABSTRACT

We present the case of a 32-year-old man with a diagnosis of type-III osteogenesis imperfecta who developed a telangiectatic osteosarcoma in the proximal right tibia. An above-knee amputation was performed and after one-year follow-up, pulmonary metastatic lesions were detected on the thoracic CT scan. Palliative chemotherapy was proposed and to date the patient is still living and is under medical treatment.

The association between osteogenesis imperfecta and osteosarcoma is rare. There are only ten confirmed reports of this unusual situation, but to our knowledge this is the first case reported with a telangiectatic osteosarcoma arising in this particular setting.

Keywords: Telangiectatic osteosarcoma; Osteogenesis imperfect; Diagnosis; Management; Outcomes.

INTRODUCTION

Despite the common belief in the general medical community of an association between osteogenesis imperfecta (OI) and osteosarcoma (OS), this is a rare finding. In fact, to date there are only ten proven cases published in the English literature¹. Both conditions are extremely rare and for that reason it is difficult to document a real association between the two diseases²-⁵. Nonetheless, most authors agree that the likelihood of an osteosarcoma developing in patients with OI is probably no greater than that found for the general population⁶. Meanwhile, for those rare patients with an osteosarcoma arising in osteogenesis imperfecta, a classic delay in diagnosis is usually described, mainly due to two major factors: the difficulty in differentiating an hyperplastic callus from an osteogenic tumor on plain x-rays, and symptoms that can be very similar and non-characteristic¹. These issues make proper management and good outcomes even more difficult.

Herein, the authors present a case of an OS arising in type III OI, more specifically, a case of telangiectatic osteosarcoma (TO). To our knowledge, this is the first case of this OS subtype to be found in the setting of OI.

CASE PRESENTATION

This is the case of a 32-year-old male patient who was born with full-term and normal delivery, however, with growth characterized by short stature, frontal bossing, and thoracic and limb dysmorphism. These features, associated with multiple non-traumatic fractures, were eventually responsible for the patient’s total dependence. A diagnosis of type-III OI was made after medical investigation. There was no family history of this disease. This patient had initial follow-up care in a pediatric hospital, but he was lost to regular follow-up in adulthood.

In November 2018, the patient started to have pain, tenderness and progressive swelling in his proximal right leg. There was no previous history of any traumatic injury. Due to the persistence of symptoms for a month, the patient sought medical attention at his regional hospital. After plain X-rays and magnetic resonance imaging (MRI), an orthopedic surgeon requested referral to our hospital.

At our institution the examination identified an increased volume in the patient’s right upper leg, associated with pain on palpation and a visible neovascularization (Fig.1). The plain X-rays (Figure 1) showed a neoformative process around the knee, the origin of which was probably at the proximal tibia. These findings were consistent with malignant bone tumor be-
behavior and further studies were requested. The studies performed included thoracic, abdominal and pelvic staging via computed tomography (CT scan), bone scintigraphy, and biopsy of the lesion. The CT scan and bone scintigraphy showed no signs of multifocal disease, and the MRI revealed features of fluid-fluid levels, suggesting the possibility of telangiectatic osteosarcoma, an aneurismatic bone cyst, or the event of a bony giant-cell tumor (Figure 2). The biopsy identified a hyalinized stroma with loci of calcification and scattered cells, with hyperchromatic and pleomorphic nuclei. The histological aspects were suggestive of malignancy, namely a bone malignancy such as osteosarcoma (Figure 3). Neoadjuvant chemotherapy before surgery was proposed, however this was refused by the patient. Nonetheless, the proposal for surgical above-knee amputation was accepted to better control the pain generated by the tumor.

The specimen in pathology confirmed the osteosarcoma diagnosis, namely a telangiectatic osteosarcoma (Figure 4). There were no complications with the stump and the patient was indicated for follow-up every three-months. Unfortunately, one year after surgery, metastatic lesions were detected in the

**FIGURE 1.** Left - Clinical photography showing a dysmorphic limb with increased volume and visible vascularization associated with a tumor/lesion in the right upper leg. Right - Plain X-ray showing severely dysmorphic bone structure and a neoformative process of the proximal right tibia.

**FIGURE 2.** Upper left - T1-weight coronal imaging showing an aggressive bone neoplasm arising from the proximal tibia. Lower left - T1-weight axial imaging showing the aggressive bone neoplasm with fluid-fluid levels with visible septae. Right - T1-weight sagittal imaging showing the same aggressive bone neoplasm arising from the proximal tibia.
which is a rare high-grade malignant neoplasm accounting for less than 4% of all cases of OS\textsuperscript{16}. This non-conventional subtype of OS usually occurs in the first and second decades of life\textsuperscript{17}. Clinically, there is no difference in the presentation between telangiectatic and conventional osteosarcoma. The most common symptoms are local pain (especially during the night), tenderness, and the presence of a soft tissue mass\textsuperscript{18}. The most common anatomic sites for telangiectatic osteosarcoma are the distal femoral metaphysis (42%) and proximal tibia (17%), which was the case for our patient\textsuperscript{16}.

A crucial aspect of evaluating an OS arising in the setting of OI is the diagnostic challenge. In fact, during the course of OI, as stated by Takahashi et al\textsuperscript{,}, there may be difficulty interpreting old and new radiographic changes due to the distorted bony morphology resulting from disease progression and recurrent fractures. Additionally, the plethora of symptoms of OI and its complications can be very similar to those of OS in its early stages\textsuperscript{1}. Unlike most cases reported in the literature regarding conventional OS in the setting of OI, where diagnostic difficulties are systematically present, our case was not affected by this phenomena\textsuperscript{1}. In fact, the different radiologic and histopathologic features of

FIGURE 3. Biopsy of the proximal tibia neoplasm showing atypical polygonal cells and sclerotic stroma (A – 25X amplification; B – 400X amplification)
Telangiectatic osteosarcoma facilitated a distinction from the cases of conventional OS or hyperplastic callus formation that were found related to OI. On the other hand, other challenges were raised by the findings during clinical investigation, such as the need to differentiate a telangiectatic osteosarcoma from other entities like an aneurysmal bone cyst (ABC) or a giant-cell tumor (GCT), in order to facilitate adequate and prompt management. However, the evidence of a tumor with clinically malignant behavior, the presence of a radiographically destructive and osteolytic neoplasm with little or no matrix mineralization, an MRI showing fluid-fluid levels with septae, and a bone scan with an intense uptake, made us suspect a telangiectatic osteosarcoma. Eventually, this suspicion was confirmed by the biopsy and final specimen histologic analysis.

Several studies in the literature concluded a similar prognosis for telangiectatic osteosarcoma and conventional osteogenic OS. The advent of neoadjuvant chemotherapy greatly improved the prognosis for all these patients, but surgery still has a decisive role. Despite limb salvage and reconstructive surgery as the current gold standard for any given limb with OS, our particular patient had severe dysmorphism which made limb salvage impossible. An above-knee amputation was performed instead, and despite a specimen with clear margins, metastatic disease was found one year after surgery, which was not a surprise in the absence of chemotherapy.

The data collected in Table 1 regarding age, gender,

![Figure 4](image-url)

**FIGURE 4.** On top – Proximal tibia tumor in section: it is possible to observe the hemorrhagic aspect of the tumor and the typical cystic cavities seen in telangiectatic osteosarcomas; on bottom – Microscopy image showing mononuclear ovoid and fusiform cells, some dispersed multinuclear cells and atypical cells in the cavities filled with blood (A – 200X amplification; B – 400X amplification).

![Figure 5](image-url)

**FIGURE 5.** Left - One year post-operative thoracic CT scan showing metastatic lesions affecting the right lung. Right - One year post-operative thoracic CT scan showing severe metastatic lesions affecting the left lung.
and location of OS in patients with OI, presented no significant differences when compared with the general population. In fact, there is a predominance of males in the first two decades of life, and osteosarcomas arising in the long bone metaphysis of lower limbs. Regarding the treatment modality and oncologic outcomes obtained in the population described in table 1, proper comparison with general population is not possible, since at least half of the reports are previous to the introduction of chemotherapy and multimodal therapies, which represented the leap forward in osteosarcoma treatment. Additionally, demographic data, histologic findings, the presence of metastases and the response to chemotherapy are the greatest predictors of survival, which are not related to the OI diagnosis.

The clinical case presented above illustrates the need for awareness of this rare event: OS arising in the setting of OI. Furthermore, we believe we describe the first case of telangiectatic osteosarcoma arising with the diagnosis of OI. This information gives practitioners additional knowledge to better understand this uncommon association.

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**REFERENCES**

<table>
<thead>
<tr>
<th>Year</th>
<th>Reference first author</th>
<th>OS subtype <em>(extrapolated from imaging and histologic findings)</em></th>
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**Table 1. Cases reported in the literature of osteosarcoma in the setting of osteogenesis imperfecta**
Telangiectatic osteosarcoma arising in osteogenesis imperfecta


