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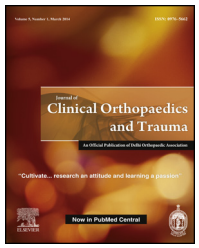

Case Report

Osteosarcoma in identical twins: A case report

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ABSTRACT

Osteosarcoma (OS) is the most frequent primary malignant bone tumor, if we exclude myeloma, a hematologic systemic disease. OS is relatively uncommon, with an estimated incidence of 600 cases per year in the United States. Among siblings is an even rarer phenomenon, with scattered reports throughout the English literature[1].

We report the incidence of OS in identical twins. The first case is a low-grade OS arisen in the proximal tibia of a 25-year-old man, treated with en-bloc resection and reconstruction with allograft. The second one is a high-grade OS of the distal tibia of the 33-year-old twin, developed in a previous non-ossifying fibroma (NOF) followed over the time. The patient was treated with neo-adjuvant chemotherapy, en-bloc resection and reconstruction with allograft. Our literature review did not find any case of OS in identical twins, while 26 reports of OS in siblings are described.

1. Introduction

Osteosarcoma (OS) is the most frequent primary malignant bone tumor, if we exclude myeloma, a hematologic systemic disease. OS is relatively uncommon, with an estimated incidence of 600 cases per year in the United States. Among siblings is an even rarer phenomenon, with scattered reports throughout the English literature.[1]

We report the incidence of OS in identical twins. The first case is a low-grade OS arisen in the proximal tibia of a 25-year-old man, treated with en-bloc resection and reconstruction with allograft. The second one is a high-grade OS of the distal tibia of the 33-year-old twin, developed in a previous non-ossifying fibroma (NOF) followed over the time. The patient was treated with neo-adjuvant chemotherapy, en-bloc resection and reconstruction with allograft.

Our literature review did not find any case of OS in identical twins, while 26 reports of OS in siblings are described.

2. Case-reports

2.1. *Case 1*

In 2005, a twenty-five-year-old man was admitted at our Institute for 6 months-history of knee pain without trauma. He referred gradual increase of pain and swelling. No history of irradiation, infection or cancer was found. Antero-posterior and lateral plain radiographs (Fig. 1) of the right knee revealed a radiolucent lesion in the metaphysis of the proximal tibia.

Computer Tomography (CT) examination (Fig. 2) showed a radiolucent cortical lesion of the proximal tibia with extension

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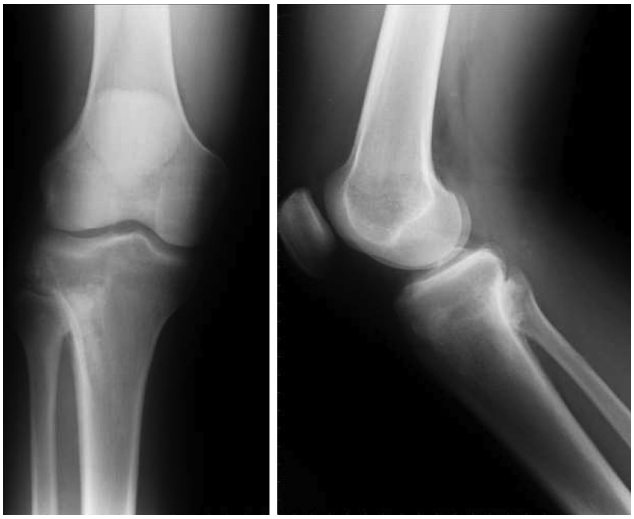

Fig. 1 – Antero-posterior and lateral plain radiographs show radiolucent lesion of the proximal tibia, near to the tibiofibular articulation.

to the proximal fibula. A CT-guided biopsy was performed with diagnosis of low-grade osteosarcoma (parosteal osteosarcoma). So the staging was performed with CT of the lungs, negative for metastases, and bone CT-scans, negative for bone metastasis. The patient underwent resection of the proximal tibia and fibula and reconstruction with homologous allograft bone and plate. Then, he presented wound dehiscence and two surgical debridements were performed.

At last follow-up in September 2013, the patient was continuous disease-free and without functional deficits. Postoperative radiograph demonstrated good integration of the allograft (Fig. 3).

2.2. *Case 2*

In September 2013, the thirty-three-year-old twin of the first patient was admitted at our institute for 4-months history of left ankle pain. The patient was followed by our surgeons for a NOF of the left distal tibia, as showed in the X-rays of 2005 (Fig. 4).

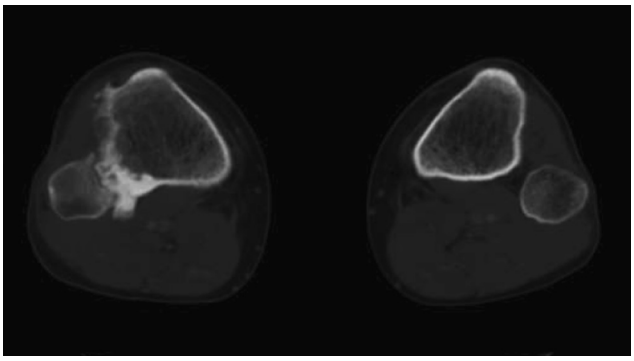

Fig. 2 – CT scan of the knee shows a cortical lesion of the proximal tibia which produces bone and violates the tibiofibular articulation.

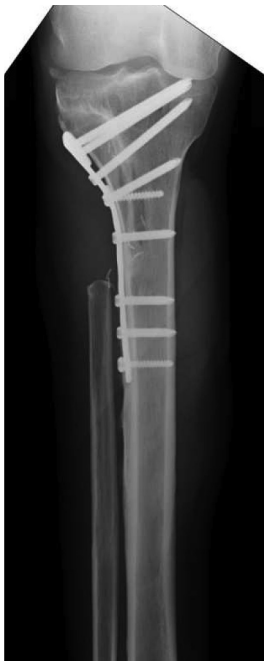

Fig. 3 – Eight-years follow-up X-ray.

The new radiographs (Fig. 5) showed osteolytic lesion of the distal tibia, near to the NOF. The Magnetic Resonance Imaging (MRI, Fig. 6) showed a destructive lesion of the distal tibia extending through the cortex in the soft tissues and the NOF adjacent to the lesion. A CT-guided biopsy was performed with diagnosis of high-grade OS. The staging of the disease was completed with CT of the lungs and Positron Emission Tomography (PET) with Fluorodeoxi-D-Glucose (FDG), negatives for metastatic disease. So the patient started standard protocol treatment with four cycles of chemotherapy, 2 with methotrexate and 2 with cisplatin and adriamycin. Then he underwent intercalary tibia resection and reconstruction with homologous bone allograft and plate with translation of the fibula to ensure more stability.

Histological examination of the entire specimen (Fig. 7a,b) demonstrated poor response to chemotherapy (30% of

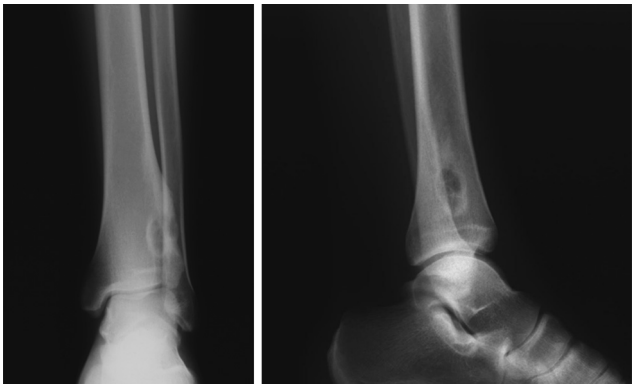

Fig. 4 – Anteroposterior and lateral plain radiographs of the left ankle performed in 2005 after accidental fall show well-defined osteolytic lesion with cortical reaction of the distal tibia, diagnosed as NOF.

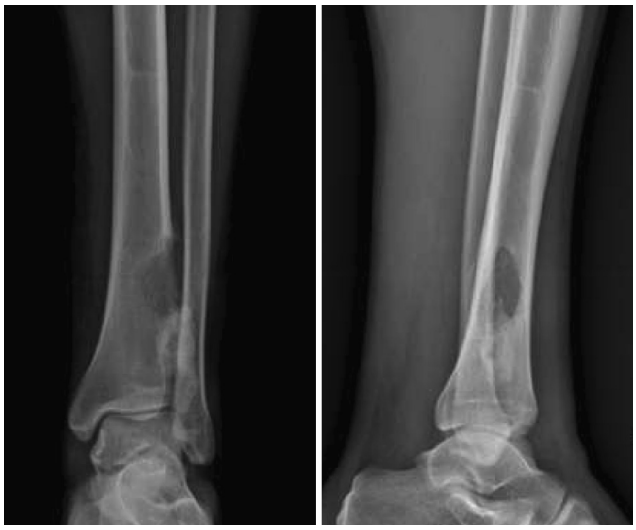

Fig. 5 – Anteroposterior and lateral X-rays show osteolytic lesion with no cortical and periosteal reaction, just above the NOF.

necrosis) and wide margins of excision. Then the patient began postoperative chemotherapy.

3. Discussion

The cause of OS is unknown but the tendency to develop in sites and age of most rapid growth points to a defect in cell growth and division. The cause of this cellular defect is still under investigation but recent advances in molecular genetics have implicated alterations in the retinoblastoma (Rb-1) and p53 suppressor genes, among others, as probable causative agents in the development and progression of OS.[1]

The first documented report of OS in siblings was described by Werner in 1930[2]; then Roberts and Roberts[3] in 1935 reported the occurrence of OS in non-identical siblings with no previous chronic bone disorders. Since then, other 24 documented cases of OS in siblings are reported in the English literature but none in identical twins.

Nowadays, is well documented the relationship between OS and other predispositions, such as retinoblastoma, Paget's

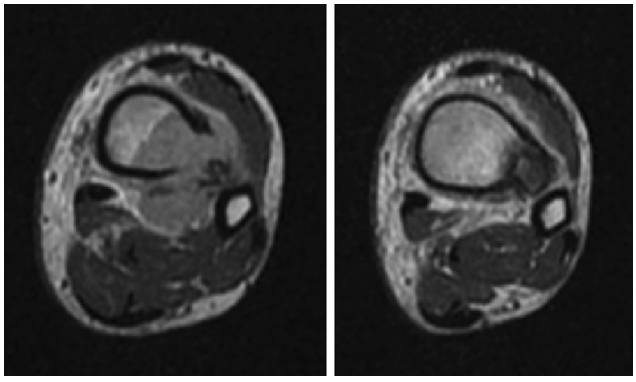

Fig. 6 – Pre-chemotherapy MRI: see on the left the destructive lesion of the tibia and on the right the NOF.

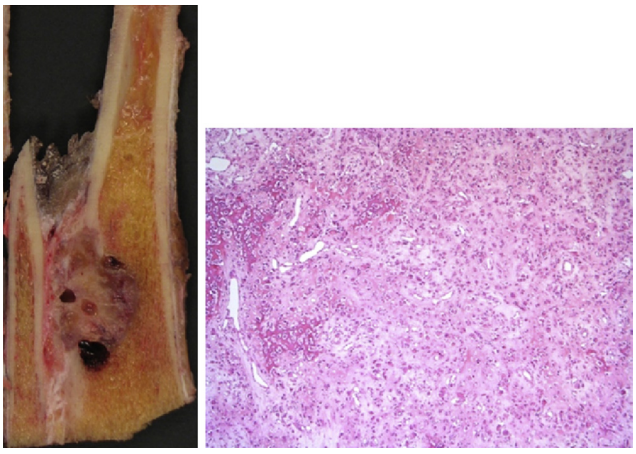

Fig. 7 – On the left, macroscopically, a tan-white solid neoformation with cystic, friable and focally hemorrhagic areas is evident. The tumor originates within the tibial distal diaphysis, erodes the cortex and forms a large soft tissue mass with involvement of fibula cortex; On the right, at histology, tumor is constituted of pleomorphic neoplastic cells that are in contact with coarse, lace-like neoplastic bone, without significative histological signs of chemotherapy response. No signs of NOF were observed (Hematoxylin and eosin, magnification 100×).

disease[4] and Li-Fraumeni syndrome while are still unknown the risk factors and causes of OS. Schimke et al.,[5] reported two cases of OS in two non-identical siblings with bilateral retinoblastoma and suggested that the retinoblastoma gene may play a role in the development of OS. Toguchida et al.,[6] reported that loss of function of both alleles of the retinoblastoma gene (Rb-1) led to the development of OS. A review of OSs[7] reported that almost 50% of second malignancies in patients with hereditary retinoblastoma are OSs and that approximately 60%–75% of sporadic OSs have an abnormality of the Rb-1 gene or do not express a functional Rb-1 product.

A recent literature review[8] of OSs arisen in the same family describes 59 cases. Paget's disease is reported as the most frequent predisposing condition (7 cases), followed by multiple fractures (3 cases) and retinoblastoma (2 cases).

The p53 gene has also been implicated in the etiology of OS and it has been estimated approximately that 50% of all human cancers have p53 defects. The incidence of p53 mutations in OS cells is estimated to be between 30% and 50%. The p53 gene produces a protein that has a cell cycle regulatory role similar to the Rb protein. Such germline mutations were first identified in families with Li-Fraumeni syndrome, characterized by a proband with a sarcoma and two or more additional first-degree relatives aged younger than 45 years with cancer.[8]

The occurrence of OS in identical twins is a rare or even unique event but may represent the best opportunity to understand the causes of the disease in humans. Further investigations and molecular analysis are necessary to clear these aspects. It would be of interest to evaluate if exposure to environmental or external factors could led to the development of OS in these twins.

Our report is the first documented case of OS in identical twins with no previous chronic bone disorders.

The final message is that a detailed family history should be obtained from every new patient with OS and parents should be urged to schedule early evaluation of siblings or twins with complaints of painful extremities.

Conflicts of interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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