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Case Report

# Silent Osteonecrosis in a Young Osteosarcoma Survivor: A Case Report of Chemotherapy-Associated Osteonecrosis

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## Abstract

Chemotherapy-associated osteonecrosis is a rare but significant complication of cancer treatment, characterized by bone necrosis resulting from disrupted vascular supply. This condition is most often associated with cytotoxic agents such as doxorubicin, cisplatin, and ifosfamide, which are known to inhibit angiogenesis, induce osteocyte apoptosis, and impair bone metabolism. MRI plays a crucial role in the early diagnosis with characteristic findings including serpiginous borders and distinct signal abnormalities on T1- and T2-weighted sequences. Although typically asymptomatic in its early stages, undetected osteonecrosis may progress to joint collapse, significantly impacting a patient's quality of life. We report the case of a 28 years-old asymptomatic male, treated with chemotherapy for an osteosarcoma without any other relevant medical history, presenting imaging signs of osteonecrosis.

***Keywords:*** *Osteonecrosis; Osteosarcoma; Chemotherapy; MRI*

## Introduction

Chemotherapy-associated osteonecrosis is an uncommon but significant complication associated to cancer treatment. Osteonecrosis, also known as avascular necrosis, is characterized by bone tissue death due to compromised blood supply, leading to cellular death and structural collapse. Although the condition is well-documented in patients receiving corticosteroids, its association with cytotoxic chemotherapy in solid tumor cases remains relatively underexplored. We present a case of a 28 years old man who developed osteonecrosis of the femur and tibia as an incidental finding on follow up MRI for his osteosarcoma.

## Case Report

A 28-year-old man with no significant medical history presented with progressive pain and swelling in his left ankle. Initial clinical, radiological and pathological investigations revealed a diagnosis of high-grade chondroblastic osteosarcoma involving the distal tibia. Following a multidisciplinary discussion, the patient was initiated on a neoadjuvant chemotherapy regimen comprising three cycles of API-AI (doxorubicin, cisplatin, and ifosfamide followed by doxorubicin and ifosfamide). After completing neoadjuvant chemotherapy, the patient underwent a below-knee amputation as definitive surgical management. Histopathological examination confirmed clear surgical margins, and he subsequently received three cycles of adjuvant EI (etoposide and ifosfamide) chemotherapy to minimize the risk of recurrence. The patient tolerated the chemotherapy regimen well without immediate complications.

Post-surgical rehabilitation involved the fitting of a prosthesis and initiation of physical therapy, which allowed the patient to regain functional mobility. Six months after completing chemotherapy, a routine follow-up magnetic resonance imaging (MRI) of the lower limbs was performed.

Although the patient was asymptomatic, the MRI revealed multiple areas of map-like bone signal abnormalities demonstrating high-intensity signals on both T1- and T2-weighted images, surrounded by a low-signal rim of sclerosis, and peripheral enhancement on Gadolinium injection. These findings included the distal epiphysis and articular surface of the femur, indicative of subchondral necrosis, and the proximal metaphyseal-diaphyseal region of the tibia corresponding to bone infarcts. There was no evidence of restricted diffusion or any signs of malignancy recurrence in the left lower limb.

These findings display characteristic features of ischemic bone damage. Given the absence of symptoms, the patient was managed conservatively with ongoing monitoring and periodic imaging to assess disease progression.

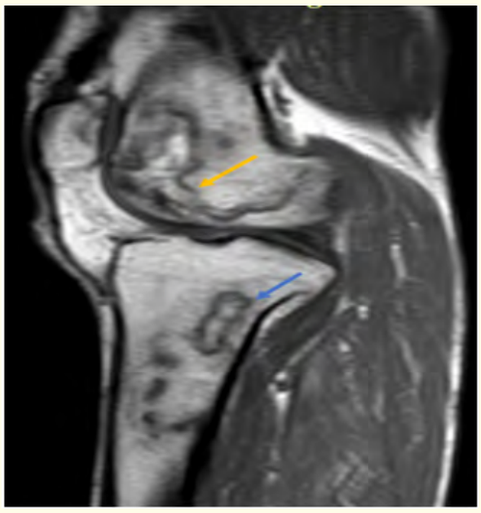

***Figure 1:*** *Sagittal T1 image of the patient's right knee showing subchondral osteonecrosis (Yellow arrow) and medullary bone infarcts (Blue arrow).*

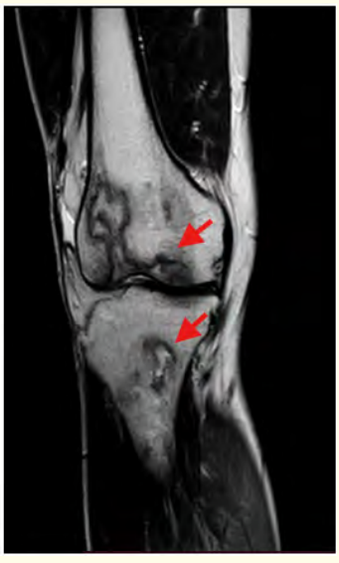

***Figure 2:*** *Coronal T2-weighted image of the patient's right knee showing osteonecrosis.*

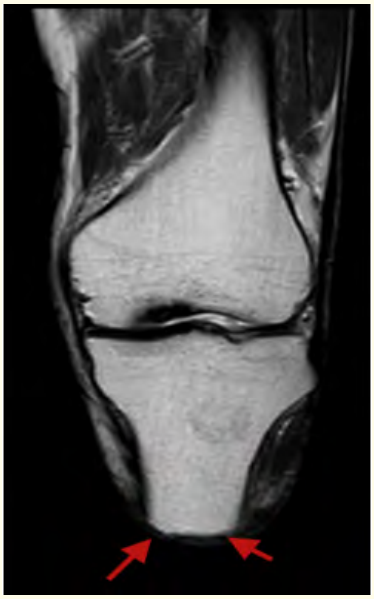

***Figure 3:*** *Coronal T2 weighted image of the left limb showing clear amputation section, with no evidence of malignancy.*

## Discussion

Chemotherapy-associated osteonecrosis is a rare but well-recognized complication of cancer treatment, particularly in patients receiving regimens that include corticosteroids or cytotoxic agents [1]. The case presented highlights the asymptomatic development of osteonecrosis in the contralateral limb of a 28-year-old man treated for osteosarcoma with a combination of doxorubicin, cisplatin, ifosfamide, and etoposide. Routine imaging six months after treatment revealed typical radiological features of osteonecrosis in the distal femur and proximal tibia of the right lower limb, underscoring the importance of vigilance in long-term follow-up of cancer survivors. The timing of osteonecrosis, its contralateral localization, and the absence of other known risk factors, such as corticosteroid use, alcoholism, or hematological disorders, strongly suggest chemotherapy as a significant contributor.

The exact pathophysiology of chemotherapy-associated ischemic bone damage is multifactorial and poorly understood. Proposed mechanisms include direct cytotoxic effects of agents like doxorubicin and cisplatin on bone cells inducing osteoblast apoptosis, ischemia due to angiogenesis inhibition and hypercoagulability [2]. Moreover, ifosfamide is associated with cumulative bone marrow toxicity, which may exacerbate the risk of osteonecrosis [3].

On imaging, osteonecrosis presents with characteristic features. It may affect the subarticular region of a joint, commonly termed avascular necrosis, or involve the metaphyseal regions of long bones, in which case it is referred to as a bone infarct.

In both situations, early lesions may be occult on radiography, ranging from subtle ill-defined radiolucencies to the more classic appearance of well-defined shell-like sclerosis. The visibility of the classic “crescent sign”, a subchondral radiolucent line, indicate imminent collapse of the articular surface.

However, magnetic resonance imaging (MRI) is very sensitive in identifying and characterizing osteonecrosis. Bone infarcts on MRI are characterized by a “map-like” rim of low signal intensity on T1- and T2-weighted images, encircling a central region that often follows

the signal intensity of fat. The central area may vary from hyperintense (fat necrosis) to hypointense (marrow fibrosis or sclerosis). The hallmark "double line sign," consisting of an inner high-signal-intensity line and an outer low-signal-intensity line on T2-weighted imaging, is considered pathognomonic for osteonecrosis [4].

Beyond diagnosing ischemic bone damage, MRI surveillance plays a crucial role in detecting potential malignancies arising from chronic bone infarcts [5]. Although rare, bone infarct-associated osteosarcoma has been reported in patients with longstanding infarcts or prior cancer diagnoses. The population most at risk primarily consists of men around the age of 55. The most frequently affected locations are bone infarcts in the proximal tibia and distal femur [6]. Although our patient is younger than the average reported cases, the localization of his bone infarcts in these high-risk anatomical regions in addition to his history of osteosarcoma, may constitute a predisposing factor, warranting close surveillance.

Management of osteonecrosis depends on the stage of disease and clinical presentation. In asymptomatic cases without joint collapse, conservative measures such as activity modification, weight-bearing restrictions, and periodic monitoring are recommended. For symptomatic cases or those with advanced disease, surgical interventions such as core decompression or joint replacement may be necessary. In this patient, conservative management was deemed appropriate given the early stage of osteonecrosis and the lack of symptoms.

Early detection through routine imaging allows for timely intervention, which may prevent joint collapse and preserve function. Although rare, chemotherapy's potential to induce osteonecrosis warrants increased awareness among clinicians, particularly as cancer survivorship grows. Further research is needed to elucidate the underlying mechanisms and identify preventive strategies [7].

## Conclusion

Chemotherapy-associated osteonecrosis, though rare, is a debilitating complication that warrants greater attention in oncology. This case highlights the dual role of MRI in diagnosing ischemic bone damage and screening for infarct-related malignancy and underscores its importance in the comprehensive care of cancer survivors.

## Patient Consent

An appropriate written consent was obtained from the patient for the publication of this case report.

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