

# Development of a Non-ossifying Fibroma in the Same Femur 6 Years after Limb-Salvage Surgery for Osteosarcoma: A Case Report

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## Learning Point of the Article:

A new lytic lesion in a previously treated osteosarcoma-bearing femur may represent a benign lesion; careful multimodal assessment can prevent unnecessary biopsy or aggressive treatment.

## Abstract

**Introduction:** A new osteolytic lesion detected during surveillance after osteosarcoma treatment usually raises concern for local recurrence, a skip lesion, metastasis, or a treatment-related secondary process. Non-ossifying fibroma (NOF) is a common benign fibrous lesion in children and adolescents, but its delayed appearance in the same surgically reconstructed femur is unusual and may create a major diagnostic dilemma.

**Case Report:** A 12-year-old child presented with a 4-month history of pain and swelling in the right thigh. Imaging and core needle biopsy confirmed osteosarcoma of the femur. The patient received three cycles of doxorubicin- and cisplatin-based neoadjuvant chemotherapy, followed by wide resection, extracorporeal radiotherapy of the resected segment, reimplantation, and plate fixation. The patient remained symptom-free with good limb function for 6 years. Routine surveillance then identified a new, well-defined cortically based osteolytic lesion in the distal femoral metaphysis. Computed tomography (CT) demonstrated sclerotic margins without cortical breach or a soft-tissue component, while positron emission tomography-CT showed only low-grade metabolic activity. Serial imaging and the absence of symptoms supported a radiological diagnosis of NOF, and observation was continued. At 8 years of follow-up, the patient remained asymptomatic with satisfactory knee motion and no evidence of osteosarcoma recurrence.

**Conclusion:** Benign lesions should remain in the differential diagnosis when a new lytic lesion is detected during long-term osteosarcoma surveillance. Correlation of lesion morphology, metabolic activity, clinical findings, and interval behavior is essential to avoid misdiagnosis and overtreatment.

**Keywords:** Osteosarcoma, non-ossifying fibroma, extracorporeal radiotherapy, limb salvage, femur, case report.

## Introduction

Osteosarcoma is the most common primary malignant bone tumor in children and adolescents. A non-ossifying fibroma (NOF) is a benign fibrous lesion that typically occurs in the metaphysis of long bones and is frequently discovered incidentally [1, 2]. The simultaneous or sequential occurrence of

osteosarcoma and NOF in the same bone is rare and can complicate surveillance, particularly when a new lesion appears after successful oncological treatment [3,4].

NOF is one of the most common benign fibrous lesions of childhood, typically arising in the metaphysis of long bones and exhibiting a characteristic natural history of spontaneous

## Author's Photo Gallery



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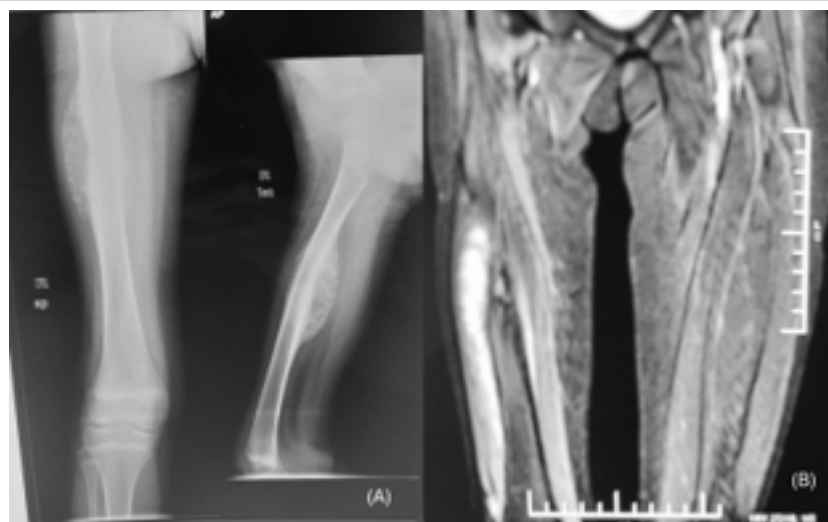
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**Figure 1:** Pre-operative imaging demonstrating the primary malignant lesion of the right femur. (a) Anteroposterior and lateral radiographs showing an aggressive osteolytic lesion involving the femoral shaft with cortical destruction and periosteal reaction, suggestive of a malignant bone tumor. (b) Coronal magnetic resonance image demonstrating marrow involvement with extension into the adjacent soft tissues, consistent with a high-grade primary bone malignancy.

regression. Although NOF is generally regarded as a benign developmental lesion with an excellent prognosis, uncommon presentations, including occurrence at unusual anatomical sites and exceptionally rare sarcomatous transformation, have been reported. These observations emphasize that atypical NOFs may pose important diagnostic challenges, particularly in patients with a previous history of malignant bone tumors

[2,5,6].

The detection of a new osteolytic lesion during surveillance in an osteosarcoma survivor immediately raises concern for local recurrence, skip lesions, metastasis, infection, or treatment-related secondary neoplasms. Distinguishing these entities from a benign developmental lesion is crucial, as an incorrect diagnosis may lead to unnecessary biopsy, aggressive surgery, or systemic therapy. We report the delayed development of an imaging-defined NOF in the same femur 6 years after limb-salvage surgery with extracorporeal radiotherapy (ECRT) and biological reimplantation for osteosarcoma, highlighting the importance of multimodal imaging and careful clinicoradiological correlation in avoiding overtreatment.

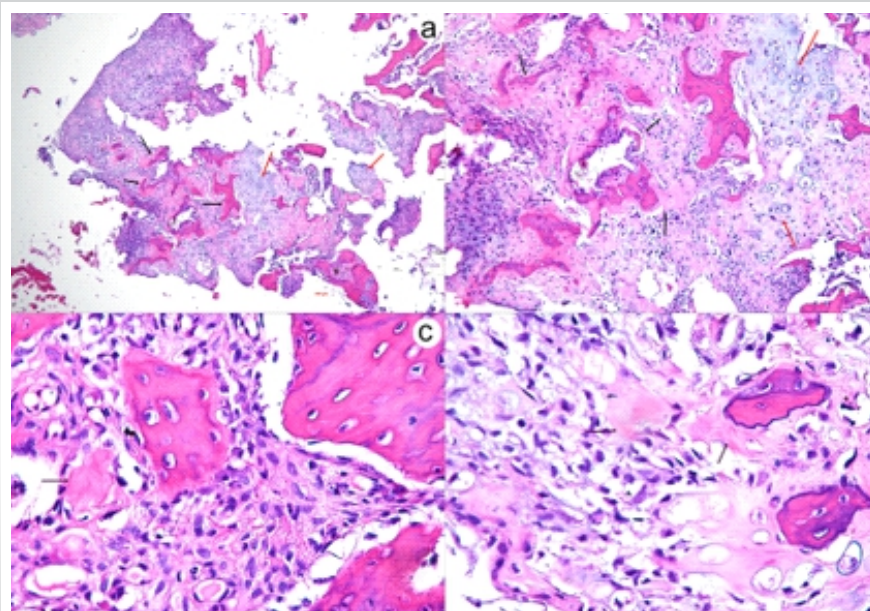
### Case Report

A 12-year-old presented with a 4-month history of pain and swelling in the right thigh. Orthogonal radiographs demonstrated an aggressive osteolytic lesion of the femur with cortical destruction and periosteal reaction. Magnetic resonance imaging showed marrow involvement with extension into the adjacent soft tissues, consistent with a high-grade primary bone malignancy (Fig. 1). Core needle biopsy

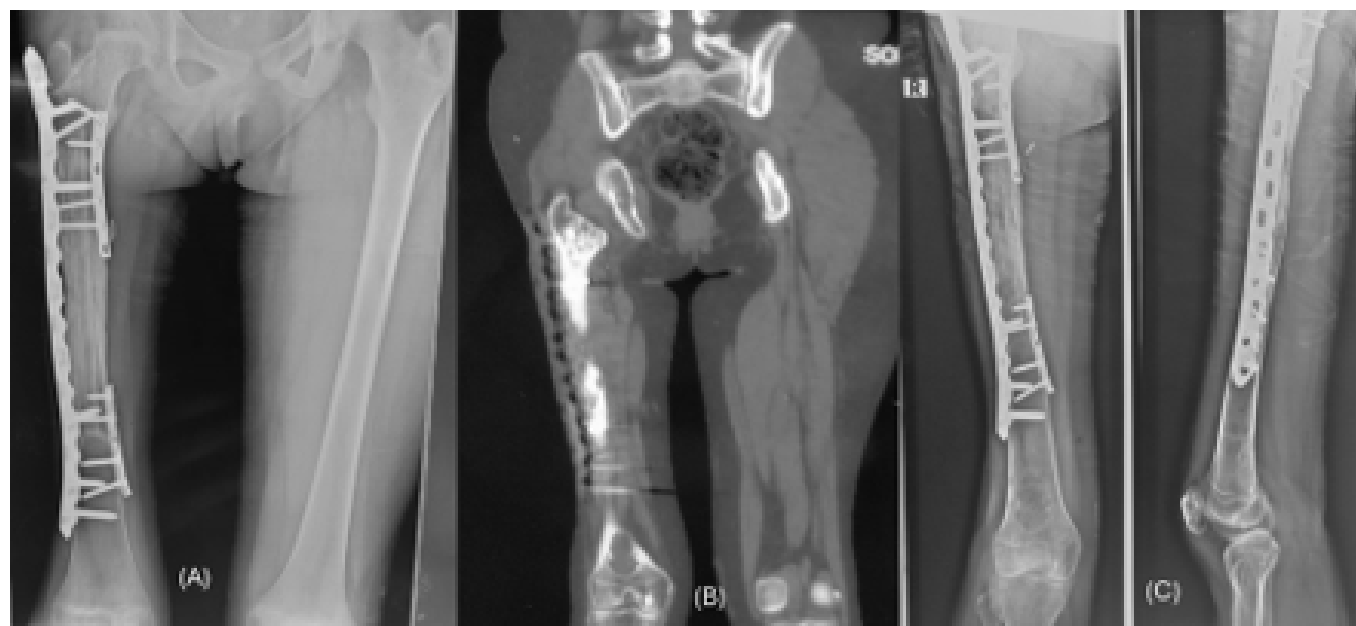
confirmed osteosarcoma, with histopathology demonstrating malignant mesenchymal cells and irregular osteoid deposition with areas of chondroid differentiation (Fig. 2).

The patient received three cycles of doxorubicin- and cisplatin-based neoadjuvant chemotherapy. After repeat imaging and pre-operative evaluation, including two-dimensional echocardiography, wide tumor resection was performed. The resected femoral segment was treated with ECRT, reimplanted, and stabilized using a 3.5-mm locking compression plate and a one-third tubular plate (Fig. 3a). The post-operative course was uneventful, and the patient remained symptom-free with good limb function for 6 years.

During routine long-term surveillance 6 years after surgery, radiographs revealed a new, well-defined osteolytic lesion in the metaphyseal region of the ipsilateral distal femur. Non-



**Figure 2:** Histopathological features of the primary lesion. (a) Hematoxylin and eosin (H and E), ×40 and (b) ×100 magnification showing a mesenchymal neoplasm with irregular osteoid deposition (black arrows) and areas of chondroid differentiation (red arrow). The osteoid is predominantly woven and appears as eosinophilic, haphazard, lace-like structures. Tumor cells show marked nuclear hyperchromasia and an increased nuclear-to-cytoplasmic ratio. (c and d) H and E, ×400 magnification showing atypical spindle-to-polygonal tumor cells embedded within a chondroid matrix.



**Figure 3:** Post-operative imaging demonstrating interval development of a distal femoral lesion. (a) Immediate post-operative radiograph after wide resection, ECRT, and reimplantation with internal fixation, showing no distal femoral lesion. (b) Coronal computed tomography image demonstrating a well-defined cortically based metaphyseal lesion in the distal femur. (c) Follow-up radiographs showing persistence of the distal femoral lesion with healing and incorporation of the ECRT -treated femoral segment. ECRT: Extracorporeal radiotherapy.

contrast computed tomography (CT) showed a cortically based lesion with sclerotic margins, without cortical breach or an associated soft-tissue component (Fig. 3b and c). Positron emission tomography-CT demonstrated low-grade metabolic activity without features strongly suggestive of malignancy.

Although histological confirmation remains the gold standard for diagnosis of a new bone lesion in an osteosarcoma survivor, biopsy was deferred in this patient because all imaging modalities consistently demonstrated benign characteristics; there was no cortical destruction or soft tissue component, metabolic activity remained low, and serial imaging showed stability. The potential morbidity of biopsy in a previously reconstructed femur also favored continued surveillance.

The differential diagnosis included osteosarcoma recurrence, a skip or metastatic lesion, NOF, fibrous dysplasia, a simple bone cyst, and osteomyelitis. In view of the benign imaging characteristics, absence of symptoms, and stable interval appearance, the lesion was considered radiologically most consistent with a benign NOF. Continued clinical and radiological surveillance was advised rather than immediate biopsy or operative intervention.

At 8 years after the index procedure, the patient remained asymptomatic with no pain, swelling, or functional limitation. Knee range of motion was

satisfactory (Fig. 4); the ECRT-treated segment showed healing and incorporation, and there was no evidence of local recurrence or metastatic disease. Observation was continued.

### Discussion

This case illustrates the diagnostic complexity created by a new osteolytic lesion in a previously treated bone in an osteosarcoma survivor. Osteosarcoma carries a recognized risk of local recurrence, skip lesions, and distant metastasis, and therefore any new lesion detected during surveillance requires careful evaluation [7]. Nevertheless, benign entities such as



**Figure 4:** Clinical photographs at final follow-up demonstrating satisfactory post-operative knee range of motion. (a) Knee flexion. (b) Knee extension.

NOF must remain in the differential diagnosis, particularly in children and adolescents. Typical NOFs are well-defined, eccentric or cortically based lytic lesions with a sclerotic margin and usually lack aggressive cortical destruction or a soft-tissue mass [2,6].

Sharma et al. described a NOF that mimicked distant skeletal metastasis of recurrent osteosarcoma on bone scintigraphy, emphasizing the potential for benign lesions to simulate metastatic disease during oncological surveillance [3]. Similarly, Kyriakos and Resnick reported the concurrence of metaphyseal fibrous defects and osteosarcoma in the same bone, demonstrating that benign fibrous lesions may coexist with malignant tumors and complicate diagnostic interpretation [4]. Although NOF is generally regarded as a benign developmental lesion, Biazzo et al. reported an exceptional case of spindle cell sarcoma arising in association with a pre-existing NOF, highlighting the need for histopathological confirmation whenever imaging findings are atypical or progressive [5]. Likewise, Bowers et al., in their review of an unusual maxillary NOF, emphasized that these lesions may occasionally occur at uncommon anatomical sites and mimic more aggressive pathology, necessitating careful clinicoradiological correlation [6]. Unlike these previously reported scenarios, our patient developed a new radiologically characteristic NOF in the same reconstructed femur 6 years after limb-salvage surgery for osteosarcoma, without radiological or metabolic evidence of recurrent malignancy. To our knowledge, this represents the first reported case of such a presentation following ECRT-assisted biological reconstruction.

Multimodal imaging is central to differentiation. Lesion margins, cortical integrity, presence or absence of a soft-tissue component, metabolic activity, and interval change should be interpreted together with the clinical examination [7,8]. In the present case, the well-defined cortically based morphology, sclerotic margin, low-grade metabolic activity, absence of symptoms, and stable follow-up behavior favored a benign diagnosis. A multidisciplinary review involving orthopedic oncologists, musculoskeletal radiologists, pathologists, and pediatric oncologists can reduce the risk of both undertreatment and overtreatment.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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ECRT and reimplantation provide a biologic reconstruction with exact anatomical fit after wide resection of selected malignant bone tumors [9,10]. Long-term surveillance remains necessary after this procedure to evaluate oncological status, graft incorporation, mechanical complications, and any new osseous lesion. The present observation broadens the spectrum of benign findings that may appear during follow-up after limb-salvage reconstruction.

The principal limitation of this report is that the NOF diagnosis was based on characteristic imaging and interval stability rather than histopathological confirmation. However, biopsy was deferred because the lesion lacked aggressive features and the patient was asymptomatic. Continued surveillance remains important, and biopsy would be warranted if the lesion enlarges, becomes symptomatic, develops cortical destruction, or acquires a soft-tissue component.

To the best of our knowledge, no previous report has described the delayed appearance of a radiologically characteristic NOF in the same reconstructed femur following ECRT-assisted limb-salvage surgery for osteosarcoma.

## Conclusion

A new lytic lesion in an osteosarcoma survivor should not automatically be considered recurrent malignancy. Benign lesions such as NOF may occur in the same femur even years after limb-salvage treatment. Careful multimodal imaging, clinical correlation, interval assessment, and multidisciplinary review can establish an appropriate working diagnosis and prevent unnecessary invasive or aggressive treatment.

## Clinical Message

Every newly detected osteolytic lesion during osteosarcoma surveillance should undergo systematic assessment using clinical findings, radiographs, cross-sectional imaging, and metabolic imaging before recurrence is presumed. Recognition of the characteristic appearance of NOF may prevent unnecessary biopsy and repeat oncological surgery.



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