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Case Report

Extraskeletal osteosarcoma misdiagnosed as heterotopic ossification after periprosthetic femoral fracture: A case report

Il-Hoon Sung[1], Hee-Jung Son[2], Jin-Sung Park[2], Young-Sik Song[2], Ki-Chul Park[2]

[1]*Department of Orthopedic Surgery, Hanyang University, College of Medicine, Seoul Hospital, Seoul, Korea*
[2]*Department of Orthopedic Surgery, Hanyang University, College of Medicine, Guri Hospital, Gyeonggi, Korea*

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ORCID IDs of the authors:
I.H.N. 0000-0002-4757-5210;
H.J.S. 0000-0002-0180-8744;
J.S.P. 0000-0001-6517-8609;
Y.S.S. 0000-0002-7148-8221;
K.C.P. 0000-0003-0938-8040.

Corresponding Author:
Ki-Chul Park
kcpark722@gmail.com

ABSTRACT

Extraskeletal osteosarcoma is a malignant tumor of soft tissue characterized by osteoid production and has a very low prevalence, comprising approximately 4% of all osteosarcomas and about 1% of all soft tissue sarcomas, and a total of about 350 cases have been reported until now. Heterotopic ossification is a pathological finding of bony tissue in soft tissue regions such as muscle, skin and subcutaneous tissue. We report a case of an 86-year-old woman with a history of total hip arthroplasty (THA), in which open reduction and internal fixation were done for periprosthetic femoral Fracture. The ossified lesion misdiagnosed as heterotopic ossification initially was diagnosed as extraskeletal osteosarcoma at 6 months after the surgery. Both extraskeletal osteosarcoma and heterotopic ossification have no definite symptoms, but show radiopaque shadows on simple radiograph. Therefore, careful attention and thorough evaluation with multiple imaging tests may be necessary for the differential diagnosis of these entities

Extraskeletal osteosarcoma, also known as extraosseous osteosarcoma, is a malignant tumor of soft tissue characterized by osteoid production, and has no connection with bone or periosteum (1). This malignancy is rare compared to skeletal osteosarcoma, accounting for approximately 4% of all osteosarcomas and 1% of all soft tissue sarcomas (2). In contrast to the bone-invading osteosarcoma that commonly affects teenagers and young adults, extraskeletal osteosarcoma occurs predominantly in men and women older than 40 years of age (3, 4).

Heterotopic ossification, also referred to as heterotopic bone formation, is a pathological finding of bony tissue in soft tissue regions such as muscle, skin, and subcutaneous tissue, among others, frequently occurring around joints. To date, the exact mechanism of heterotopic ossification remains unidentified. However, it is related to several factors, including hematoma after soft tissue trauma, injury to the central nervous system, and passive physical therapy to a stiff joint (5, 6).

Both extraskeletal osteosarcoma and heterotopic ossification display no definite symptoms, but produce radiopaque shadows on a simple radiograph. When a radiopaque lesion is observed on a plain radiograph, further evaluation and operative excisional biopsy should be performed if required.

A case involving a patient with a periprosthetic femoral fracture is presented, wherein open reduction and internal fixation were conducted. The case was initially misdiagnosed as heterotopic ossification but subsequently diagnosed as extraskeletal osteosarcoma 6 months after the operation.

Case Presentation

An 86-year-old woman arrived at the emergency department with severe pain in the right thigh, right wrist, and both knees after falling down. The patient had undergone a THA (brand name unknown due to lack of record) of her right hip in another hospital 17 years prior to the presentation described herein. Additionally, she had

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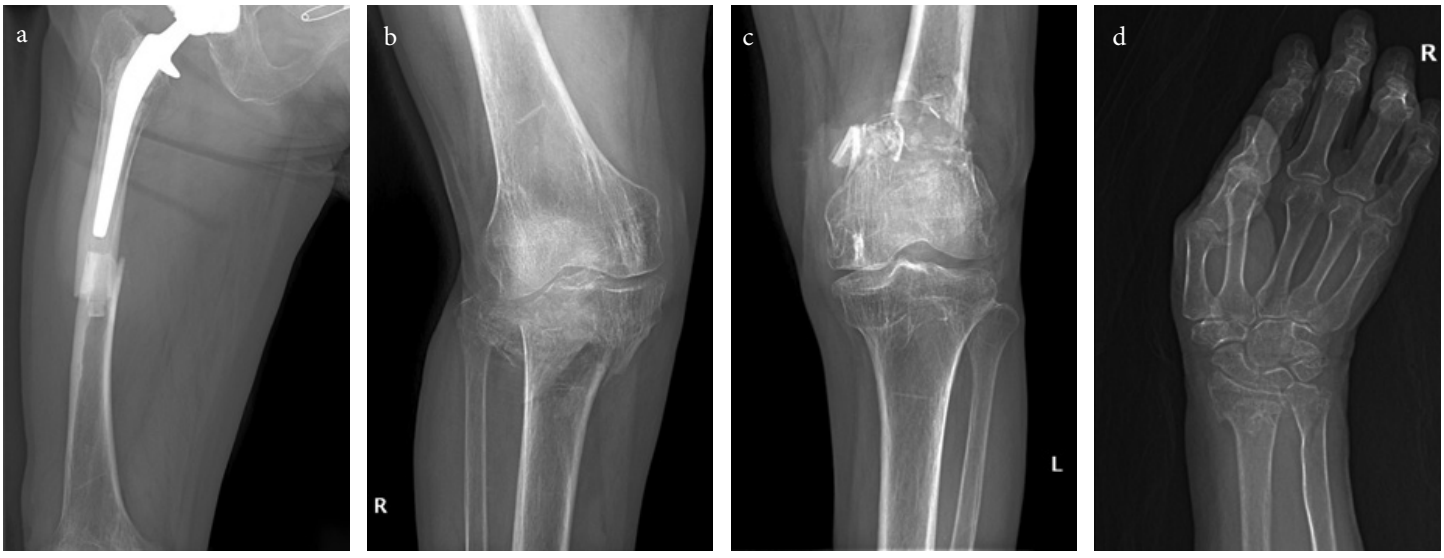


Figure 1. a-d. Preoperative AP radiographs showing a periprosthetic fracture of the right femur (Vancouver classification C) (a), right proximal tibial fracture (b), left distal femoral fracture (c), and right distal radial fracture (d)

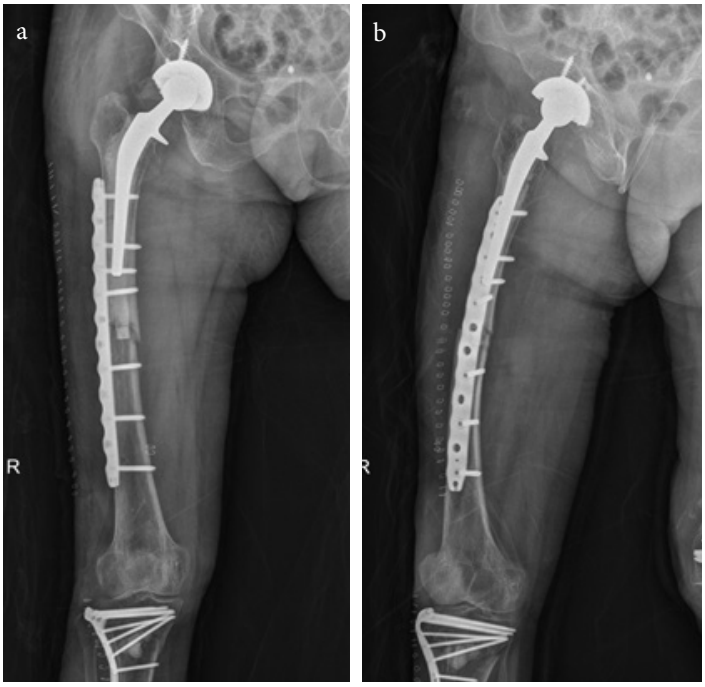


Figure 2. a, b. Postoperative AP (a) and oblique radiograph showing appropriate reduction and fixation (b)

taken warfarin due to atrial fibrillation. Initial anteroposterior and lateral radiographs after the injury showed a periprosthetic fracture of the right femur (Vancouver classification C), right proximal tibial fracture, left distal femoral fracture, and right distal radial fracture (Figure 1). Subsequently, the patient underwent open reduction and internal fixation for each fracture. The right periprosthetic femoral fracture was repaired with a Non-Contact Bridging (NCB) plate (Zimmer, Warsaw, Indiana, USA) (Figure 2).

Postoperatively, the patient had mild pain, but experienced no difficulty in performing daily activities. Simple radiographs performed periodically showed radiopaque lesions around the right femoral fracture site 4 weeks postoperatively. At 8 weeks postoperative, there was mild soft tissue swelling on the right thigh and the radiopaque shadow had slightly increased, but no definite bridging of the radiopaque lesion with the callus was observed. A physical examination performed 12 weeks postoperatively revealed moderate soft tissue swelling, local heat, and redness on the right thigh and knee. In addition to the mild callus formation around the femoral fracture site, multiple radiopaque mass-like lesions with increased soft tissue swelling were observed on the follow-up simple radiograph (Figure 3). Laboratory findings showed an erythrocyte sedimentation rate (ESR) of 69 mm/hr and a mildly elevated level of C-reactive protein (CRP) of 2.60 mg/dL. It was thought that the symptoms were due to a superficial infection of the wound, while the multiple radiopaque mass-like lesions observed through the simple radiograph represented heterotopic ossification. Antibiotics were prescribed, and the patient's condition was observed. At 6 months after surgery, a fistula was observed, which suggested the possibility of infection around the knee, and the patient's symptoms became aggravated. Therefore, operative treatment was performed because of the suspected postoperative infection around the knee and heterotopic ossification of the thigh.

MAIN POINTS

- The p16 and CD34 expressions are valuable in the differential diagnosis of lipomatous tumors
- Spindle cell lipoma is often localized in the subcutaneous superficial soft tissue of the neck, back, or shoulder and Dedifferentiated liposarcoma is often located in the retroperitoneum.
- Atypical lipomatous tumor/well differentiated liposarcoma and Dedifferentiated liposarcoma constitute diameter greater than 10 cm.

Under general anesthesia, a lateral approach to the femoral shaft revealed no definite evidence of infection. However, several of the mass-like lesions that appeared on the simple radiograph were similar to calcified cartilage mixed with fatty tissue, which had no attachment to bone or periosteum (Figure 4). Therefore, an excisional biopsy was performed. In addition, the implant in the tibia was removed, and the surgical area was completely irrigated and debrided. There was no infection found in the surgical area; only a change in the amount of inflammation was observed.

The specimens were analyzed by a pathologist. The largest specimen was approximately 7×5.6×2.8 and the weight of all specimens was 160 g. Gross findings showed that the tumor surface was white or light gray and relatively soft, while the localized calcified tumor lesion was hard. A cross section of the tumor revealed a light gray or yellow color with multiple calcifications (Figure 5). Finally, microscopic immunohistochemistry findings showed malignant and anaplastic spindle cell proliferation with the presence of osteoid or immature bone, leading to the diagnosis of the tumor as extraskeletal osteosarcoma (chondroblastic) (Figure 6).

After the final diagnosis, a bone scan of the entire body was performed, but no lesions were observed in other parts of the body. Chemotherapy and radiotherapy were planned in consultation with a hemato-oncology specialist. However, the patient and her family refused aggressive treatment because of the patient's deteriorated physical condition (Eastern Cooperative Oncology Group scale performance 4 [ECOG 4]). Therefore, besides pain control, no treatment was administered. Four months after the final operation, pulmonary metastasis was found on a chest radiograph. The patient died 5 months postoperatively.

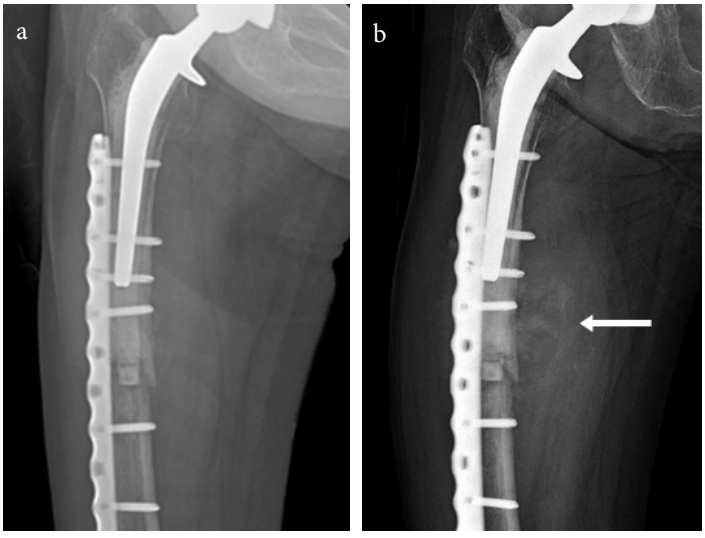


Figure 3. a, b. Radiopaque shadow on AP radiograph 2 months postoperatively (a) and 4 months postoperatively (arrow indicates multiple radiopaque mass-like lesions) (b)

Discussion

In this case, the patient underwent an excisional biopsy for multiple radiopaque tumors; heterotopic ossification was initially suspected after open reduction and internal fixation were performed for a periprosthetic femoral fracture (Vancouver classification C), and she was eventually diagnosed with extraskeletal osteosarcoma. Heterotopic ossification describes bone formation outside the skeletal system, and commonly occurs in sites adjacent to joints. Although its exact pathogenetic mechanism has not been established, it is known to be associated with hematoma following trauma, injury to the central nervous system, and aggressive application of passive range of motion to stiff joints (5, 6). It has been reported that severe heterotopic ossification may develop in 9% of patients who undergo THA, and many of them may need to undergo a further operation due to limited range of motion or painful impingement (7).

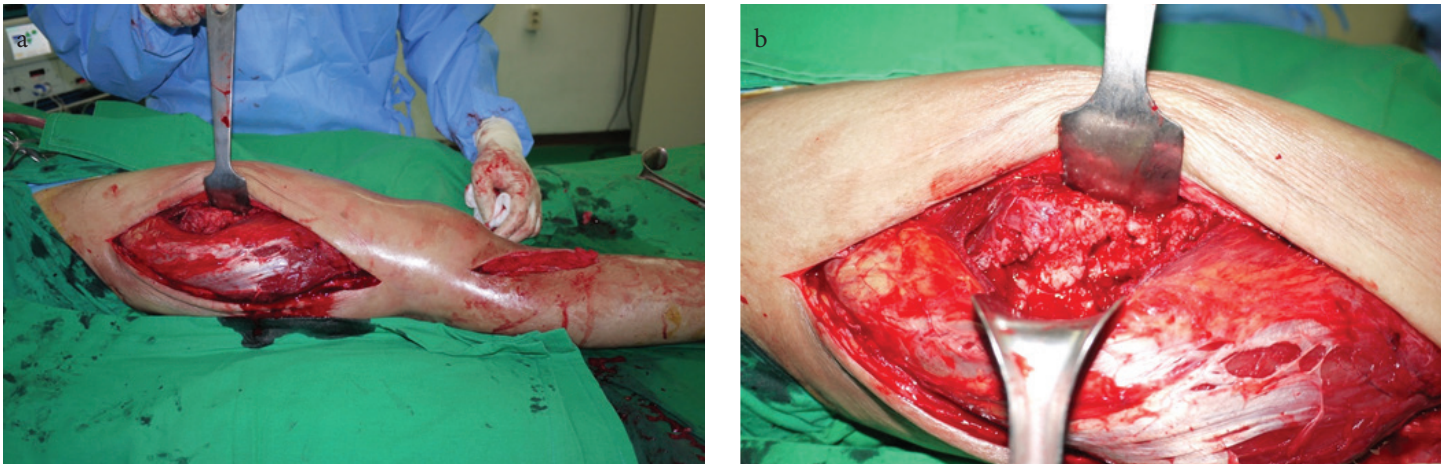
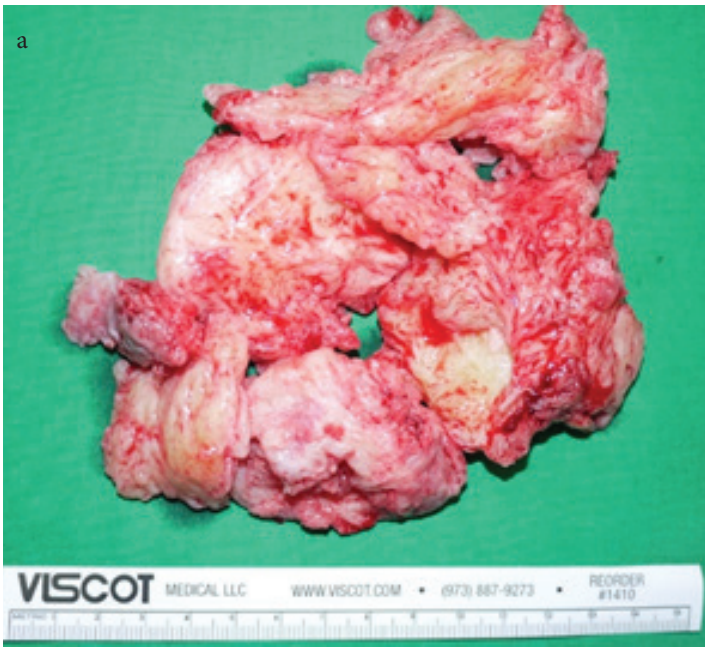


Figure 4. a, b. Intraoperative finding of multiple mass-like lesions shown on the simple radiograph, which had no attachment to bone or periosteum (a, b)



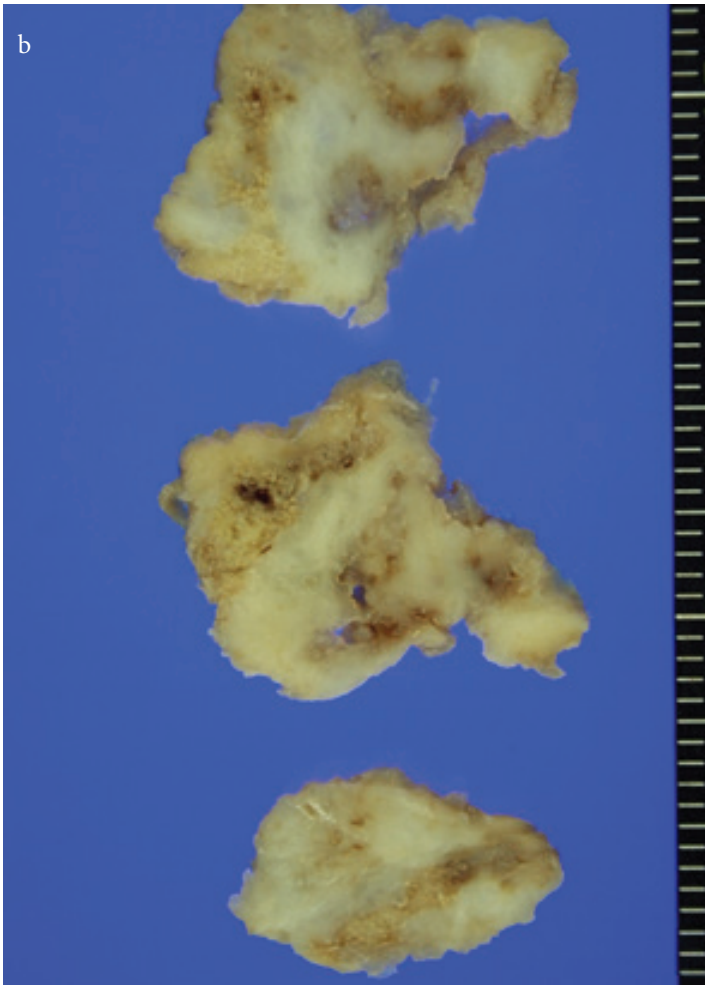


Figure 5. a, b. The observed macroscopic specimen, similar to calcified cartilage mixed with fat tissue with a white or light gray and relatively soft surface, whereas the localized calcified lesion was hard (a). The tumor cross section appeared light gray or yellow in color, with multiple calcifications (b)

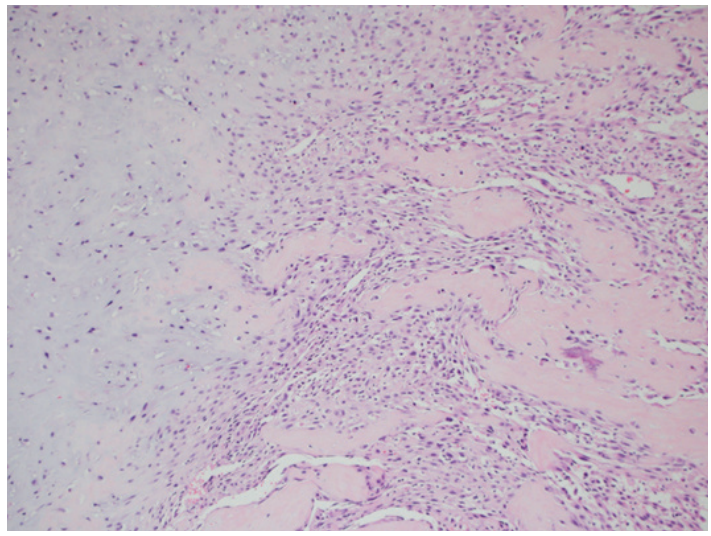


Figure 6. Microscopic image (HE, 100×) showing a malignant, anaplastic spindle cell proliferation with the presence of osteoid or immature bone

Conversely, extraskeletal osteosarcoma is a malignant tumor of the soft tissue that produces an osteoid with no attachment to bone or periosteum (1). This tumor has a very low prevalence, constituting approximately 4% of all osteosarcomas and about 1% of all soft tissue sarcomas; until the present, a total of about 350 cases have been reported (2). Unlike skeletal osteosarcoma, which occurs primarily in adolescents and young adults, extraskeletal osteosarcoma is common in persons over 40-years-old, and it is most often found in the soft tissue of the lower extremities, including the buttocks and thigh (3, 4). Although trauma, myositis ossificans, and a history of radiotherapy, among others, have been proposed as predisposing factors for extraskeletal osteosarcoma, the pathogenesis is not precisely understood (8, 9). Pathologic findings are similar to that of skeletal osteosarcoma, but the prognosis remains very poor, with a 5-year survival rate of 28%–45% (9, 10). The chief symptom reported is a soft tissue mass, and one-third of patients suffer from localized pain (3). On simple radiographs, a focal or diffused calcification in soft tissue appears, characterized by no change in bone or periosteum.

In addition to radiation exposure and chronic osteomyelitis, implanted foreign bodies are also known to be a cause of osteosarcoma (11). Furthermore, the carcinogenic potential of metallic debris from hip prostheses after THA could be considered, though this has not yet been fully investigated. A previous study reported 46 total cases of malignant disease after THA, including 10 cases of skeletal osteosarcoma, but no case of extraskeletal osteosarcoma was reported (12). Some metals, ceramics, and plastic materials, which are generally believed to be nontoxic, have been shown to induce neoplastic processes in animal studies (13), though there is no definite evidence of their carcinogenic potential in humans (14). In addition, high concentrations

of prosthetic metallic debris in the capsule tissue and synovial fluids have been reported due to the continuous friction around artificial (15). In the cases of such implants, circulating metallic debris can be detected in the liver, spleen, and abdominal lymph nodes (16). It is not fully understood whether the aforementioned prosthetic metallic debris has adverse and carcinogenic effects. Hence, further studies are necessary.

In the case studied, the hip prosthesis may not have been the cause of the extraskeletal osteosarcoma, despite the patient's history of THA, because this malignancy was not detected around the hip prosthesis, but at a distal location. Although the pathogenesis of extraskeletal osteosarcoma is not yet fully understood, the traumatic injury in this case represents one of the possible causes of the malignant neoplasm, considering both the recent trauma history and the 17-year gap between the THA procedure and the malignancy occurrence.

In general, a radiopaque shadow around a fracture site displayed on a plain radiograph could be callus formation or heterotopic ossification. However, tumors, including malignant fibrous histiocytoma and extraskeletal osteosarcoma, must be suspected despite their low prevalence, because these kinds of diseases are life-threatening (17). As demonstrated by this case, careful attention and thorough evaluation are required to detect the development of extraskeletal osteosarcoma near a fracture site, because the presentation of the disease on a simple radiograph could be confused with callus formation or heterotrophic ossification. Therefore, obtaining a definite diagnosis requires performing not only additional image studies, such as computed tomography (CT) or magnetic resonance imaging (MRI), but also a pathologic study after biopsy if the lesion is confusing (18).

Conclusion

A case of extraskeletal osteosarcoma that was mistaken as a callus formation or heterotrophic ossification surrounding a recent fracture site has been discussed. Based on this case and the review of several studies investigating extraskeletal osteosarcoma, it is recommended that clinicians suspect a bone tumor. The appearance of images such as those seen in this study must be investigated as possible malignancies, including extraskeletal osteosarcoma, not just as callus and heterotopic ossification formation, and additional imaging tests should be performed.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Author Contributions: Concept - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Design - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Supervision - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Resources - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Materials - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Data Collection and/or Processing - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Analysis and/or Interpretation - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Literature Search - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Writing Manuscript - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.; Critical Review - I.H.N., H.J.S., J.S.P., Y.S.S., K.C.P.

Conflict of Interest: The authors have no conflicts of interest to declare.

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