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Case report

# Myelolipoma mimicking osteosarcoma in the distal femur

Takao Sakai [a], Hisaki Aiba [a,*], Motoo Nakagawa [b], Hideo Hattori [c], Hideki Murakami [a], Hiroaki Kimura [a]

[a] Department of Orthopaedic Surgery, Nagoya City University, 1, Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi 467-8601, Japan
[b] Department of Radiology, Nagoya City University, 1, Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi 467-8601, Japan
[c] Department of Pathology and Molecular Diagnostics, Nagoya City University, 1, Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi 467-8601, Japan

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ABSTRACT

*Introduction and importance:* Periosteal reactions indicate malignant bone tumors, including osteosarcoma; establishing an accurate diagnosis is key to determining the most appropriate treatment strategy. We describe a rare case of myelolipoma in the distal femur metaphysis with massive extraskeletal lesions and periosteal reactions.

*Case presentation:* A 25-year-old woman was referred to our hospital to treat a gradually expanding mass around her knee that grew to the size of a baby's head. She had a history of hydrocephalus caused by congenital cytomegalovirus infection and was bedridden for life. Radiography showed a prominent osteoblastic rim and osteolytic lesion with a moth-eaten appearance. Osteosarcoma was suspected due to excessive extraskeletal invasion and periosteal reactions. T1- and T2-weighted magnetic resonance images showed a high-signal-intensity homologous lesion. Biopsy specimens contained adipose and hematopoietic tissues. A myelolipoma was diagnosed. Due to her fragility, surgical intervention was suspended. Two years after diagnosis, the tumor size did not change.

*Clinical discussion:* Myelolipomas are benign tumors that typically arise from the adrenal gland and rarely develop in the extremities. This type of tumor typically does not cause any tumor-related symptoms or endocrine disturbances and has been reported as a type of incidentaloma. To effectively manage myelolipoma patients, differential diagnosis of tumors mimicking malignant bone tumors is important.

*Conclusion:* We successfully managed a destructive ectopic myelolipoma in the distal femoral metaphysis, with massive extraskeletal lesions and periosteal reactions. Clinicians should appropriately differentiate myelolipoma from tumors mimicking malignant bone tumors.

## 1. Introduction

The distal femoral metaphysis is the most frequent site of osteosarcoma. Extraskeletal lesions with periosteal reactions should be carefully differentiated from other primary bone tumors to determine an appropriate treatment strategy. Myelolipomas typically occur in the adrenal glands and have no endocrine function. Extra-adrenal myelolipoma (EAM) occurs mostly in the presacral or peritoneal cavities [1]. We describe a very rare case of EAM with massive distal femoral periosteal reactions, that mimicked a malignant bone tumor. The work has been reported in line with the SCARE 2020 criteria [2].

## 2. Presentation of case

A 25-year-old woman with no remarkable family medical history or genetic disorders but who had a history of congenital cytomegalovirus hydrocephalus was referred to our hospital. She complained of a gradually increasing mass around the distal femur that had been first detected approximately 10 years ago. She received prophylactic antiepileptic drugs (zonisamide, valproate, and phenobarbital), diuretics (furosemide and spironolactone), and levothyroxine. Owing to severe atrophy of the cerebral cortex and brainstem, she was dependent on mechanical ventilatory support and had restricted communication and ambulation. Physical examination of the distal femur revealed a tense baby-head-sized mass with spider telangiectasia and distended

*Abbreviations:* CT, computed tomography; EAM, extra-adrenal myelolipoma; MRI, magnetic resonance imaging.

* Corresponding author.
*E-mail address:* h-aiba@med.nagoya-cu.ac.jp (H. Aiba).

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epidermis. Blood test results, including alkaline phosphatase levels, did not show any apparent abnormalities. The anesthesiologist in charge considered her to be a high-risk case for subsequent interventions and anesthesia based on her medical history, in spite of normal echocardiography, electrocardiography, and tidal volume mechanical ventilation. X-ray imaging revealed a massive osteolytic lesion (approximately 20 cm × 15 cm) without bony demarcation (Fig. 1), which strongly suggested a high-grade malignant bone tumor. The periosteal reaction had a sunburst appearance. Similarly, computed tomography (CT) indicated a destructive lesion on the distal femur with peripherally invasive progression from the bone cortex. Magnetic resonance imaging (MRI) also revealed a tumor (192 mm × 135 mm) with high signal intensity on T1- and T2-weighted images, and low signal intensity on the fat-suppression technique (Fig. 2). After eliciting the patients' perspective and importance of biopsy for establishing a definite diagnosis, needle and open biopsies were performed under local or general anesthesia by a certified orthopedic surgeon with 10 years' experience and a senior trainee who had completed 3 years of orthopedic residency in an academic regional cancer hospital. Pathological specimens contained fatty and hematopoietic tissues with no atypical cells. Therefore, the patient was diagnosed with myelolipoma by a certified pathologist with over 30 years' experience (Fig. 3). Perioperatively, the patient had prolonged hypotension, fever of unknown origin, and fatal arrhythmia possibly due to brainstem dysfunction.

Based on this diagnosis, hip disarticulation was planned for complete tumor resection owing to fears of the tumor protruding the skin. However, after thorough consideration, this strategy was suspended based on the patient's fragile condition. Two years after diagnosis, the tumor size did not change at all, and her condition has been regularly assessed by her family doctor.

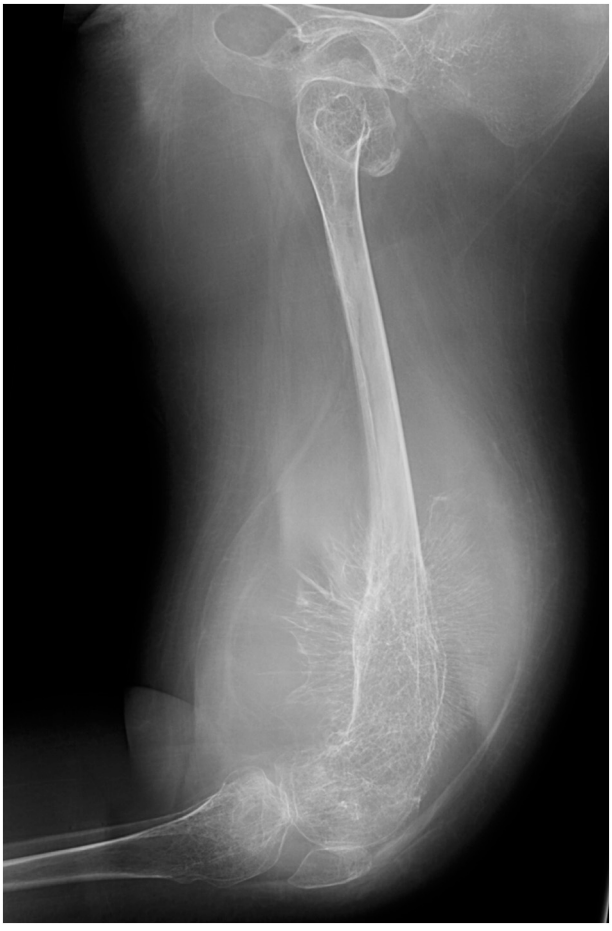

**Fig. 1.** The X-ray image (lateral view) shows a massive osteolytic lesion extending from the diaphysis to the metaphysis of the distal femur. The sunburst appearance, which typically indicates an aggressive bone tumor, is prominent. However, the density of trabeculae bone is sparse. The radiolucent area in the peripheral zones of the periosteal reaction is an unusual finding (white arrow).

## 3. Discussion

In this report, we describe the case of an EAM on the distal femur. Radiography findings mimicked those of a malignant bone tumor. However, a biopsy confirmed that the tumor was a myelolipoma, which is a benign tumor. In 1905, myelolipoma was first described by Gierke [3] who reported the histological findings of a mixed proportion of mature adipose tissues and hematopoietic elements. The most common site of occurrence is the adrenal gland, and this tumor accounts for 2–4% of all adrenal tumors [4]. Myelolipoma typically does not cause any tumor-related symptoms or endocrine disturbances and has been reported as a type of incidentaloma detected during CT for other diseases [5].

Few ectopic EAMs have been reported in previous studies; these accounted for approximately 15% of all myelolipomas. Other reported sites include the presacral space (40%), retroperitoneal space (20%), and thoracic cavity (15%) [6]. However, less than 10 cases of myelolipomas in bones have been reported until 2020 [7,8].

The true etiology of myelolipomas is unclear. However, under peculiar stimuli, stray mesenchymal stem cells may ectopically settle on connective tissue and then accumulate and arrest differentiation of hematopoietic cells [1,9]. Sundaram et al. showed the histopathological features of intraosseus myelolipoma; these included hematopoietic bone marrow (mildly hypercellular or normocellular) with interspersed adipocytes and rare bony trabeculae. Our current case showed similar features [8].

Extramedullary hematopoiesis, lipomatous tumors, and teratomas need to be considered in the differential diagnosis [10]. Myelolipomas typically occur in solitary form and have septal tissue at their border. Usually, no abnormal laboratory findings can be found in patients with myelolipomas. However, in patients with severe anemia due to thalassemia, sickle cell disease, and pernicious anemia, extramedullary hematopoiesis occurs in numerous locations with a predilection for the mediastinal, spinal, and perirenal areas [1,11]. On MRI, a lipomatous tumor appears relatively homogeneous. Several malignant forms of these tumors have myxoid components or are dedifferentiated; these manifest as multiple changes in intensity [12]. Intraosseous lipoma commonly develops in the calcaneus or metaphysis of long tubular bones. On histopathological examination, mature-appearing adipocytes exist with delicate trabeculae of woven bone. Radiography mostly reveals calcification around a well-defined margin or inside tumor [13]. These findings clearly indicate that the tumor in the current case had rare characteristics of fat-containing bone tumors; i.e., the tumor demonstrated periosteal reaction with no demarcated margin.

Surgical intervention is indicated, especially when the tumor is symptomatic, greater than 7 cm, metabolically active, or suspected of being malignant based on imaging [14]. Conservative treatment or surgical treatment may be chosen, depending on the patient's condition and risks of surgical intervention. In this patient, hip disarticulation with the ligation of major vessels and resection of muscles around the hip would have been necessary for complete tumor resection. However, our faculty determined that the patient would not have tolerated the required surgical procedures. In addition, the patient's guardians were unwilling to accept the possibility of deformity after surgery.

## 4. Conclusion

An EAM in the distal femur with X-ray imaging features similar to those of osteosarcoma has never been reported. Careful interpretation of the specific intensity of MRI indicated a fat-containing tumor; the

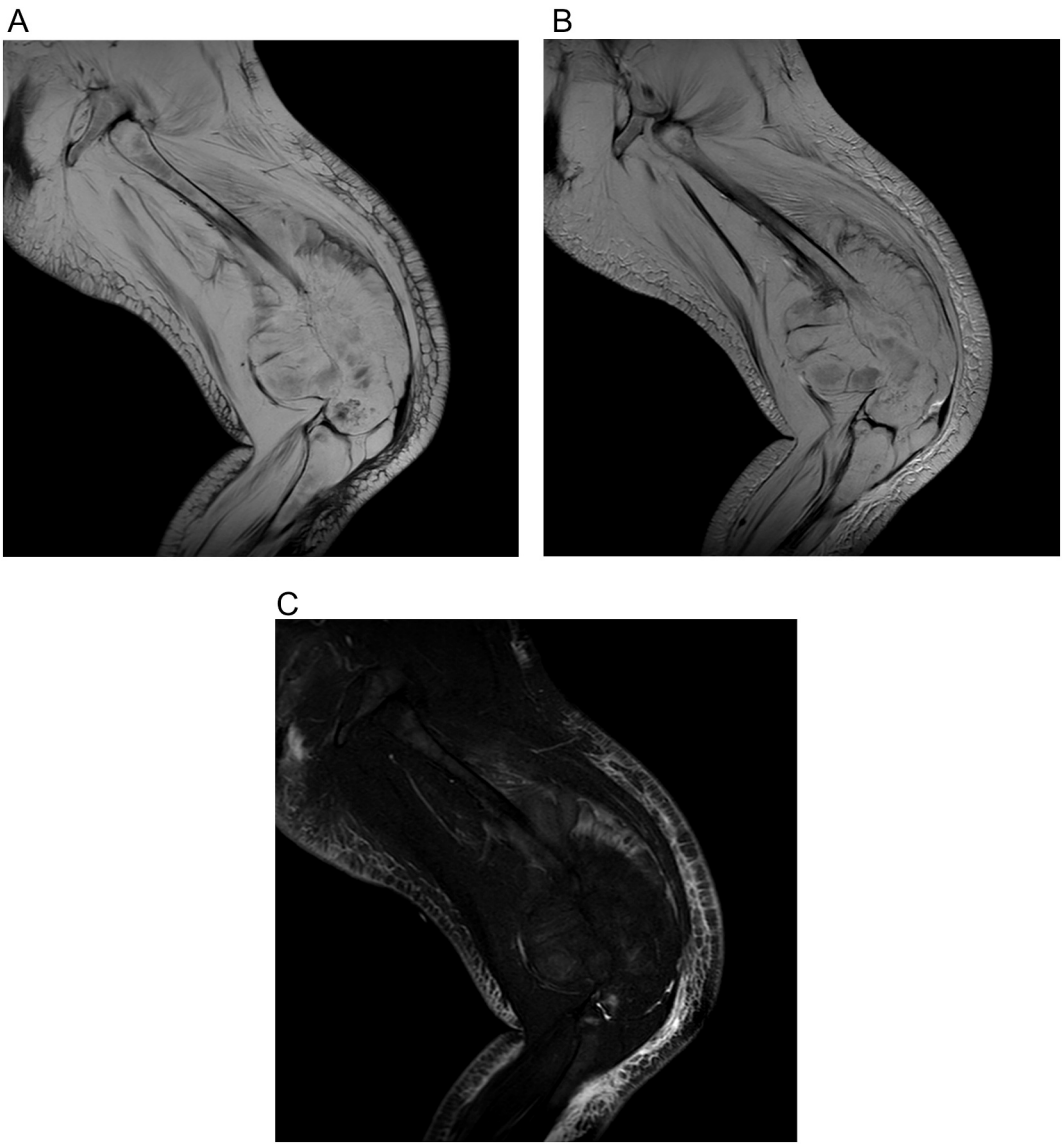


**Fig. 2.** Magnetic resonance imaging (MRI) shows a tumor (192 cm × 135 mm) with high intensity on T1- (a) and T2-weighted images (b). It is suppressed under the fat-suppression condition (c).

diagnosis should be confirmed by a biopsy in such cases. Clinicians should appropriately differentiate myelolipomas from tumors mimicking malignant bone tumors.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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## CRediT authorship contribution statement

Takao Sakai, Hisaki Aiba, Hideo Hattori, and Hideki Murakami: Conceptualization. Motoo Nakagawa and Hideo Hattori: Data curation. Hideo Hattori: Formal analysis. Hideo Hattori: Funding acquisition. Hisaki Aiba, Motoo Nakagawa, and Hideo Hattori: Investigation. Motoo Nakagawa and Hideo Hattori: Methodology. Takao Sakai, Hisaki Aiba, Hideki Murakami, and Hiroaki Kimura: Project administration. Hideki

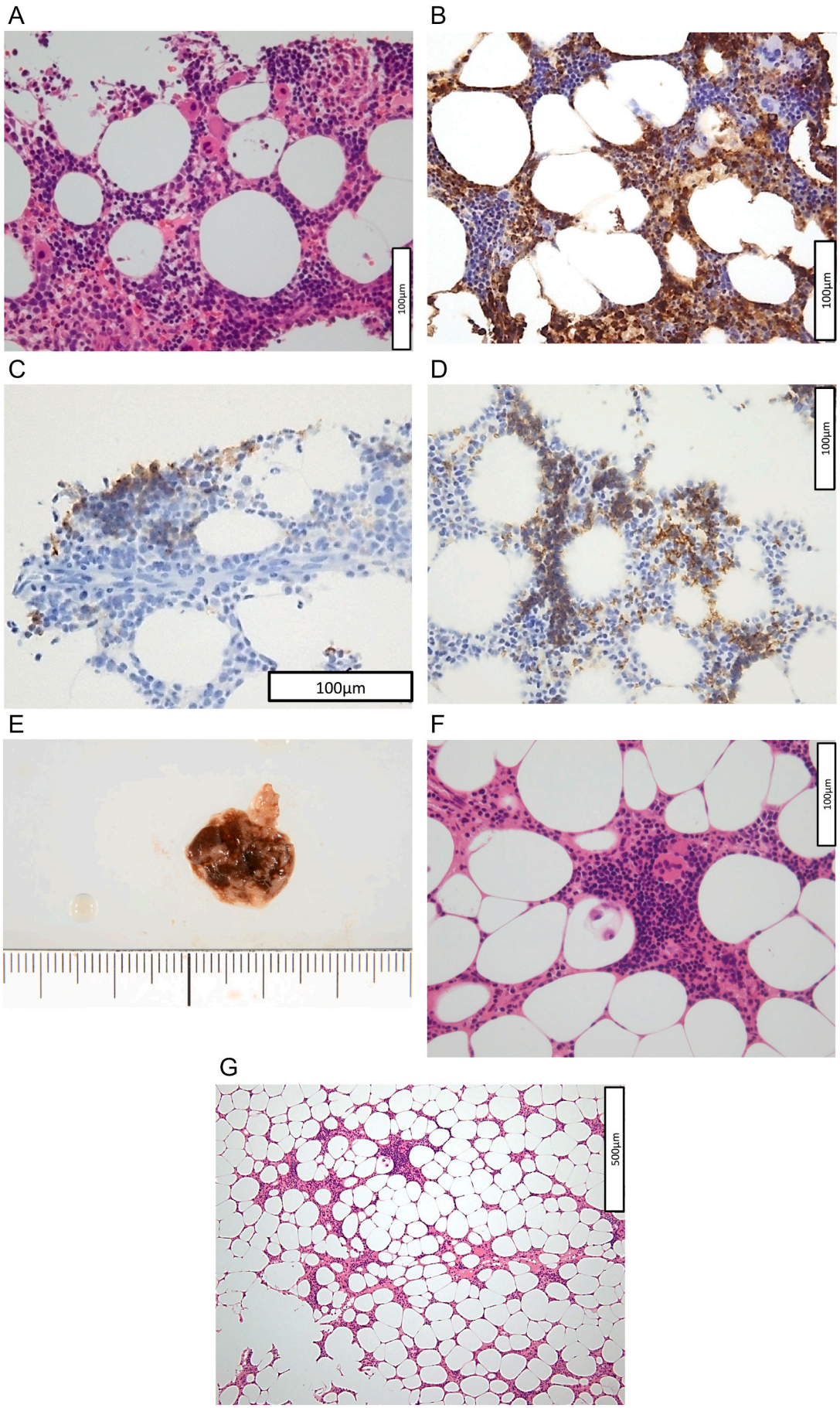


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**Fig. 3.** In needle biopsy, specimens are collected from the distal femur. The specimens consist of fatty and hematopoietic tissues (a, high-power field). There were myeloperoxidase- (b), CD71- (c), spectrin- (d), CD 42b-, and factor VIII-stained cells in the clusters of hematopoietic cells. The cellularity of the bone marrow-like area is 5%–30% with triphenotopic differentiation. Immature blastic blood cells are not prominent or dysplastic (confirmed by negative CD34 and p53 staining). Unlike the normal bone marrow, trabecular bones are not encompassed and intervened in the neoplastic lesion. To avoid a misdiagnosis owing to the lack of specimens, we repeated open biopsy under general anesthesia. As a result, the histological appearance and immunophenotype were identical to those of the biopsy specimens (e, gross appearance, f, high-power field, g, low-power field).

Murakami: Resources. Not applicable: Software. Hideki Murakami: Supervision. Motoo Nakagawa and Hideo Hattori: Validation. Motoo Nakagawa and Hideo Hattori: Visualization. Takao Sakai and Hisaki Aiba: Roles/Writing - original draft. Hisaki Aiba and Hiroaki Kimura: Writing - review & editing.

## Declaration of competing interest

None.

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