

Parosteal osteosarcoma of the fibula in a middle-aged patient

A case report

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Abstract

Rationale: Parosteal osteosarcoma (PO) is relatively rare, accounting for about 1% of primary malignant bone tumors and 4% of all osteosarcomas. Onset is generally at approximately 20 to 40 years of age; the distal posterior surface of femur is the most common site, accounting for more than 60% cases. However, PO in middle-aged or elderly patients is extremely rare and PO occurring in the fibula is even rarer. To our knowledge, this is the first case of PO occurring in the fibula of a middle-aged adult.

Patient concerns: We present a case of a 47-year-old female who had a lateral mass on her left knee for 3 months with no obvious cause.

Diagnoses: The patient was initially diagnosed with a proximal left fibula tumor via x-ray scan at a local hospital. Subsequently, osteochondroma was highly suspected through computed tomography (CT) and magnetic resonance imaging (MRI) obtained at our hospital. Finally, the postoperative pathological report confirmed PO.

Interventions: She underwent a complete resection of the left fibula tumor and received postoperative adjuvant chemotherapy.

Outcomes: The patient recovered well and was discharged on the 10th day after admission. Additionally, there was no evidence of recurrence at the 4-year follow-up after surgery.

Lessons: In middle-aged or elderly patients, early diagnosis of PO in the fibula is difficult and misdiagnosis or missed diagnosis is common. In clinical practice, PO is uncommon in middle-aged or elderly patients, occurs more rarely in the peroneal bone, and should be carefully identified. CT and MRI are essential for diagnosis, with pathological examination being effective for confirmation. Because of the limited reports of PO of the fibula in middle-aged or elderly adults, the present case raises awareness of this rare condition.

Abbreviations: CT = computed tomography, HE = hematoxylin and eosin, MRI = magnetic resonance imaging, PO = parosteal osteosarcoma.

Keywords: chemotherapy, imaging, misdiagnosis, osteosarcoma, parosteal osteosarcoma, pathology, surgery

1. Introduction

Parosteal osteosarcoma (PO), first reported by Geschichter^[1] in 1951, was initially considered to be a benign tumor. However, Jaffe et al^[2] suggested that PO was instead a low-grade malignant bone tumor in subsequent studies and adopted the term PO,

which is still used today. PO is a low-grade osteosarcoma characterized by significant mineralization of bone surface growth.^[3,4] In addition, PO is relatively rare, accounting for approximately 1% of primary bone malignancies and 4% of all osteosarcomas.^[5] The age at onset is generally between 20 to 40

Editor: N/A.

GC and QX contributed equally to this work and should be considered co-first authors.

This study was supported by Health and Family Planning Commission of Jiangxi Province on traditional Chinese medicine (2016A073) and the Education Department Project of Jiangxi Province (GJJ160127).

The study protocol was approved by the Ethical Institutional Review Board of the First Affiliated Hospital of Nanchang University and written informed consent was obtained from all study participants.

Consent for publication of the manuscript and the related images from the patients and/or their relatives has been obtained by the First Affiliated Hospital of Nanchang University.

There are no conflicts of interest to declare.

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Medicine (2019) 98:2(e13857)

Received: 5 September 2018 / Received in final form: 1 December 2018 / Accepted: 5 December 2018

<http://dx.doi.org/10.1097/MD.0000000000013857>

years and usually occurs in the lower femur, upper tibia, and popliteal fovea, rarely in the flat and short tubular bones, and 16% may undergo dedifferentiation.^[6–8] However, PO of the peroneal bone in middle-aged or elderly people is extremely rare. There are few reports on PO of the peroneal bone in middle-aged or elderly patients, and therefore, the experience of diagnosis is limited, making PO an easily misdiagnosed disease. Furthermore, it is difficult to distinguish from benign lesions such as ossifying fibroma, ossifying myositis, and exuberant reactive periostitis. Although PO is a low-grade malignant tumor, it can cause local recurrence if misdiagnosed. After multiple recurrences, the density and abnormality of the tumor cells increase, which may increase the probability of dedifferentiation and the condition being treated as classic osteosarcoma.^[9]

The diagnosis of PO is made by combining the patient's medical history, clinical symptoms, laboratory examination, and imaging analysis with histopathological examination. However, the analysis of patient history, clinical manifestations, and auxiliary examination are not very specific, as these are similar to those of benign lesions such as osteochondroma or malignant lesions such as hypermalignant osteosarcoma of the bone surface. Therefore, histopathological examination is the most critical step in the diagnosis of PO. Thus, it has been suggested that PO of the peroneal bone in middle-aged or older patients is likely to be misdiagnosed before the pathologic findings are analyzed after surgical resection of the lesion. Since 2007, we have diagnosed and treated 198 cases of osteosarcoma in our institution, with less than eight patients diagnosed with PO. However, only one patient, a middle-aged female patient over the age of 45, with a PO presented with the fibula as the primary site. To the best of our knowledge, PO occurring in the fibula has not previously been reported. Because of its less aggressive biological behavior, it is important to recognize PO that occurs in rare sites to plan appropriate treatment and avoid overtreatment. To this end, the clinical characteristics, imaging, pathologic findings, diagnosis, and treatment of a 47-year-old woman with PO of the peroneal bone are presented here. The ethical review committee of the First Affiliated Hospital of Nanchang University approved this study and written informed consent was obtained from the patient.

2. Case report

2.1. Presenting concerns

On July 28, 2014, a 47-year-old Chinese woman in the outpatient clinic of our hospital was unintentionally found to have a mass on the outside of the left knee for 3 months without fever, local pain,

and limited joint activity. She claimed that she was physically healthy and denied any history of underlying diseases such as high blood pressure, diabetes, or coronary heart disease. In addition, she had no history of injuries or illnesses and no relevant family history.

2.2. Diagnostic focus and assessment

Further specialist examination found that the lateral part of the left knee was slightly raised and identified a hard mass of approximately 5×3 cm. There was no tenderness or percussion in the knee; the knee flexion and extension were normal. The left lower extremity motion and sensation were within normal limits. There was no obvious abnormality in the remaining limbs.

The patient's erythrocyte sedimentation rate, C-reactive protein level, and serum alkaline phosphatase level were all within the normal range. The radiological report showed a multiple mass of bone with increased density on the head of the left fibula. The CT scan obtained at our hospital showed a local defect in the lateral cortex of the upper left fibula. In addition, patchy high-density shadows were seen in the left fibula head and surrounding soft tissue, with uneven internal density and spotted mixed density shadows (Fig. 1A). An MRI showed interruption of the lateral cortical continuity at the head of the left fibula and a signal shadow approximately 6.2×2.3 cm in size could be seen beside it. The boundary of the mass was clear and a patchy signal shadow was seen inside the mass (Fig. 1B). Consequently, diagnosis of osteochondroma was considered by an experienced radiologist.

2.3. Therapeutic focus and assessment

After a routine preoperative assessment, continuous spinal epidural anesthesia was administered, and the patient was placed in the supine position. First, the left lower extremity was disinfected by exposing the surgical field and a posterolateral incision of the fibula upper was made. The skin was cut layer by layer, first the subcutaneous tissue, then the superficial fascia, and finally the deep fascia. Subsequently, the peroneal nerve was exposed and the muscle attached to the peroneal nerve was peeled off. This revealed a white neoplasm on the upper fibula surface, which was smooth with a hard tissue texture. After complete removal of the tumor on the upper fibula by osteotome, the tumor was sent for pathological examination. The lateral accessory ligament and the long and short fibula tendons attached to the head of the fibula were fixed to the tibia cortex with a rivet. Finally, the wound was soaked in distilled water and repeatedly washed with hydrogen peroxide and physiological saline. A

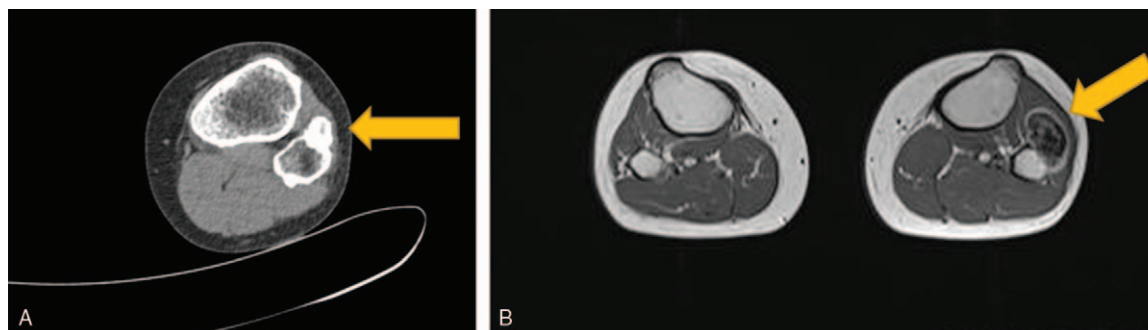


Figure 1. (A) CT: a high-density shadow on the left fibula head and surrounding soft tissue. (B) MRI: left fibula head cortical continuity was interrupted and a signal shadow 6.2×2.3 cm in size could be seen beside it.



Figure 2. The gross specimen visible to the naked eye is a large quantity of rock-like ivory with well-defined sclerotic boundaries, almost all of which is bone tissue.

drainage tube was then placed under the muscle layer and the fascia was sutured; the incision was closed layer by layer.

The pathological features of PO are visible to the naked eye (Fig. 2) with a large quantity of rock-like ivory with well-defined

scleroses, almost all of which are bone tissue. Microscopic examination of the upper left fibula tumor (Fig. 3) showed the trabecular bone was filled with fibrous interstitium, nuclei had mild atypia, and the surface of the tumor had hyperplastic fibrous tissue and an area of cartilage island. In addition, chondrocyte proliferation was atypical and there was invasive growth between the peripheral striated muscle bundles. After the operation, the patient was given 3 cycles of systemic intravenous chemotherapy of cisplatin (DDP) 120mg/day for 1 day and doxorubicin (ADM) 20mg/day for 3 days; isophosphoric acid (IFO) was administered 1g/day for 5 days after 2 weeks. The chemotherapy cycle was repeated every 2 weeks. After the 3 cycles of systemic intravenous chemotherapy, the patient was administered epirubicin (EPI) 30mg/day for 3 days and 120mg of DDP for 1 day. After 2 weeks, isophosphoric acid (IFO) was administered at 1g/day for 5 days. During the systemic chemotherapy, the patient did not have any complications.

2.4. Follow-up and outcomes

The patient was discharged without any complications 10 days after surgery. In addition, this patient's follow-up

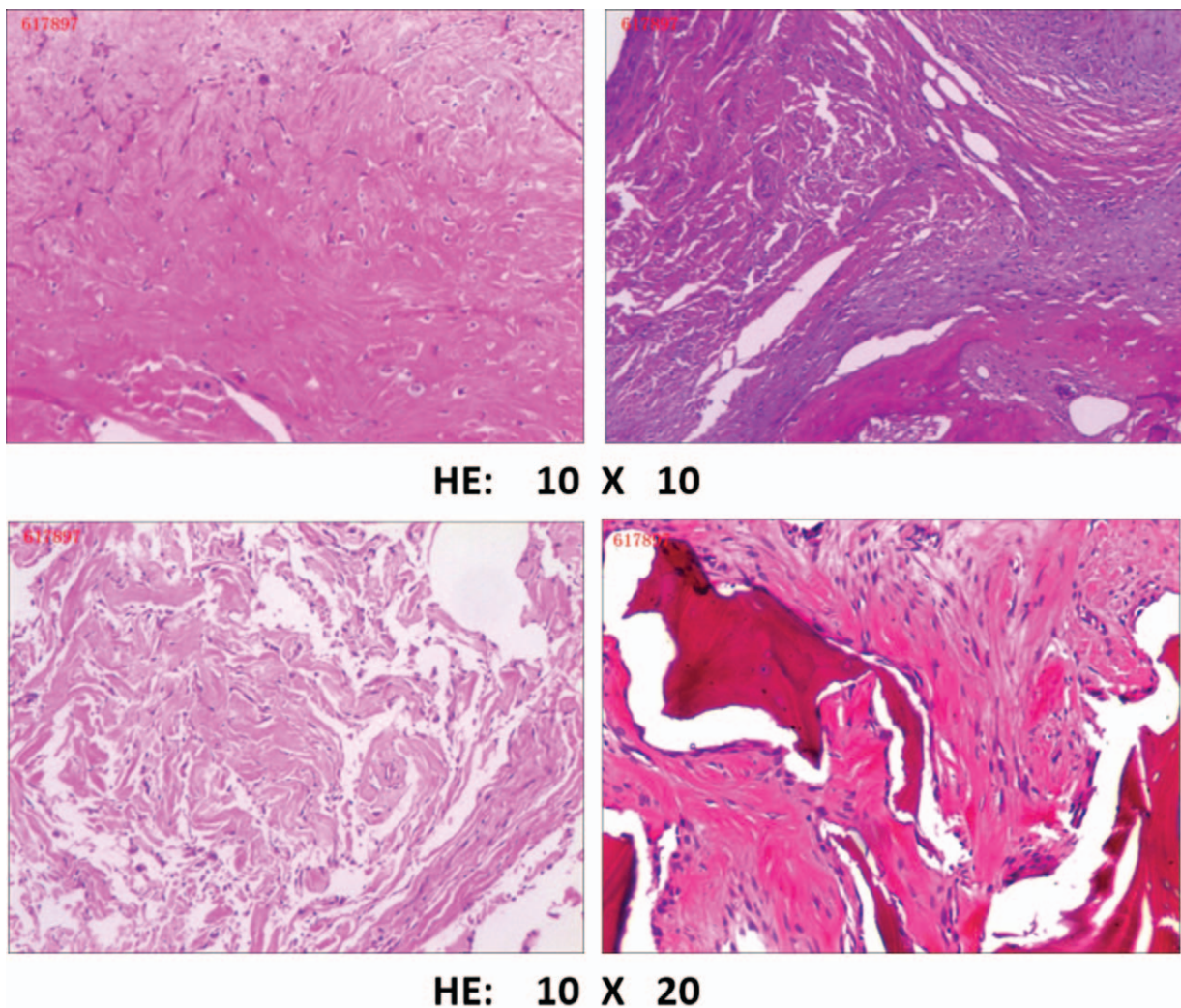


Figure 3. Histopathology (hematoxylin and eosin) showed the surface of the tumor with hyperplastic fibrous tissue and a cartilage island area. In addition, chondrocyte proliferation was atypical and there was invasive growth between the peripheral striated muscle bundles.



Figure 4. Follow-up imaging data.

after 4 years showed no signs of recurrence or metastasis (Fig. 4).

3. Discussion

PO is a rare type of bone tumor. Dwinell et al.^[10] reviewed 400 cases of osteosarcoma in 2000 cases of primary bone tumors and found 15 cases of PO, accounting for 0.75% of all primary bone tumors and 3.8% of osteosarcoma. PO onset generally occurs between the ages of 20 to 40, usually in the lower femur, upper tibia, and popliteal fovea. Therefore, most of the studies on diagnosis and treatment of PO focus on young people and the effect on the femur. However, diagnoses of PO at other ages and uncommon sites are rarely mentioned.

Diagnosis of PO emphasizes the triple combination of clinical, radiographic, and pathologic findings. The typical PO has a slow onset, mainly presenting as a painless and gradually increasing mass, with approximately 86% of cases being palpable, and about 33% of cases having adjacent joint activity limitation.^[11] In the present case, the tumor was consistent with others reported in the literature as it was a painless, palpable mass but the patient had no adjacent joint activity limitation. Generally, imaging examinations of PO show the shape and size of the bone tumor by X-ray plain film,^[12] while the CT and MRI show the relationship between the tumor and bone and the degree of invasion of the medullary cavity.^[13,14] There was a comprehensive assessment of the relationship and degree of invasion between the area of the tumor soft tissue mass and the vascular nerve, which was of significant use for the clinical diagnosis and formulation of the surgical program. The major pathologic feature of PO is that the gross tumor is a hard bone mass attached to 1 side of the epiphyseal cortex or half a week. Microscopically, the neoplastic trabeculae and active fibrous interstitium contained no obvious heterogeneity, pleomorphism, or nuclear division of tumor cells.

Hence, when clinical and imaging identification is difficult, pathological biopsy should be performed to obtain an accurate preoperative diagnosis to improve treatment planning.

Early diagnosis of PO of the peroneal bone in middle-aged or elderly patients is difficult and misdiagnosis or missed diagnosis is common. PO should be differentiated from benign tumors that mainly include ossifying myositis and florid reactive periostitis. Special attention should be paid to the identification of osteochondroma. In this case, according to the clinical history and imaging features of the patient, the experienced radiologist found that PO was misdiagnosed as osteochondroma, which may be due to the following factors: first, incidence of PO in middle-aged or elderly individuals is extremely rare; second, both osteochondroma and PO present as painless, slow-growing, textured hard masses; third, after the discovery of lesions and due to similar imaging performance, clinicians tend to focus on more common diseases. Moreover, myositis ossificans usually has a history of trauma and pain, and its ossification is around the lesion, while the ossification of PO is at the center of the tumor. Whether the tumor encroaches on normal bone is also an important basis for differentiation. Florid reactive periostitis is a common disease of the phalanx and nearly 40% of the patients have a history of trauma.^[15] Histology predominantly indicates the proliferative fibroblast lesions, which often involve osteoid tissue. However, unlike in PO, the tumor edge is the braided bone containing bone marrow and the center is the immature area with abundant cells.

On the other hand, malignant tumors primarily include periosteal osteosarcoma, high-grade surface osteosarcoma, and extracortical infiltration of intramedullary well-differentiated osteosarcoma. Periosteal osteosarcoma is generally associated with relatively small lesions and often presents with a characteristic acicular periosteum.^[14,16] In addition, PO should be differentiated from extracortical infiltration of the intra-

medullary well-differentiated osteosarcoma, which has a similar histology, although most intramedullary well-differentiated osteosarcomas are widely involved with the medullary tissue,^[17] while PO usually has focal invasion. Intramedullary well-differentiated osteosarcoma is similar to highly malignant classic osteosarcoma in both X-ray and histological morphology.^[18] Unlike PO, high-grade surface osteosarcomas are mainly osteoblast-like and contain little or no cartilage components.

PO has limited remote diffusion potential with local invasiveness.^[19] Nevertheless, the presence of bone marrow infiltration and moderate cell atypia did not correlate with a worse prognosis and it has been reported in the literature that PO has a generally good prognosis.^[11,20] Therefore, surgical treatment should be actively sought.^[11] Simple tumor resection is feasible for patients with smaller tumors and extensive and thorough resection should be performed for patients with larger tumors, invasion of adjacent bone, or recurrence. If the tumor infiltrates important blood vessels or nerves and cannot be completely removed, amputation is considered.^[11] In this case, due to moderate tumor size and the absence of vascular or nerve damage, we performed a complete resection of the tumor and a 1-week post-operative radiography showed a complete resection of the tumor. If not completely excised, recurrence may be seen, since the remaining tumor tissue can dedifferentiate and metastasize after recurrence. Hence, great care should be paid during the first operation to achieve complete excision. It has been reported that^[21] the 5-year recurrence rates following marginal and extensive resection were 10% and 8.8%, respectively. PO grows slowly, and recurrence and metastasis often occur years after surgery. Patients with incomplete surgery can have multiple recurrences, so multiple surgeries are not uncommon.^[22-24] The longest recorded recurrence was 21 years after the initial operation.^[25] Therefore, for low-grade malignant tumors of PO, the follow-up time should be long to facilitate close observation. If PO dedifferentiation occurs, it is the same as classic osteosarcoma and is treated in the same manner, with comprehensive treatment dominated by neoadjuvant chemotherapy and surgery.^[9] For the typical surgical plan of PO, we advocate that the same method should not be pursued, but full use should be made of highly developed imaging examinations to accurately judge the location, size, and boundary of the tumor, and design different individualized surgical plans. Tumor resection should have a negative resection margin to avoid recurrence and normal tissue and function should be retained as much as possible.

In short, PO of the fibula in middle-aged or elderly patients should not be ignored. Given its rarity, PO should be carefully evaluated. Any analysis based on a single factor or incomplete information may lead to arbitrary diagnosis. We believe that as long as we raise awareness, it is possible to make a correct diagnosis early. In addition, most cases of PO have a good prognosis and should be treated actively. In order to understand this condition better, we recommend that plastic surgeons and radiologists learn to recognize the possibility of PO in older age groups and uncommon locations.

Acknowledgments

We greatly appreciate the patient and her family for allowing us to make use of the medical documentation and information that led to the present article. We would also like to thank the Editage company in Shanghai, which provided English language editing, for their assistance

Author contributions

DM, and ZB performed the surgery and managed the patient postoperatively. CGP drafted the manuscript. XQ critically revised the manuscript. CGP analyzed the patient data. All authors read and approved the final manuscript.

Funding acquisition: Bin Zhang, Min Dai.

Resources: Bin Zhang, Min Dai.

Supervision: Bin Zhang, Min Dai.

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Writing – review & editing: Qiang Xu.

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