

## Case Report

# Diaphyseal osteomyelitis of femur with suspected ewing sarcoma in 8 years old children: a case report

Panji Sananta, Hidayat Rizal\*

Department of Orthopaedic and Traumatology, Saiful Anwar Hospital, Malang, East Java, Indonesia

**Received:** 05 October 2018

**Accepted:** 29 October 2018

**\*Correspondence:**

Dr. Hidayat Rizal,

E-mail: [hidayatrizal85@gmail.com](mailto:hidayatrizal85@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

Metaphyseal osteomyelitis in children due to direct bone trauma or vascular insufficiency is a frequent problem in orthopaedic surgery. In contrast, diaphyseal osteomyelitis represents a rare entity that almost exclusively affects child with bony infarct in sickle cell anemia. Differentiating neoplasm from musculoskeletal infection can sometimes be very challenging. In particular, Ewing sarcoma can masquerade as osteomyelitis with the presenting symptoms of fever, localized bone pain, and elevated inflammatory markers common to both entities, although osteomyelitis is a totally different type of disease. In this article, we report the case of chronic osteomyelitis of the femur in an immunocompetent and otherwise healthy 8 years old boy with minor inflammation signs and misleading clinical features. The X-ray showed onion skin periosteal reaction. We evacuated about 200 cc of abscess. Biopsy report revealed polymononuclear, mononuclear, and necrotic inflammatory cells. The patient was treated with antibiotic for two weeks and discharged with improved general condition. Six months follow-up shows clinical and radiological improvement. The diagnosis had to be confirmed by surgery which allowed the initiation of a targeted therapy. A case of diaphyseal osteomyelitis of a femur, lacking predisposing factors or trauma, is unique in children and never been reported previously.

**Keywords:** Ewing sarcoma, Onion skin, Osteomyelitis, Periosteal reaction

## INTRODUCTION

Metaphyseal osteomyelitis in children due to direct bone trauma or vascular insufficiency is a frequent problem in orthopaedic surgery. In contrast, diaphyseal osteomyelitis represents a rare entity that almost exclusively affects child with bony infarct in sickle cell anemia.<sup>1</sup> Predisposing factors documented were from trauma (35%), wound (13%), abscess (13%).<sup>2</sup>

Osteomyelitis is an infection that usually affects the growing skeleton, involving primarily the most vascularized regions of the bone. It is considered an acute process if the symptoms have lasted less than 2 weeks.<sup>3-5</sup>

Acute osteomyelitis has an incidence of 8-10 per 100000 in developed countries and an even higher incidence, up to 80 per 100000, in developing countries.<sup>6</sup> The incidence of acute osteomyelitis also varies according to the age and gender of the child due to processes of skeletal and vascular development.

The reported rate of acute osteomyelitis varies between 1:5000 and 1:10,000, with boys having a rate twice that of girls.<sup>7</sup> Approximately 50% of cases of osteomyelitis occur in the first 5 years of life. Boys are more likely than girls to be affected. The long bones of the lower extremities are most often involved, although any bone may be affected.<sup>8</sup>

Kremers et al, reported that majority of the infections (94%) involved only one location, and the most common anatomical sites affected were the tarsal and metatarsal bones and the toes (43%); the long bones of the lower extremities (20%); and the spine, sternum, and/or pelvis (19%). Consistent with temporal trends in the distribution of cases by underlying etiology, there was an increase in patients with osteomyelitis of the feet and/or toes and axial locations, but a decline in lower-extremity osteomyelitis of the long bones. In the latest time period, 42% of the cases involved the feet and toes, and 28% involved the axial locations, mostly hematogenous infections of the spine. A small number of patients (6%) had infections in more than one location. In these patients, each location was identified as a primary location.<sup>9</sup>

The diagnosis of osteomyelitis was favored in the presented patient due to the clinical, laboratory and radiographic findings. The natural behavior of the disease that was slowly progressive over a year's period was indicative of a nonaggressive lesion. The localized bone pain and swelling, the associated fever and the elevated inflammatory markers led to a presumed diagnosis of chronic osteomyelitis. In addition, the radiographic findings were also consistent with chronic osteomyelitis.<sup>10</sup>

Chronic osteomyelitis deserves many of the same clinical considerations as malignant tumors. C-reactive protein, procalcitonin and other inflammatory cytokine levels are reliably elevated in the setting of acute, posttraumatic extremity infections but have not been fully evaluated in the setting of chronic osteomyelitis.<sup>11</sup>

Differentiating neoplasm from musculoskeletal infection can sometimes be very challenging. In particular, Ewing sarcoma can masquerade as osteomyelitis with the presenting symptoms of fever, localized bone pain, and elevated inflammatory markers common to both entities, although osteomyelitis is a totally different type of disease.<sup>12</sup> Ewing's sarcoma is the fourth most common primary malignancy of the bone. The incidence is about 9-11% of primary malignancy of the bone and approximately 90% of cases present themselves before the age of 20. Diaphyses of the long bones (femur, tibia, and humerus), the ribs, and the flat bones, such as the scapula and the pelvis, are the preferred sites.<sup>7</sup> Involvement of proximal metaphyses of tibia is rare with an incidence frequency of about 4-11%. Although metaphyses of the long bones may occasionally be affected, the epiphyseal involvement is rare (2%).<sup>13,14</sup> The average delay from onset of symptoms to the diagnosis is about eight months.<sup>15</sup>

In some cases, it is difficult to distinguish between osteomyelitis of the femur and bone tumors by plain film radiography, and this condition commonly mimics Ewing sarcoma. Accurate diagnosis of this condition is also difficult by using MRI, which is believed to be a sensitive

and useful modality. The penumbra sign on MRI, which is reported to be highly specific for osteomyelitis, is difficult to detect. However, elevated CRP levels and ESRs found to be consistent among the cases with this condition are relatively sensitive indicators for distinguishing osteomyelitis from bone tumors. But sometimes, Ewing sarcoma can present with similar laboratory data. Hence, it is recommended that open biopsy should be performed in all cases for accurate diagnosis and for obtaining an adequate specimen for culture.<sup>16</sup>

## CASE REPORT

Eight years old boy with chief complain of pain in his thigh since 1month ago after was kicked by his friends. This patient can still walk after the incident although with a limp. Swelling occurred 1month after the incident. The patient complained difficulty to walk 2weeks after the incident.

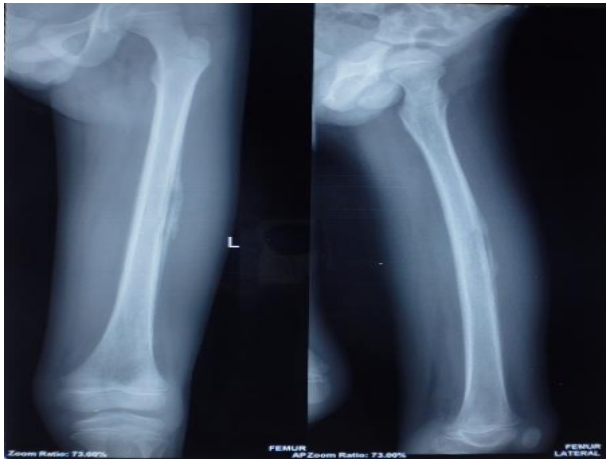


**Figure 1: Clinical appearance of the patient when he first came to the hospital.**

From physical examination, we found thigh circumference was 25 cm when healthy side was 20cm (Figure 1), hip flexion 30-60°, extension 60-30°, abduction 0-5°. Leucosytosis was found in the first laboratory test while patient was hospitalized. Lactate dehydrogenase (LDH) and alkaline phosphatase levels are increased. In the x rays we found a Periosteal reaction and an "onion skin appearance" (Figure 2). The patient and his family have no history of bone tumour before. We performed a Fine Needle Aspiration Biopsy (FNAB) to diagnose the patient. During the aspiration we found a pus. Patient underwent debridement surgery and abscess evacuation (Figure 3).

We evacuated about 200 cc of pus (Fig. 4). The pain and swelling were decreased after the surgery and leucocyte level was back to normal. From the biopsy we found

there was chronic inflammation that can be seen in (Figure 5 and 6).



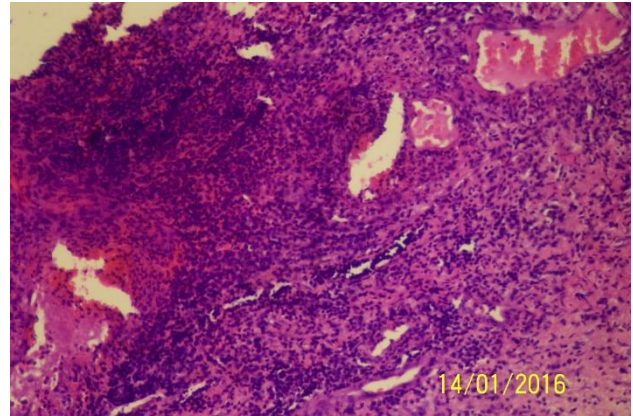
**Figure 2: Initial x-ray image of the femur. In diaphysis of femur we can see periosteal reaction and “onion skin appearance”.**



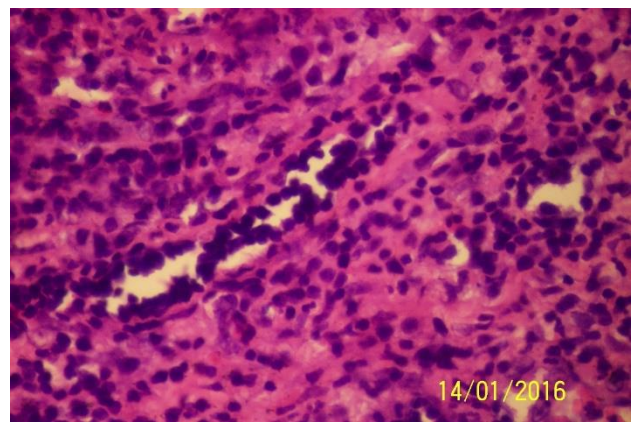
**Figure 3: Open biopsy and evacuated abscess during the surgery.**



**Figure 4: Abscess was evacuated about 200 cc.**



**Figure 5: Histopathological image as the result from open biopsy of the femoral bone.**



**Figure 6: Histopathology of polymononuclear, mononuclear, and necrotic inflammatory cells. There is a group of irregular round nucleated cells that are mostly coagulative necrosis.**

Biopsy report revealed polymononuclear, mononuclear, and necrotic inflammatory cells. There is a group of irregular round nucleated cells that are mostly coagulative necrosis. There was no evidence of spindle cell hypercellularity, nuclear atypia, or mitotic activity suggestive of sarcoma. The findings were lead to chronic inflammation and negative malignancy. The patient were treated with antibiotic for two weeks and discharged with improved general condition. Six months follow-up shows clinical and radiological improvement.

## DISCUSSION

In this case, according to the physical examination, x ray, and laboratory findings, initially we diagnosed the patient with primary bone tumour suspected ewing sarcoma, but from surgery showed pus which was confirmed from biopsy as suppurative chronic inflammation. This final diagnosis is diaphyseal chronic osteomyelitis of the femur. This is interesting case, because of diaphyseal osteomyelitis appearance that mimicking to bone tumor.



Children with acute osteomyelitis typically have symptoms 3 to 4 days prior to presentation. Abdi et al, reported that infection is more common in lower extremities than upper extremities, with the 3 most common sites the femur (27%), tibia (22%), and humerus (12%). Single-bone involvement is more common than multifocal infection. More than 50% of cases occur in children under the age of 5 years.<sup>7</sup>

Patients with symptoms pain, swelling, fever, and pathological fractures, where fever is associated with disseminated disease. Radiographs feature lytic destruction and subperiosteal new bone formation skin to 'onion skinning'. These non-specific findings may be present in many conditions such as metastatic carcinoma, malignant lymphoma, and osteomyelitis, necessitating open biopsy to confirm the diagnosis.<sup>17</sup> Misdiagnosis of Ewing's sarcoma as osteomyelitis has been reported in several cases. Reasons reported for the misdiagnoses include a low level of suspicion, occurrence at an atypical site, and the lack of or insufficient histologic specimens.<sup>17</sup>

The radiographic appearance of Ewing's sarcoma is fairly characteristic but not pathognomonic. Mottled destruction of medulla and erosion of the cortex with some expansion of bone accompanied by deposition of periosteal new bone in parallel layers ('onion-peel' appearance) is the typical appearance of Ewing's sarcoma, although a substantial proportion of cases have no characteristic appearance.<sup>10</sup> Laminated periostitis occurs in 57% of lesions; multiple layers of new bone formation lead to an 'onion skin' appearance. Uncommon appearances include speculated periostitis in 28% and pure osteolysis in 19% of lesions. Pathological fracture is unusual occurring in 15% of lesions.<sup>18</sup>

Other nonpredictive radiographic parameters that we observed in subjects with osteomyelitis and that have been reported as being typical of this diagnosis, included a cavity in bone and cortical sequestrum; however, few subjects had these findings. Lamellar periosteal reaction was seen in 13 subjects with Ewing's sarcoma and five with osteomyelitis, spiculated periosteal reaction was seen in five subjects with Ewing's sarcoma and one with osteomyelitis, and a serpiginous medullary or cortical tract (i.e., a longitudinally oriented tortuous medullary or cortical lucency seen on radiographs or signal abnormality seen on MR images traversing the medulla and cortex) was seen in none of the subjects with Ewing's sarcoma and in four subjects with osteomyelitis.<sup>19</sup>

McCarville reported that nonpredictive MRI parameters included cortical thinning (in 17 subjects with Ewing's sarcoma and seven subjects with osteomyelitis) ( $p = 0.08$ ), spiculated periosteal reaction (in five subjects with Ewing's sarcoma and in none of the subjects with osteomyelitis) ( $p = 0.06$ ), and a cavity in bone (in one subject with Ewing's sarcoma and three subjects with osteomyelitis) ( $p = 0.33$ ). Two of the three cavities in bone in patients with osteomyelitis (67%) showed the

penumbra sign (a peripheral hyperintense layer on unenhanced T1-weighted images that shows intense enhancement on contrast-enhanced images).<sup>19</sup>

Plain film findings of osteomyelitis lag the onset of infection by days to weeks. Initial findings may include only subtle soft tissue edema near the involved metaphysis. Radiographically evident bone destruction and periosteal reaction take 2-3 weeks to develop. Eventually metaphyseal lucencies with varying degrees of cortical destruction and periosteal new bone develop. The periosteal reaction can appear as lamellated, onion-skin or spiculated new bone or a Codman's triangle due to subperiosteal abscess.<sup>20</sup>

Shimose et al, reported on 244 cases that were tentatively diagnosed as malignant bone tumor based on imaging results; however, 15 of these cases were osteomyelitis. The clinical symptom of pain was noted in all osteomyelitis cases and swelling of the limb was present in eight cases. In their study, laboratory data showed elevated CRP levels in nine (60%) patients and leukocytosis in three (20%).<sup>21</sup> Huang et al, reported that only 40% of patients had leukocytosis, and this may not have been indicative of osteomyelitis. However, other studies have shown that laboratory investigations were inconsistent and did not aid in diagnosing subacute osteomyelitis.<sup>22</sup> The reasons for positive uptake of leucocytes by this Ewing's sarcoma are not clear. Review of the histological appearance reveals no unusual morphological features. Areas of necrosis are common in Ewing's tumours, possibly due to compression and thrombosis of blood vessels by the rapidly expanding neoplasm, and some degree of inflammation is usually present throughout the lesion.<sup>23</sup>

Cottias et al, also reported on 21 osteomyelitis cases mimicking bone tumor. Pain was also noted in all cases, but only half complained of nocturnal pain. Two of twenty-one (9%) patients had leukocytosis, and 30% had elevated ESRs.<sup>24</sup>

Ewing's sarcoma has been described as a tumor that may involve only the diaphysis, sparing the metaphysis, whereas osteomyelitis typically originates in the highly vascular metaphysis and later spreads through the Haversian canals into the subperiosteum, through the medullary space into the diaphysis, or across the physis into the epiphysis.<sup>19</sup> Radiographs of the osteomyelitis cases showed osteolysis in 12 (80%) patients. Pathogens were found in 11 of 15 patients, including *Staphylococcus aureus* in eight patients, *Salmonella* in two patients, and *Staphylococcus epidermidis* in one patient.<sup>21</sup>

Biopsy is mandatory and specimens should always be sent for both microbiology and histology. If the local pathologist is not appropriately experienced, referral to the local bone tumour treatment centre should be considered for a second opinion.<sup>18</sup>

Successful treatment of osteomyelitis depends on the appropriate selection and administration of antibiotic therapy and surgical intervention as needed. Empirical antibiotics in pediatric patients with osteomyelitis should be treated with antibiotics that have excellent coverage against *S. aureus*, *S. agalactiae*, and enteric gram-negative bacteria.<sup>8</sup>

Duration of therapy depends on extent of infection, clinical response, and presence of underlying risk factors. In general, 3 to 6 weeks of antibiotic therapy is given depending on the clinical response. There is good evidence that treatment for less than 3 weeks results in an unacceptably high rate of relapse. Chronic infection is reported in 19% of children treated for less than 3 weeks compared with 2% in children treated longer than 3 weeks.<sup>25</sup>

Authors relied on clinical judgment and a low level of suspicion of Ewing's. Osteomyelitis is difficult to differentiate from malignant bone tumors, as it lacks specific signs and symptoms. Distinguishing between the two potential diagnoses is important in order to initiate proper clinical management.

## CONCLUSION

The presentation of osteomyelitis of the femur mimicking bone tumors emphasizes the importance of clinical history, laboratory investigations, and radiographic interpretations in the diagnosis of this condition, which is generally difficult to detect. Moreover, it is difficult to distinguish between osteomyelitis of the femur and bone tumors by plain film radiography, and this condition commonly mimics Ewing sarcoma. MRI is believed to be a sensitive and useful modality for this condition. When all imaging and clinical features were considered together, only ethnicity and the presence of a soft-tissue mass were predictive of the diagnosis. Although open biopsy provided a higher diagnostic yield, we still support performing percutaneous biopsy first to avoid the risk of morbidity associated with surgical procedures. We recommend that a surgical consultation be obtained before percutaneous biopsy to ensure that the patient quickly undergoes an open procedure if the results of the initial biopsy are inconclusive.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

- Tountas AA, Kwok JM. Acute hematogenous diaphyseal osteomyelitis in childhood. Canadian Medical Association J. 1985 Jun 1;132(11):1287.
- Patzakis MJ, Zalavras CG. Chronic posttraumatic osteomyelitis and infected nonunion of the tibia: current management concepts. JAAOS. 2005 Oct 1;13(6):417-27.
- McCarville MB. The child with bone pain: malignancies and mimickers. Cancer Imaging. 2009(9):S115-21.
- Frank G, Mahoney HM, Eppes SC. Musculoskeletal infections in children. Pediatr Clin North Am. 2005;52(4):1083-106.
- Gutierrez K. Bone and joint infections in children. Pediatric Clinics. 2005 Jun 1;52(3):779-94.
- Yeo A, Ramachandran M. Acute haematogenous osteomyelitis in children. BMJ. 2014 Jan 20;348(315):g666.
- Abdi R, Taheri MMH. A case report of ewing's sarcoma of tibial epiphysis with retrobulbar mass. J Surg and Trauma. 2015;3(1-2):23-5.
- Peltola H, Pääkkönen M. Acute osteomyelitis in children. N Engl J Med. 2014;370(4):352-60.
- Kremers HM, Nwojo ME, Ransom JE, Wood-Wentz CM, Melton III LJ, Huddleston III PM. Trends in the epidemiology of osteomyelitis: a population-based study, 1969 to 2009. J Bone Joint Surg Am. 2015;97:837-45.
- Sferopoulos NK. Ewing's sarcoma of the pubis in a child misdiagnosed as osteomyelitis: a case report. Res Rev Ortho. 2017;1(2):4-8.
- Forsberg JA, Kyle Potter MAJB, Cierny III G, Webb L. Diagnosis and management of chronic infection. J Am Acad Orthop Surg. 2009:8-19.
- Henninger B, Glodny B, Rudisch A, Trieb T, Loizides A, Putzer D, Judmaier W, Schocke MF. Ewing sarcoma versus osteomyelitis: differential diagnosis with magnetic resonance imaging. Skeletal Radiol. 2013(42):1097-104.
- Nesbit ME Jr, Gehan EA, Burgert EO Jr, Vietti TJ, Cangir A, Tefft M, et al. Multimodal therapy for the management of primary, non metastatic Ewing's sarcoma of bone: a long-term follow-up of the First Intergroup study. J Clin Oncol. 1990;8(10):1664-74.
- Widhe B, Widhe T. Initial symptoms and features in osteosarcoma and Ewing sarcoma. J Bone Joint Surg Am. 2000;82(5):667-74.
- Heck Jr RK. Malignant tumors of bone. In: Terry Canale S, Beaty JH. Campbell's operative orthopedics. 11th ed. Philadelphia: Mosby;2008:901-38.
- Varunjikar MD, Jayan BE. Osteomyelitis of femur mimicking ewings sarcoma-a case report. Sch J Med Case Rep. 2014;2(2):118-21.
- Tow BPB, Tan MH. Delayed diagnosis of Ewing's sarcoma of the right humerus initially treated as chronic osteomyelitis: A case report. J Orthop Surg. 2005;13(1):88-92.
- Metcalfe JE, Grimer RJ. Ewing's sarcoma of the foot masquerading as osteomyelitis. Euro Foot Ankle Soc. 2004(10):29-33.
- McCarville MB, Chen JY, Coleman JL, Li Y, Li X, Adderson EE, et al. Distinguishing osteomyelitis from ewing sarcoma on radiography and MRI. AJR Am J Roentgenol 2015;205(3):640-51.
- Funk SS, Copley LAB. Acute hematogenous osteomyelitis in children pathogenesis, diagnosis,

- and treatment. *Orthop Clin N Am.* 2017;48:199-208.
21. Shimose S, Sugita T, Kubo T, Matsuo T, Nobuto H, Ochi M: Differential diagnosis between osteomyelitis and bone tumors. *Acta Radiol.* 2008(49):928-33.
  22. Huang PY, Wu PK, Chen CF, Lee FT, Wu HT, Liu CL, et al. Osteomyelitis of the femur mimicking bone tumors: a review of 10 cases. *World J Surg Oncol.* 2013(11):283-91.
  23. Lyall HA, Constant CR, Wraight EP. Case report: ewing's sarcoma in distal tibial metaphysis mimicking osteomyelitis. *Clin Radiol.* 1993(48):140-42.
  24. Cottias P, Tomeno B, Anract P, Vinh TS, Forest M. Subacute osteomyelitis presenting as a bone tumour. A review of 21 cases. *Int Ortho.* 1997(21):243-8.
  25. Dich VQ, Nelson JD, Haltalin KC. Osteomyelitis in infants and children: a review of 163 cases. *Am J Dis Child.* 1975;(129):1273-8.

**Cite this article as:** Sananta P, Rizal H. Diaphyseal osteomyelitis of femur with suspected ewing sarcoma in 8 years old children: a case report. *Int J Res Med Sci* 2018;6:4110-5.