

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Low-grade intramedullary osteosarcoma presenting with multiple sclerotic bone lesions

Akbar Rizki Beni Asdi, Achmad Fauzi Kamal*

Department of Orthopaedic and Traumatology, Cipto Mangunkusumo National Central Hospital and Faculty of Medicine, Universitas Indonesia, Jalan Diponegoro No. 71, Central Jakarta 10430, Indonesia

ARTICLE INFO

Article history:

Received 9 February 2018

Accepted 6 April 2018

Available online 1 June 2018

Keywords:

Low-grade intramedullary osteosarcoma
Multiple sclerotic lesions

ABSTRACT

Low-grade intramedullary osteosarcoma is a less-aggressive type of osteosarcoma for which delays in diagnosis are common. We present the case of a 42-year-old woman with complaints of low back pain. Multiple imaging evaluations and biopsy procedures were necessary to make the final diagnosis. The key radiologic feature was multiple sclerotic lesions throughout the skeleton, best seen on the bone scan. The difficulties in diagnosing this condition are evident in this case.

© 2018 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license.

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

1. Introduction

Low-grade intramedullary osteosarcoma (also known as low-grade central osteosarcoma) is a rare variant of osteosarcoma. It accounts only for 1–2% of all osteosarcomas. It has an equal gender distribution and the majority of cases occur in the second and third decade. The main difficulty in diagnosing low-grade intramedullary osteosarcoma is the noncharacteristic features of a malignant neoplasm in the radiological and histological examination. Pathological diagnosis is also difficult due to its resemblance to benign lesions. Cytological atypia is minimal and only fibroblastic stroma is present [1]. Also, because of the difficulty of diagnosing this cancer, the patient often comes in late stages and with various secondary complications. We present a case of low-grade intramedullary osteosarcoma with an emphasis on diagnostic workup and further planning.

2. Case report

A 42-year-old female was referred to our institution, mainly complaining about pain in her lower back extending to her right upper thigh. The pain was mainly felt during standing up from a sitting position since 4 months before admission and with experienced weight loss of about 5 kg. From the physical examination, there was no mass or deformity found in the extremities. She felt pain scaling 6–7 based on the visual analogue scale. The range of motion of both lower extremities was within normal limits. On laboratory examinations, lactic dehydrogenase was 1485 U/L (normal: <480) and alkaline phosphatase was 1234 U/L (normal: <95).

Radiographs, magnetic resonance imaging (MRI) and bone scintigraphy (Fig. 1) performed from another hospital with radiographs revealed multiple sclerotic lesions on multiple bones from lumbar vertebrae to both femurs. The whole spine

* Corresponding author.

E-mail address: fauzi.kamal@ui.ac.id (A.F. Kamal).<https://doi.org/10.1016/j.radcr.2018.04.012>1930-0433/© 2018 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

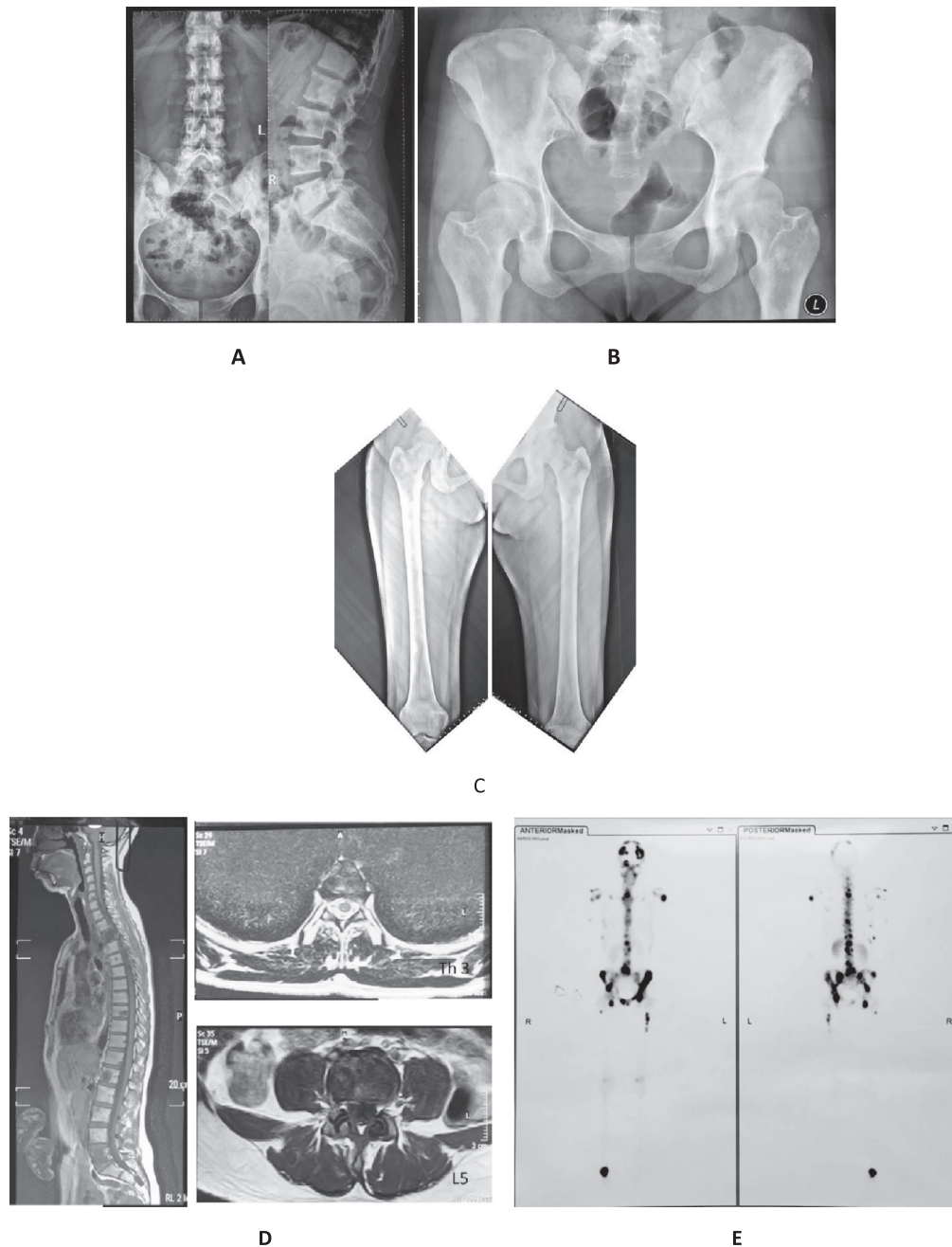
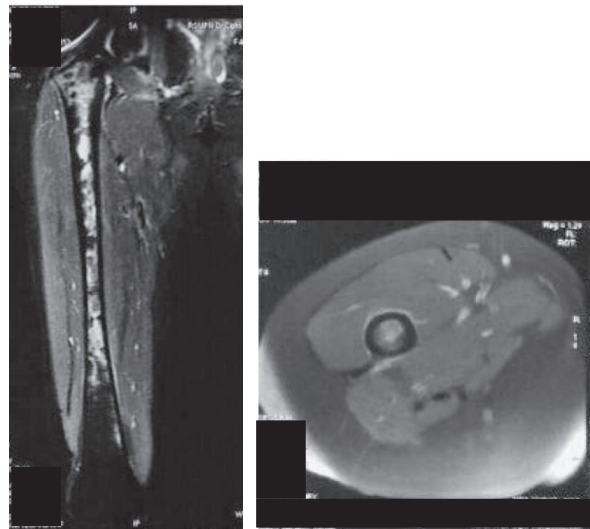


Fig. 1 – Radiological examinations were performed including radiographs, magnetic resonance imaging (MRI), bone scintigraphy, and positron emission tomography scan. (A) Radiographs of the lumbosacral spine revealed multiple sclerotic lesions on lumbar 1, 2, 5. (B) Pelvic X-ray demonstrated sclerotic lesions on left iliac wing, at the left periacetabulum, sacrum, and bilateral trochanters. (C) Radiographs of the femur showed increasing multiple blastic lesions on both femurs. (D) Whole spine MRI showed a hypointense lesions, on the multiple levels of vertebral bodies with diffused lesion on thoracal 3 and lumbar 5 with minimal soft tissue involvement. (E) Bone scanning showed an active blastic process at the hip, multiple levels of the spine, proximal femur, humerus, distal tibia, cranium, and other places. The multiple lesions were suspected as metastasis bone disease or metabolic bone disease or osteopoikilosis.

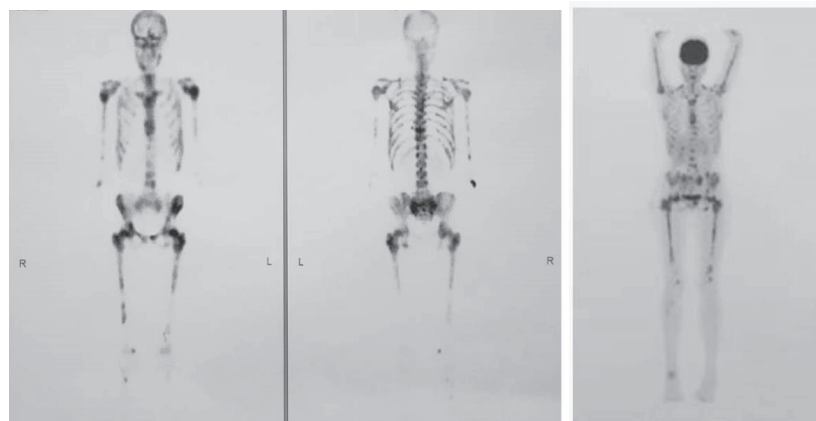
MRI showed hypointense lesions, on the multiple levels of vertebral bodies with the diffused lesion. However, the bone scanning demonstrated an active blastic process at multiple bones.

Additional serial femur radiographs showed increasing multiple blastic lesions on both femurs. The MRI of the femur

revealed increasing heterogeneous signal on the bone marrow with slightly hyperintense image post contrast (Fig 2). An open biopsy of the iliac bone was performed in the previous hospital and it showed necrotizing fibrosis, bone-forming lesions, without any evidence of malignant cells.



A



B

C

Fig. 2 – Additional magnetic resonance imaging (MRI) of the femur, bone scan, and positron emission tomography (PET) scan were performed 3 months later. (A) MRI of the femur revealed increasing heterogeneous signal on the bone marrow with slightly hyperintense image post contrast. (B) Showed an increasing blastic lesion at the skull, ribs, humerus, multiple vertebrae from cervical VII to lumbar V, sacroiliac joint, acetabulum, sacrum, iliaca, pubic, right ischium, proximal femur, and right distal tibia. (C) PET scan showed lesions on mandibula, both of ischium, proximal humerus, clavicle, scapula, ribs, sternum, all vertebrae, pubis, acetabulum, bilateral femur, and right talus.

We compared the bone scan results from the previous hospital and from our center, and they showed an increasing blastic lesion at the skull, ribs, humerus, multiple vertebrae from cervical VII to lumbar V, sacroiliac joint, acetabulum, sacrum, iliaca, pubic, right ischium, proximal femur, and right distal tibia (Fig. 2). The positron emission tomography scan also showed mix lesions on mandibula, both of ischium, proximal humerus, clavicle, scapula, ribs, sternum, all vertebrae, pubis, acetabulum, bilateral femur, and right talus (Fig. 2). Based on these data, we concluded that the lesion was growing progressively, suggesting a malignant lesion.

Thus, a second open biopsy was performed on the right proximal femur. The histopathological specimen showed spindle cells surrounded by osteoid that formed lace-like structure (Fig. 3). After reviewing patient's data on the

clinic-pathological conference, we concluded that it was consistent with a low-grade intramedullary osteosarcoma.

She was treated with a chemotherapy regimen consisting of doxorubicin and cisplatin. During the first 2 out of 6 cycles, she felt improvement with decreased pain and increased appetite. After she finished all cycles of the chemotherapy, there was marked general improvement; she did not feel pain anymore with visual analogue scale 0–1, no activity limitation, and the body weight increased about 10 kg. On laboratory examinations, lactic dehydrogenase was 628 U/L and alkaline phosphatase was 549 U/L. Bone scan showed decreasing uptake of the blastic lesion on the mandibula, both of ischium, proximal humerus, clavicle, scapula, ribs, sternum, all vertebrae, pubis, acetabulum, bilateral femur, and right talus (Fig. 4).

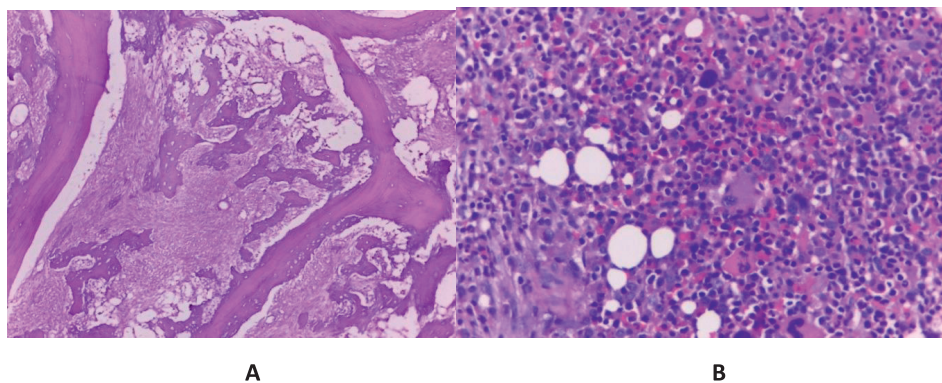


Fig. 3 – (A) Histological features of the first biopsy, on 400x magnification showing a bone-forming lesions that did not has the typical features of malignancy. The biopsy was taken from the lesion on the iliac crest. (B) Histopathology from rebiopsy of right femur right on 400x magnification, the spindle cells showed multiple nuclear form, round and oval shaped with osteoid formation. It was consistent with osteosarcoma.

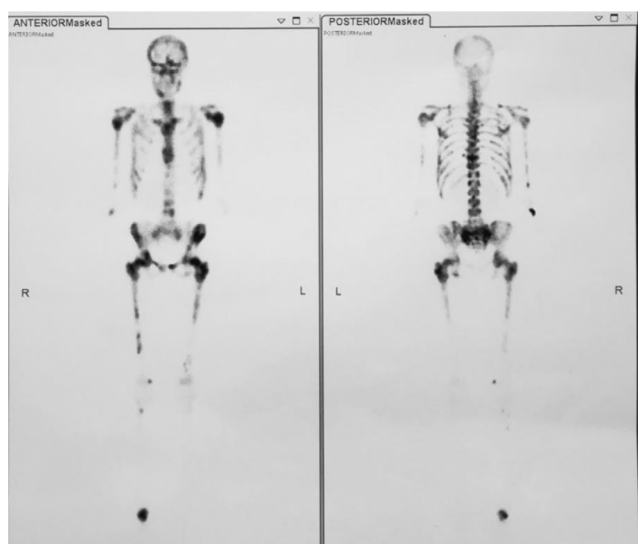


Fig. 4 – Bone scan after chemotherapy showed decreasing a blastic lesion at the hip, acetabulum, femur, multiple level of the spine, ribs, sternum, scapula, humerus, tibial distal, and cranium.

3. Discussion

A low-grade osteosarcoma possesses nonrapidly progressing symptoms and innocuous histological features, especially comprising spindle cells with minimal malignant cells (nuclear atypia and mitosis). Referring to subtle signs, it is not always easy to establish a diagnosis as it also requires accurate timing and procedure [2]. Most of the time patients with low-grade osteosarcoma were misdiagnosed as other diagnosis and were treated by other means. Therefore, when the diagnosis of low-grade intramedullary osteosarcoma is established, the patient will already have terminal conditions. The patient came to our outpatient clinic after several visits to var-

ious doctors. Various diagnoses were established and several treatment modalities were carried out.

Atypical low-grade osteosarcoma is located in the intramedullary compartment and often the metaphysis or metadiaphysis around the knee frequently extends to the end of the bone, is large, and has an aggressive feature such as poor margination [3,4]. In our case, the age of the patient was 42 years old, in accordance with literature. The symptoms were also subtle and not as clear as conventional osteosarcoma. The symptoms were not in accordance to general anamnesis of cancer patients, with no subjective and objective signs and symptoms thus making lack of evidence of neoplasm lesions [5,6].

The radiological appearance of low-grade osteosarcoma are variable, the most common appearance is lytic bone destruction with the variable of coarse thick or thin trabeculation. The dense sclerotic pattern is less common. Cortical destruction and soft tissue extension is a common finding with the variable stage of periosteal reactions. On radiographs, the densely sclerotic pattern of the sarcoma is usually eccentric and expansive, with homogenously dense sclerotic matrix production [7,8]. In a study by Arslan et al. in a series of low-grade central osteosarcoma in the Turkish population, the most common form of radiographic appearance is multiple permeative sclerotic foci with extension to surrounding tissue [9]. In our case, there was a widespread of sclerotic lesion all over the bone, from head to toe. This phenomenon was complemented with various active lesions shown in the bone scan.

Pathologically, the lesion showed spindle cells surrounded by osteoid that formed lace-like structure. Nuclear cell atypia was not found, although various shapes existed (oval, vesicular). In literature, spindle cells with osteoid formation are usually the hallmark of typical low-grade intramedullary osteosarcoma. Cellular atypia is present but is usually scarce [10]. The osteoid production is a typical presentation in osteosarcoma, as matrix production is almost never present in malignant lymphoma of the bone. The cell type in lymphoma of the bone is usually presented as a mixed type of large

and small cells. It is possible, however, that a low-grade osteosarcoma infiltrates a lymphoid structure as shown by Ostrowski et al. [11].

Most of the time, the patients require more than one biopsy. The timing of the biopsy and the location of the biopsy play an important role in achieving a correct diagnosis. In our case, the patient was diagnosed with osteosarcoma after several attempts of biopsies. This proved it was difficult to achieve a correct diagnosis for this disease as it slowly progresses. This probably is because the tumor has a finely differentiated morphology. Macroscopically it is a whitish mass with well-demarcated edges and fibrous whorled appearance [6]. She had a fine needle biopsy and failed to establish a diagnosis afterward. It is in fact, difficult to achieve a diagnosis of low-grade osteosarcoma by solely relying on fine needle biopsy, even harder to differentiate it with other conditions, such as fibrous dysplasia [12]. The biopsy was first taken from the pelvis and the second one was from the proximal of the right thigh. The decision of the location was influenced by the activity of the lesion shown by the bone scan. However, the proximal of right thigh was later especially noted due to an intramedullary lesion and the progress of the lesion.

The current steps for treating osteosarcoma include neoadjuvant chemotherapy, surgery and adjuvant chemotherapy. While adjuvant chemotherapy is a must, neoadjuvant is not as urgent as the aforementioned chemotherapy. For an adult, the standardized treatment for osteosarcoma is adriamycin (doxorubicin), high-dose methotrexate, and cisplatin. The addition of ifosfamide-based therapy improved the relapse-free survival rate, but only when used in conjunction with the mifamurtide. Therefore, some clinicians only prefer the dual therapy of doxorubicin and cisplatin [13]. Our patient was treated with chemotherapy, one time every 3 weeks, the total number of chemotherapy was six cycles while the regimen was doxorubicin and cisplatin. After the chemotherapy, she did not feel pain anymore and increased the body weight about 10 kg, no limitation of activity. Bone scintigraphy showed decreasing uptake of the blastic lesion on the mandibula, both of ischium, proximal humerus, clavicle, scapula, ribs, sternum, all vertebrae, pubis, acetabulum, bilateral femur, and right talus

The advanced technology and medical research in osteosarcoma treatment are largely dependent on its clinical stage. The prognosis will be worse if it is found at a later stage. Therefore, the burden of misdiagnosis and mistreatment is larger than other diseases. In a study by Yang and Feng, the rate of misdiagnosis is as high 36%. Primary practitioners are usually the main area where the diagnosis is stagnant. The average delay until rightly treated is 57 days. The reasons for lack of diagnosis were unclear imagery of X-ray examination and clear pathology on early stage. From the anamnesis, mostly the patient will state that it was probably due to a household accident, misdirecting the physician to a common trauma. Most of the time, the misdiagnosis will occur in the earlier stage because no sign will be prominent, and the anamnesis will be insignificant [14].

4. Conclusions

A low-grade osteosarcoma is a rare variety of osteosarcoma and a challenge for every clinician to diagnose. Many physicians had several failed to diagnose this tumor due to the very slow progression of symptoms, insignificance of laboratory markers, nonpathognomonic radiographical appearance, and failed biopsies. The complicated process of diagnosing the condition is evident in this case and should be underlined in deciding a lesion to be a benign lesion or malignant.

Conflict of interest

Declaration of interest: none.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.radcr.2018.04.012](https://doi.org/10.1016/j.radcr.2018.04.012).

REFERENCES

- [1] Malhas AM, Sumathi VP, James SL, Menna C, Carter SR, Tillman RM, et al. Low-grade central osteosarcoma: a difficult condition to diagnose. *Sarcoma* 2012;5:1–7.
- [2] Bonar SF. Central low-grade osteosarcoma: a diagnostic challenge. *Skeletal Radiol* 2012;41(2):365–7.
- [3] Moghadamfalahi M, Alatassi H. Low-grade central osteosarcoma of the rib: a case report and brief review of the literature. *Case Rep Pathol* 2013;4:1–3.
- [4] Sinha R, Chowdhury SKR, Chattopadhyay PK, Rajkumar K. Low-grade osteosarcoma of the mandible. *J Maxillofac Oral Surg* 2010;9:186–90.
- [5] Kurt AM, Unni KK, McLeod RA, Pritchard DJ. Low-grade intraosseous osteosarcoma. *Cancer* 1990;65:1418–28.
- [6] Fletcher CDM, Unni KK. Pathology and genetics of tumours of soft tissue and bone. In: Fletcher CDM, Unni KK, Mertens F, editors. *World Health Organization classification of tumours, vol. 4. Lyon: International Agency for Research on Cancer (IARC); 2002. p. 264–86.*
- [7] Yarmish G, Klein MJ, Landa J, Lefkowitz RA, Hwang S. Imaging characteristics of primary osteosarcoma: nonconventional subtypes. *Radiographics* 2010;6:1653–72.
- [8] Andresen KJ, Sundaran M, Unni KK, Sim FH. Imaging features of low-grade central osteosarcoma of the long bones and pelvis. *Skeletal Radiol* 2004;33:373–9.
- [9] Arslan HS, Aydin O, Dervisoglu S, Oksuz DC, Kantarci F, Hiz M, et al. Low-grade osteosarcoma, review of 15 cases in a series of 156 osteosarcoma cases. *Turkish J Pathol* 2011;27:138–43.
- [10] Klein MJ, Siegal GP. Osteosarcoma: anatomic and histologic variants. *Am J Clin Pathol* 2006;125:555–81.
- [11] Ostrowski ML, Johnson ME, Smith PD, Barrios PC, Spjut HJ. Low-grade intraosseous osteosarcoma with prominent lymphoid infiltrate. *Arch Pathol Lab Med* 2000;124:868–71.

-
- [12] Bertoni F, Bacchini P, Fabbri N, Mercuri M, Picci P, Ruggieri P, et al. Osteosarcoma: low-grade intraosseous type osteosarcoma, histologically resembling parosteal osteosarcoma, fibrous dysplasia, and desmoplastic fibroma. *Cancer* 1993;71(2):338–45.
- [13] Asha K, Sachin A, Muzammil S. Chemotherapy in osteosarcoma. In: Agarwal M, editor. *Osteosarcoma*, vol. 9. InTech; 2012. p. 93–108.
- [14] Yang Y, Feng L. Misdiagnosis and mistreatment for osteosarcoma: analysis of cause and its strategy. In: Agarwal M, editor. *Osteosarcoma*, vol. 9. InTech; 2012. p. 85–92.