Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
49(10) 1–5

DOI: 10.1177/03000605211052229
journals.sagepub.com/home/imr
SAGE

Multiple osteolytic primary peripheral T-cell bone lymphoma: the first case report

Chen Li[1], Weiguo Wang[2], Lingyun Xu[1], Dingyun Zheng[1], Miao Zhang[1], Qin Zhang[1], Xiaoqian Wu[1], Yue Yao[1], Wenyue Huang[1], Xue Li[1], Peipei Ying[1], Xiuxiu Wang[1], Liu Shang[1] and Yuhu Feng[1]

Abstract

Peripheral T-cell lymphoma accounts for about 10% of all cases of non-Hodgkin's lymphoma. However, less than 5% of patients with non-Hodgkin's lymphoma present with hypercalcaemia as the initial symptom, and less than 1% present with primary bone lesions. We herein describe a 76-year-old Chinese man who was diagnosed with primary bone adult T-cell lymphoma with extensive osteolysis, including bone loss in the radius, as the initial manifestation. He had developed severe generalised bone pain and an inability to raise his arms. X-ray examination revealed osteolytic destruction of the forearm with loss of the radial diaphysis. The patient was diagnosed with peripheral T-cell lymphoma based on his immunohistochemical results. He began treatment with the CHOPE chemotherapy regimen, which resulted in significant improvement of his bone pain.

Keywords

Lymphoma, T-cell lymphoma, peripheral T-cell lymphoma, primary bone lymphoma, osteolysis, chemotherapy, case report

Date received: 12 January 2021; accepted: 27 August 2021

[1]Department of Hematology, Fuyang People's Hospital (The Affiliated Fuyang People's Hospital of Anhui Medical University), Fuyang City, Anhui Province, China

[2]Department of Clinical Laboratory, Fuyang People's Hospital, Fuyang City, Anhui Province, China

Corresponding author:
Yuhu Feng, Department of Hematology, The Affiliated Fuyang People's Hospital of Anhui Medical University, No. 501, Sanqing Road, Fuyang City, Anhui Province 236000, China.
Email: 18997080097@163.com

Introduction

Primary bone lymphoma is a rare disease that accounts for <2% of all lymphomas in adults.[1] Primary bone lymphoma is estimated to account for 3% to 7% of all primary bone tumours and 3% to 5% of all cases of extranodal non-Hodgkin's lymphoma.[2,3] Osteolytic bone lesions are rare initial symptoms of primary bone adult T-cell lymphoma. Severe osteolytic destruction characterised by loss of the radial diaphysis is even more rare in patients with primary bone adult T-cell lymphoma.

We herein report a case of primary bone adult T-cell lymphoma with loss of the radial diaphysis. This is the first report of severe osteolytic destruction in a patient with this type of lymphoma.

Case report

A 76-year-old man presented to the orthopaedic department of a hospital with generalised bone pain. He reported severe generalised bone pain and an inability to raise his arms, and he had no medical history of bone disease. The patient had mild anaemia (haemoglobin concentration of 90 g/L), marked hypercalcaemia (blood calcium concentration of 3.9 mmol/L), and elevated concentrations of lactate dehydrogenase (1158 U/L) and alkaline phosphatase (188 U/L). His concentrations of parathyroid hormone (5.0 ng/L), serum immunoglobulins (IgG, IgA, and IgM), complement C, creatinine, uric acid, and serum and urine light chains were normal. The orthopaedist performed various tests, including computed tomography (CT) and X-ray examinations. The X-ray examination revealed osteolytic destruction of the forearm characterised by loss of the radial diaphysis (Figure 1) and signs of multiple bone lesions throughout the body; in particular, some of the ribs and thoracic vertebrae showed signs of osteolytic bone destruction. Multiple small regular translucent shadows were seen in the iliac bones, thoracolumbar vertebrae, and ribs. Circumferential hyperdense shadowing was also seen in some of the lumbar vertebrae. There were no signs of enlarged

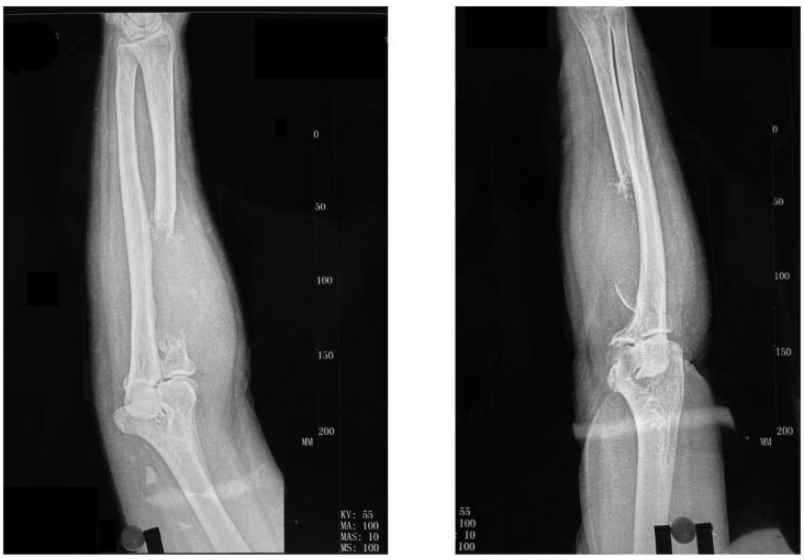

Figure 1. Forearm X-ray showing bilateral radial diaphysis loss.

lymph nodes. The orthopaedist suspected multiple myeloma and immediately referred him to our haematology department for treatment.

The patient developed nausea, vomiting, polyuria, and polydipsia in the haematology department of our hospital. He had an albumin concentration of 21 g/L on admission. His calibrated calcium concentration was 4.42 mmol/L (reference range, 2.25–2.75 mmol/L), vitamin D/calcitriol concentration was 80 ng/mL, and parathyroid hormone concentration was 8.30 pg/mL (reference range, 17–73 pg/mL). Positron emission tomography–computed tomography examination at the first visit showed multiple bone lesions with no obvious solid tumours (Figure 2). Given the symptoms of hypercalcaemia, anaemia, and bone lesions, our differential diagnoses were metastases, multiple myeloma, and lymphoma. The patient's blood and urine immunofixation electrophoresis results were normal; thus, we ruled out multiple myeloma. We also ruled out metastases because positron emission tomography–CT examination showed no solid tumours.

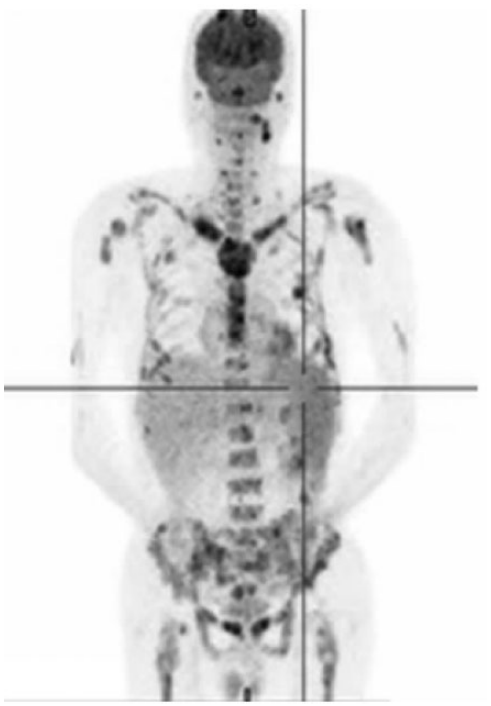

Figure 2. Whole-body fluorodeoxyglucose-positron emission tomography image showing sternum, ribs, spine, and pelvis fixation.

We then performed bone marrow aspiration, and no significant abnormalities were seen. Bone marrow biopsy suggested a localised lymphocytic excess (Figure 3).

The patient had no fever, night sweats, or weight loss. The results of brain magnetic resonance imaging were normal.[4,5] We obtained the patient's consent for treatment. He began the CHOPE chemotherapy regimen (cyclophosphamide at 750 mg/m^2 on day 1, vincristine at 1.4 mg/m^2 on day 1, doxorubicin at 10 mg/m^2 on days 1–4, dexamethasone at 40 mg on days 2–5, and etoposide at 100 mg/m^2 on days 1–3), which resulted in significant improvement of his bone pain. His hypercalcaemia was managed with treatments targeting the primary cause, massive fluid replacement, diuresis, diphosphonates, and calcitonin. We proposed surgical treatment involving external fixation, an internal fixator, a prosthetic joint, and arthroplasty for the radial bone loss, but the patient refused for financial reasons. He had a stable forearm with anterior and posterior rotation, and he and his family requested that he be discharged from the hospital without further review or follow-up treatment. The patient died of respiratory failure due to pulmonary infection 1 month later. The reporting of this study conforms to the CARE guidelines.[14] We have de-identified all patient details.

Discussion

We have presented a case involving a 76-year-old man with extensive osteolysis, including radial diaphysis bone loss, as a main feature of fatal primary peripheral T-cell bone lymphoma and paraneoplastic

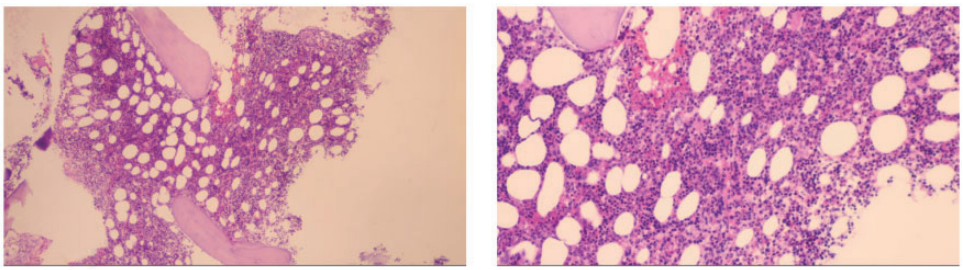

Figure 3. Histologic images of iliac crest showing T lymphocyte hyperplasia. (a) Histopathology. (b) Immunohistochemistry. Initial immunohistochemistry of a bone marrow biopsy specimen showed CD34 small vessels (+), round nucleated cells occasionally (+), CD117 occasional (+), CD61 megakaryocytes (+), no single round nucleus, CD3 multifocal (+), CD20 small clusters and scattered few (+), CD56 (−), E-cadherin small clusters (+), and myeloperoxidase scattered (+). Bone marrow biopsy and immunohistochemistry demonstrated multifocal T-lymphocyte hyperplasia and a high probability of T-cell lymphoma. Further immunohistochemistry showed CD3 diffuse (+), CD20 individually (+), CD4 diffuse (+), CD8 scattered sparingly (+), terminal deoxynucleotidyl transferase (−), CD30 occasional (+), CD5 diffuse (+), anaplastic lymphoma kinase (−), CD56 (−), and Ki-67 (approximately 50%–60% +). In addition, positive T-cell receptor β clonal rearrangements were detected. Finally, the patient was diagnosed with peripheral T-cell lymphoma based on these immunohistochemical results.

syndrome characterised by severe hypercalcaemia.

It is not uncommon for patients with lymphoma to develop osteolytic damage. However, the rarity of the present case involves the loss of the radial diaphysis. Such serious osteolytic destruction has not been reported in previous cases. This is the first report of bilateral loss of radial bone in a patient with lymphoma. The pathophysiology of osteolysis in peripheral primary T-cell bone lymphoma is complex. In brief, lymphoma cells increase osteoclast activation by secreting receptor activator of nuclear factor-κB ligand (RANK-L), which activates RANK signalling in bone. The cytokines macrophage inflammatory protein 1α (MIP-1α)[10] and MIP-1β[11] and the protein Wnt-5a[12] promote osteoclast formation by upregulating RANK expression. Lymphoma cells also secrete the viral protein gp46 as an osteoprotective protein antagonist, thereby promoting bone destruction.[13]

Severe hypercalcaemia and Ki-67 are vital markers of a poor prognosis. Bilateral loss of the radial diaphysis is a sign of a poor functional prognosis and was debilitating in the present case. The patient's hypercalcaemia was due to osteolysis,[6,7] which is most often seen in the late stages of the disease and develops by many pathomechanisms.[8,9]

Peripheral T-cell bone lymphoma should be considered a differential diagnosis of diffuse bone pain, notably in older men. Peripheral T-cell bone lymphoma can lead to bone loss and is a debilitating condition if left untreated. Early diagnosis of peripheral T-cell bone lymphoma is therefore warranted. There were some limitations in the management of the present case, including the late diagnosis and unclear follow-up.

Conclusion

This older man presented with severe osteolytic destruction and hypercalcaemia as features of primary peripheral T-cell bone lymphoma. In the future, RANK-L inhibitors could be considered in the treatment of

primary bone lymphoma in addition to chemotherapy.

Consent and ethics statement

The patient provided written informed consent for treatment and publication of this case report. The requirement for review board approval was waived because of the nature of this study (case report).

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Yuhu Feng https://orcid.org/0000-0002-6016-7588

References

1. Hayase E, Kurosawa M, Suzuki H, et al. Primary bone lymphoma: a clinical analysis of 17 patients in a single institution. *Acta Haematol* 2015; 134: 80–85.
2. Pilorge S, Harel S, Ribrag V, et al. Primary bone diffuse large B-cell lymphoma: a retrospective evaluation on 76 cases from French institutional and LYSA studies. *Leuk Lymphoma* 2016; 57: 2820–2826.
3. Yagi S, Zheng R, Nishiyama S, et al. Osteolytic primary bone lymphoma in the multiple bones. *J Med Invest* 2019; 66: 347–350. doi: 10.2152/jmi.66.347.
4. Essouma M, Soh DM, Temgoua MN, et al. Adult T-type lymphoblastic lymphoma presenting as hypercalcemic crisis and aplastic anemia: a case report. *J Med Case Rep* 2019; 13: 305. https://doi.org/10.1186/s13256-019-2225-2
5. Wagner J and Arora S. Oncologic metabolic emergencies. *Emerg Med Clin North Am* 2014; 32: 509–525.
6. Takasaki H, Kanamori H, Takabayashi M, et al. Non-Hodgkin's lymphoma presenting as multiple bone lesions and hypercalcemia. *Am J Hematol* 2006; 81: 439–442. https://doi.org/10.1002/ajh.20559.
7. Schöttker B, Heinz W, Weissinger F, et al. Parathyroid-hormone-related-protein-associated hypercalcemia in a patient with CLL-type low-grade leukemic B-cell lymphoma. *Haematologica* 2006; 91: ECR45.
8. Tebben PJ, Singh RJ and Kumar R. Vitamin D-mediated hypercalcemia: mechanisms, diagnosis, and treatment. *Endocr Rev* 2016; 37: 521–547. https://doi.org/10.1210/er.2016-1070.
9. Hewison M, Kantorovich V, Liker HR, et al. Vitamin D-mediated hypercalcemia in lymphoma: evidence for hormone production by tumor-adjacent macrophages. *J Bone Miner Res* 2003; 18: 579–582. https://doi.org/10.1359/jbmr.2003.18.3.579.
10. Okada Y, Tsukada J, Nakano K, et al. Macrophage inflammatory protein-1α induces hypercalcemia in adult T-cell leukemia. *J Bone Miner Res* 2004; 19: 1105–1111. https://doi.org/10.1359/JBMR.040314.
11. Matsuhashi Y, Tasaka T, Uehara E, et al. Diffuse large B-cell lymphoma presenting with hypercalcemia and multiple osteolysis. *Leuk Lymphoma* 2004; 45: 397–400. https://doi.org/10.1080/10428190310001593139.
12. Bellon M, Ko NL, Lee MJ, et al. Adult T-cell leukemia cells overexpress Wnt5a and promote osteoclast differentiation *Blood* 2013; 121: 5045–5054. https://doi.org/10.1182/blood-2012-07-439109.
13. Sagara Y, Inoue Y, Ohshima K, et al. Antibody to the central region of human T-lymphotropic virus type 1 gp46 is associated with the progression of adult T-cell leukemia. *Cancer Sci* 2007; 98: 240–245. https://doi.org/10.1111/j.1349-7006.2006.00370.x.
14. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.