CASE REPORT

Multifocal primary bone lymphoma: durable complete remission after R-CHOP chemotherapy

Muhajir Mohamed,¹ Terry Brain,² Sharad Sharma³¹Department of Haematology, Launceston General Hospital, Launceston, Tasmania, Australia²Department of Pathology, Launceston General Hospital, Launceston, Tasmania, Australia³Department of Medicine, Launceston General Hospital, Launceston, Tasmania, Australia**Correspondence to**
Dr Muhajir Mohamed,
muhajirbm@yahoo.com**SUMMARY**

Primary bone lymphoma (PBL) is a type of non-Hodgkin's lymphoma predominantly affecting the skeletal system. PBL is an extremely rare cancer in adults affecting mainly the axial skeleton. The extent of bone involvement in these patients is variable. Most of the cases reported had single or a few skeletal lesions. We report a patient who had extensive multifocal lymphoma involving the axial skeleton and a very good and durable response to R-CHOP chemotherapy.

BACKGROUND

This case report will enlighten the readers on this rare subtype of non-Hodgkins lymphoma. This patient had a very good and durable response to conventional therapy and this was very apparent when comparing the pretreatment and post-treatment positron emission tomography-CT (PET-CT) scan. To our knowledge, a case of extensive primary bone lymphoma (PBL) demonstrating

excellent therapeutic response on the imaging studies has not been reported till date.

CASE PRESENTATION

A 59-year-old Caucasian male patient presented in November 2010 with back pain, weight loss and drenching night sweats of 2 weeks duration. He did not have any significant comorbid illnesses in the past. Clinical examination revealed normal cardiac, respiratory, neurological statuses. There was a firm non-tender mass on the right side of his chest wall anteriorly, measuring approximately 6 cm horizontally and 4 cm vertically in size. There were no palpable lymphadenopathy or organomegaly and no other masses were felt. His performance status on Eastern Cooperative Oncology Group (ECOG) scale was 2.

INVESTIGATIONS

Full blood counts revealed low haemoglobin (120 g/l), high white cell count ($13.4 \times 10^9/l$) with neutrophilia ($10.2 \times 10^9/l$) and high platelet count ($495 \times 10^9/l$). The erythrocyte sedimentation rate

Figure 1 Histopathological examination of the core biopsy specimen from chest wall mass showing features consistent with diffuse large B-cell lymphoma. (A) H&E stain (magnification $\times 400$), large lymphoid cells in the background of fibrosis. The larger lymphoid cells resemble centroblasts (blue arrows). (B) CD20 immunohistochemical stain (magnification $\times 400$), Strong and uniform surface positivity. (C) CD10 immunohistochemical stain (magnification $\times 400$). Surface positivity in approximately 75% of the lymphoid cells. (D) BCL-6 immunohistochemical stain (magnification $\times 400$), nuclear positivity in approximately 60% of the lymphoid cells.

To cite: Mohamed M, Brain T, Sharma S. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009809

(ESR) was high (50 mm/h). Biochemical tests showed very high lactate dehydrogenase (LDH) level (2198 U/l), high calcium level (2.90 mmol/l) and high alkaline phosphatase (ALP) level (624 U/l) with a normal uric acid level. The viral serologies for HIV, Epstein-Barr virus, Hepatitis B and Hepatitis C were negative.

A CT scan of chest showed a lenticular shape mass lesion originating from the posterior aspects of the right 10th rib with features of pathological fracture and an extrapleural mass which measured 68×32×59 mm in size. No other similar masses, bone lesions or organomegaly were detected in the contrast CT scans of chest, abdomen and pelvis. However, bone scan with single-photon emission CT (SPECT) revealed areas of increased isotope uptake in manubrium, ribs, multiple vertebrae and pelvic bones. A core biopsy of the chest wall mass was performed under CT guidance. On histological examination, pleomorphic large lymphoid cells were present interspersed in a background of fibrosis (Figure 1A). These cells had variable sizes and shapes with minimal cytoplasm. The nucleoli were relatively inconspicuous. A few larger cells appearing like centroblasts with fine chromatin and prominent nucleoli were also seen (Figure 1A—blue arrows). Immunohistochemistry performed on fixed, paraffin-embedded tissue sections demonstrated strongly positive surface staining of CD20 antigen on almost 100% of the lymphoid cells (Figure 1B). CD10 surface stain was positive in the majority of the cells (Figure 1C) and bcl-6 was positive in the nuclei of about 60% of the cells

(Figure 1D). These morphological and immunohistochemical features were consistent with a diffuse large B-cell lymphoma (DLBCL). A staging bone marrow biopsy from right posterior superior iliac spine showed a reactive marrow without any involvement by lymphoma. PET-CT using ^{18}F -FDG demonstrated a very high fluorodeoxyglucose (FDG) uptake in the right chest wall soft tissue mass centred at the 10th posterior rib. There was also extensive skeletal lesions with high FDG uptake noted throughout all regions of the spine, the manubrium, sternum, bilateral ribs, both clavicles, both scapulae, throughout the right and left hemipelvis, both proximal humeri and both proximal femora. There were no similar lesions found in the lymph nodes or any internal organs (Figure 2). Since the lymphoma was mainly localised to the bones, a diagnosis of PBL was made. On the basis of the imaging studies, the lymphoma was found to be multifocal and predominantly in the axial skeleton. There were multiple PET-avid lesions in the spine extending from cervical vertebrae to the sacrum. The lymphoma was classified as stage-IV (Ann-Arbor staging) and the patient's revised-International Prognostic Index (R-IPI) score was 3, indicating a poor prognostic category.

TREATMENT

The patient was treated with cyclophosphamide, doxorubicin, vincristine, prednisone and rituximab (R-CHOP) chemotherapy. There was evidence of tumour lysis with hyperphosphataemia and increase in LDH levels despite receiving allopurinol,

Figure 2 Positron emission tomography (PET)-CT views at diagnosis (November 2010). PET-CT showed extensive fluorodeoxyglucose uptake over the bones of axial skeleton.

Figure 3 Positron emission tomography (PET)-CT views after completion of chemotherapy (March 2011). Post-treatment PET-CT showed complete metabolic response at the previously involved sites.

aggressive intravenous hydration and sodium bicarbonate. Within the first week of chemotherapy he had a very good symptomatic improvement and a reduction in the size of the chest wall mass clinically. All the abnormal biochemical tests, namely LDH, ALP and calcium levels, returned to normal levels within 6 weeks of the first cycle of the chemotherapy.

OUTCOME AND FOLLOW-UP

All the abnormal biochemical tests, namely LDH, ALP and calcium levels, returned to normal levels within 6 weeks of the first cycle of the chemotherapy. After completion of third cycle of chemotherapy, an interval PET-CT scan showed that most of the FDG avid lesions had resolved, consistent with an excellent response. The patient received a total of six cycles of chemotherapy at 14 day intervals, which was tolerated well without any significant side effects. PET-CT scan repeated after the completion of the sixth cycle of chemotherapy, 4 months after the diagnosis revealed a complete resolution in FDG avid lesions when compared with the baseline and interval PET scans, consistent with a complete metabolic response (Figure 3). After the completion of chemotherapy no further treatment was given and the patient did not receive any radiation therapy for his lymphoma. He is being observed regularly and currently more than 2 years after diagnosis, he continues to be healthy and in clinical remission.

DISCUSSION

PBL is a very rare condition constituting 3% of all primary bone malignancies¹ and less than 2% of all the adult lymphomas.² Majority of the patients (~92%) present over the age of 30 years.³ The axial skeleton is affected more commonly than the appendicular skeleton (63% vs 37%, respectively).³ Soft tissue extension of the bony disease can occur in about 50% of the cases producing a palpable mass.⁴ The common clinical presentations are swelling, pathological fracture, cord compression and systemic 'B' symptoms (ie, fever, weight loss and night sweats). Histologically diffuse large-B-cell lymphoma accounts for the majority of cases of PBL.⁵ Rarely follicular lymphoma, small lymphocytic lymphoma, marginal zone lymphoma and Burkitt's lymphoma may present as PBL. The Ann-Arbor classification is used for staging of PBL. PBL presenting as solitary bone lesion is Stage-IE and multifocal bone disease presenting solely in the bone is classified as Stage-IV.⁵ A large proportion of patients with PBL present with stage IV disease.⁶ PET-CT examination is useful to determine the presence of distant disease since bone lymphomas are generally FDG avid. PET-CT scan is also the imaging study of choice for assessing the disease

response after treatment.⁷ Many studies prior to the use of rituximab demonstrated an improvement in overall survival using combined modality therapy (chemotherapy + radiation) over chemotherapy or radiation alone.^{8–10} However, in a case series, it has been shown that the addition of rituximab to chemotherapy had a significant benefit with a 3-year progression-free survival of 52% and 88% for those who received cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or R-CHOP, respectively ($p = 0.025$).⁶ Surgical procedure is necessary mainly for performing a diagnostic biopsy or stabilisation of a pathological fracture. The overall prognosis of PBL and long-term survival are generally good with low relapse rates.⁸ However, it was noted that patients over 60-year-old and those with high IPI scores had poorer outcomes.⁶ Our patient had symptoms and presentation similar to those mentioned in the literature. He also had a soft tissue extension of lymphoma from the rib. There were numerous lesions found in the axial skeleton with an extensive multifocal involvement of the entire spine. The response to R-CHOP chemotherapy was very good and the remission is durable. To our knowledge, a case of extensive PBL demonstrating excellent therapeutic response on the imaging studies has not been reported till date.

Learning points

- ▶ Primary bone lymphoma (PBL) is a rare subtype of non-Hodgkin's lymphoma.
- ▶ Positron emission tomography-CT scan is very useful in staging and monitoring of response of PBL.
- ▶ Combination of rituximab with chemotherapy has improved the outcome in patients with PBL.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Limb D, Dregghorn C, Murphy JK, et al. Primary lymphoma of bone. *Int Orthop* 1994;18:180–3.
- 2 Dubey P, Ha CS, Besa PC, et al. Localized primary malignant lymphoma of bone. *Int J Radiat Oncol Biol Phys* 1997;37:1087–93.
- 3 Jawad MU, Schneiderbauer MM, Min ES, et al. Primary lymphoma of bone in adult patients. *Cancer* 2010;116:871–9.
- 4 Mulligan ME, McRae GA, Murphey MD. Imaging features of primary lymphoma of bone. *AJR Am J Roentgenol* 1999;173:1691–7.

- 5 Ferreri AJ, Reni M, Ceresoli GL, *et al.* Therapeutic management with adriamycin-containing chemotherapy and radiotherapy of monostotic and polyostotic primary non-Hodgkin's lymphoma of bone in adults. *Cancer Invest* 1998;16:554–61.
- 6 Ramadan KM, Shenkier T, Sehn LH, *et al.* A clinicopathological retrospective study of 131 patients with primary bone lymphoma: a population-based study of successively treated cohorts from the British Columbia Cancer Agency. *Ann Oncol* 2007;18:129–35.
- 7 Juweid ME, Stroobants S, Hoekstra OS, *et al.* Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. *J Clin Oncol* 2007;25:571–8.
- 8 Beal K, Allen L, Yahalom J. Primary bone lymphoma: treatment results and prognostic factors with long-term follow-up of 82 patients. *Cancer* 2006;106:2652–6.
- 9 Catlett JP, Williams SA, O'Connor SC, *et al.* Primary lymphoma of bone: an institutional experience. *Leuk Lymphoma* 2008;49:2125–32.
- 10 Power DG, McVey GP, Korpanty G, *et al.* Primary bone lymphoma: single institution case series. *Ir J Med Sci* 2008;177:247–51.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow