CASE REPORT

Two diagnoses from bone marrow biopsy: multiple myeloma and Paget's disease of bone

Muhajir Mohamed^{1,2}¹Department of Haematology, Launceston General Hospital, Launceston, Tasmania, Australia²University of Tasmania, Launceston, Tasmania, Australia**Correspondence to**
Dr Muhajir Mohamed,
muhajirbm@yahoo.co

Accepted 7 February 2016

SUMMARY

Multiple myeloma and Paget's disease of bone show certain similarities such as increased osteoclastic activity and predilection to the axial skeleton. However, pathological and radiological changes of the bones are distinctive between multiple myeloma and Paget's disease of bone. This case report describes a patient who had a concomitant diagnosis of multiple myeloma and Paget's disease evidenced from bone marrow biopsy. Such a co-existence is rare, with only a few cases reported so far.

BACKGROUND

Distinctive pathological and radiological changes of the bones are observed in multiple myeloma and Paget's disease of bone. This case report describes a patient who had incidental diagnosis of Paget's disease of bone demonstrated from bone marrow biopsy while he was being evaluated for multiple myeloma.

CASE PRESENTATION

A 62-year-old man reported of exercise intolerance of 3 month's duration. There were no other symptoms. He did not have any medical illness in the past and was not taking any regular medications. He was an ex-smoker and consumed alcohol on a social basis. There was no significant family history. General clinical examination was unremarkable except for a mild conjunctival pallor, and systemic examination was unremarkable.

INVESTIGATIONS

Full blood counts showed low haemoglobin of 98 g/L with normal mean corpuscular volume of 85 fL. The patient's white cell count was normal ($6.4 \times 10^9/L$) with normal differential counts and

platelet count was also normal ($162 \times 10^9/L$). His erythrocyte sedimentation rate was high (84 mm/h, normal range: 0–22). The renal parameters and calcium level were within normal range. Liver function tests showed normal bilirubin, alanine transaminase and aspartate transaminase levels. However, the serum alkaline phosphatase level was elevated at 326 U/L (reference range: 50–130 U/L). Since the erythrocyte sedimentation rate was high, serum protein electrophoresis was performed, which showed a monoclonal band in the gamma region. Immunofixation electrophoresis confirmed IgG paraprotein of 36 g/L. Urine protein electrophoresis also was positive for κ light chain (Bence-Jones proteinuria).

Skeletal survey X-rays performed for work up of multiple myeloma did not show lytic lesions. However, X-rays of the pelvis, skull and vertebral bones, showed increased bone densities, with an abnormal sclerotic bony trabecular pattern (figures 1–3). The prostate specific antigen and parathyroid hormone were within normal limits.

Bone marrow biopsy showed thickened trabecular bone with irregularities of cement lines, resembling a 'mosaic' pattern, and numerous large multinucleated osteoclasts within the Howship's lacunae (figure 4, 100 $\times$ magnification). These features were consistent with Paget's disease of bone. Marrow infiltration by malignant plasma cells of approximately 40% was also evident (figure 5, $\times 400$ magnification). In this patient, Paget's disease was incidentally detected, coexisting with multiple myeloma.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of this condition includes bony metastases of prostate or other cancers,

Figure 1 X-ray of pelvis showing sclerotic changes.

Figure 2 X-ray of skull showing sclerotic changes.

To cite: Mohamed M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-213809

Figure 3 X-ray of lumbar spine showing sclerotic changes.

hyperparathyroidism and eosinophilic granuloma, which is a subtype of Langerhan's cell histiocytosis.

TREATMENT

Soon after diagnosis, our patient was started on a bortezomib and dexamethasone regimen for treatment of multiple myeloma. Zoledronic acid infusions were also administered for management of the bone abnormalities. He completed four cycles of bortezomib-based treatment, which he tolerated well without significant side effects, and maintenance therapy with thalidomide was started after that.

Figure 4 Bone marrow biopsy (×100 magnification) showing irregularities of trabecular bone and 40% malignant plasma cells.

Figure 5 Bone marrow biopsy (×400 magnification) showing irregularities of trabecular bone and 40% malignant plasma cells.

OUTCOME AND FOLLOW-UP

After the start of bortezomib-based treatment, the patient's para-protein levels started to drop rapidly, and after four cycles, the IgG paraprotein was 2.2 g/L and remained consistently low. His haemoglobin was 120 g/L, with normal renal function and calcium levels. This was consistent with very good partial remission (VGPR) of multiple myeloma.

With regard to Paget's disease of bone, the serum alkaline phosphatase values normalised and repeat X-rays showed a mild improvement in the sclerotic bone changes.

Our patient was clinically well with unremarkable full blood counts, biochemical parameters and low IgG paraprotein levels suggestive of ongoing VGPR, during his last clinical review 24 months after diagnosis.

DISCUSSION

In multiple myeloma, a bone marrow microenvironment—comprising of malignant plasma cells and bone marrow stromal cells—plays an important role in the bone pathophysiology. These secrete osteoclast activating factors (OAF), which lead to increase in osteoclastic activity.¹ These OAF are cytokines and chemokines, which include interleukins (IL-6, IL-1 α , IL-1 β , IL-11), macrophage-colony stimulating factor, tumour necrosis factors (TNF- α and TNF- β), macrophage inflammatory protein (MIP-1 α and MIP- β), vascular endothelial growth factor, stromal-cell-derived factor-1 α , etc.² A receptor activator of nuclear factor- κ B (RANK) and osteoprotegerin (OPG) system have been identified to play key roles in promoting osteoclastic hyperactivity in multiple myeloma. RANK ligand binding to RANK on osteoclasts and OPG (a soluble receptor for RANKL) lead to alteration of the physiological balance between bone resorption and deposition.³

Paget's disease of the bone is characterised by excessive osteoclast-mediated bone resorption, which is followed by defective osteoblast-mediated bone repair. The resultant deranged skeletal remodelling leads to bone pain, fractures and deformities. Paget's disease shows characteristic radiological features, namely focal osteolysis with irregularities of the bony trabecular pattern, bone expansion and cortical thickening.⁴

In both, multiple myeloma and Paget's disease of bone, the bone marrow microenvironment plays a critical role causing increased expression of cytokines that enhance osteoclastic activity leading to alteration of the physiological balance between

bone resorption and deposition.⁵ However, pathological and radiological changes are different in these conditions. In multiple myeloma, malignant plasma cells promote increase in osteoclastic activity, leading to osteolysis, with lytic bone lesions and osteoporosis as the characteristic radiological changes. However, Paget's disease is a disorder of bone remodelling characterised by excessive bone resorption due to osteoclastic overactivity followed by increase in bone formation as the result of compensatory osteoblastic activity. This leads to disorganised structure of bones (woven bone), which are thicker but weaker, resulting in increase in susceptibility to fractures.⁴ The radiological changes of multiple myeloma may be masked or altered if associated with Paget's disease of bone.⁶ Bisphosphonates work by inhibition of osteoclastic bone resorption, and hence are effective in the management of bone lesions for multiple myeloma and Paget's disease.

Learning points

- ▶ In multiple myeloma, malignant plasma cells and bone marrow microenvironment promote increase in osteoclastic activity leading to lytic bone lesions and osteoporosis.
- ▶ Paget's disease is a disorder of bone remodelling characterised by excessive bone resorption due to osteoclastic overactivity followed by increase in bone formation as the result of compensatory osteoblastic activity.
- ▶ The pathological and radiological changes of the bones are distinctive in multiple myeloma and Paget's disease of bone.
- ▶ Co-existence of multiple myeloma and Paget's disease of bone is rare.

Coexistence of multiple myeloma and Paget's disease of bone is uncommon.^{7–9} In the few cases reported in the literature, there was variability in the clinical features, and hence the association of myeloma and Paget's disease is deemed as coincidental.¹⁰

Contributors MM is the clinical haematologist who treated the patient and wrote the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Terpos E, Dimopoulos MA. Myeloma bone disease: pathophysiology and management. *Ann Oncol* 2005;16:1223–31.
- 2 Mitsiades CS, Mitsiades NS, Munshi NC, *et al*. The role of the bone microenvironment in the pathophysiology and therapeutic management of multiple myeloma: interplay of growth factors, their receptors and stromal interactions. *Eur J Cancer* 2006;42:1564–73.
- 3 Hsu H, Lacey DL, Dunstan CR, *et al*. Tumor necrosis factor receptor family member RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand. *Proc Natl Acad Sci USA* 1999;96:3540–5.
- 4 Ralston SH. Clinical practice. Paget's disease of bone. *N Engl J Med* 2013;368:644–50.
- 5 Ehrlich LA, Roodman GD. The role of immune cells and inflammatory cytokines in Paget's disease and multiple myeloma. *Immunol Rev* 2005;208:252–66.
- 6 Maldonado A, Abdenour G, Hodes PP. The masquerading effect of Paget's disease. *Rev Interam Radiol* 1976;1:31–4.
- 7 Caravita T, Siniscalchi A, Montinaro E, *et al*. Multiple myeloma and paget disease with abnormal skull lesions and intracranial hypertension. *Mediterr J Hematol Infect Dis* 2012;4:e2012068.
- 8 Neitzschman HR. Radiology case of the month. Paget's disease with onset of increasing bone pain. Paget's disease with coexisting multiple myeloma. *J La State Med Soc* 1997;149:109–10.
- 9 Copelan HL. Coexistence of multiple myeloma and Paget's disease of bone. *Calif Med* 1964;101:118–20.
- 10 Carcassonne Y, Bouvenot G, Gastaut JA, *et al*. The association of a myeloma and Paget's disease (author's transl). *Ann Med Interne (Paris)* 1979;130:177–84.

Copyright 2016 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