ABSTRACT

Introduction: Multiple myeloma is characterized by plasma cell infiltration of the bone marrow and presence of a monoclonal protein in plasma and/or the urine. Multiple myeloma with biclonal gammopathy is rare (1%). Case Report: In this report, we describe a case of biclonal multiple myeloma having two M bands on serum protein electrophoresis. He had elevated serum IgG and IgA levels. IgG and IgA with Kappa and Lambda light chains respectively were detected by immunofixation. It is a very rare immunofixation pattern seen in any gammopathy. The patient presented with vertebral and pelvic bone involvement and neurosensory involvement of both the lower limbs. Patient has been lost for follow up at present. Conclusion: It is a very rare form of multiple myeloma accounting for 1% of all cases. Clinical presentation and response to therapy in such cases appears to be like any other multiple myeloma cases. They should be treated like any other multiple myeloma case.

Keywords: Multiple myeloma, Biclonal gammopathy

INTRODUCTION

Multiple myeloma is a neoplastic clonal disease characterised morphologically by plasma cell infiltration of the medullary space and involvement of extraosseous tissues [1]. Multiple myeloma is an uncommon malignancy accounting for approximately 10% of all haematological malignancies. It is characterised by the production of M paraprotein. Biclonal gammopathies are characterised by simultaneous appearance of different M components [2]. The prevalence is approximately 1% of monoclonal gammopathies [3]. The most common combination is IgG and IgA (53%), followed by IgM and IgG combination (24%) [2,3]. While monoclonal gammopathy characterises a group of B cell disorders which result in the production of a specific and unique M component, biclonal gammopathy is characterised by the simultaneous appearance of two different M components. Although biclonal gammopathy is relatively rare in M proteinemia, the clinical features seem to be similar to monoclonal gammopathy. It is suggested that biclonal gammopathy results from
either one monoclonal cell clone in monoclonal gammopathy or two different monoclonal cell clones. In our patient we report IgG (kappa) and IgA (lambda) type of biclonal gammopathy detected by appearance of two bands in the gamma region on serum protein electrophoresis whose classes were further confirmed by immunofixation.

CASE REPORT

A 65-year-old male patient was referred to the radiotherapy department with numbness in bilateral lower limbs for one month. He was diagnosed as case of low grade multiple myeloma for the past one year when he had initially presented to orthopaedics department with complaints of backache and a midline swelling on the back. He had initially taken thalidomide as treatment for four months but then stopped it because of financial limitations and took herbal medications intermittently on his own till date when he was referred to radiotherapy department with neurosensory involvement of both legs due to radiculopathy.

Laboratory investigations

Complete blood count revealed leucocytosis with cell count of 10,500 cells/cmm, DLC showed polymorphs 53, lymphocytes 36, eosinophils 3, monocytes 9, basophils 1. ESR was 101mm/1st Hr. Routine biochemical parameters were normal. Peripheral smear examination revealed unremarkable WBCs and adequate platelets. Bone marrow biopsy done earlier at the time of diagnosis had revealed a cellular marrow with M:E ratio of 4:1. Erythroid series showed normoblastic maturation. Myelopoiesis appeared normal. Megakaryocytes were adequate. Plasma cells were 18% of all nucleated cells including some binucelate forms. These features pointed towards multiple myeloma.

Radiological examination

X-ray skull had no osseous lesion. X ray pelvis showed lytic lesion in right ilium in supra-acetabular region. In X ray dorsal spine, lytic lesion in the body of D8 vertebra, with normal disc spaces was observed. X ray lumbar spine showed evidence of degenerative changes at L4 and L5 level.

Histopathological findings

Trucut biopsy from paravertebral soft tissue mass was taken. Microscopic examination revealed diffuse tumour made up of malignant plasma cells with uniform eccentric nuclei. Nucleoli were not prominent. Histopathological examination showed sheets of plasma cells (mature, binucleate, immature and typical) along with small trabeculae of bone. Features were compatible with plasma cell dyscrasia suggestive of multiple myeloma.

Serum protein electrophoresis and Immunofixation

Serum electrophoresis on agarose (Sebia) revealed two sharp discrete bands in the gamma globulin region (Figure 1). On being subjected to immunofixation (Sebia), serum revealed IgG- kappa and IgA- lambda gammopathy (Fig. 2).

Serum β2 microglobulin measured by chemiluminescence was 4961ng/ml (Reference range: 1556-2286 ng/ml). Serum IgG level was 23.98 gm/l (Reference range: 6.53-13.51 gm/l), IgA level was 3.71 gm/l (Reference range: 0.86-3.20 gm/l). IgM level was < 0.255 gm/l (Ref. range: 0.521-1.79 gm/l). All these parameters were assayed by nephelometry. Urine Bence –Jones protein was negative.

The patient was started on a combination of vincristine, Adriamycin and dexamethasone. However, he was lost to follow up after two cycles of therapy.
they could also represent truly independent myeloma clones, with ongoing CSR detectable in subclones derived from the same myeloma progenitor, alternatively, lack of allelic exclusion within the same myeloma cell [4].

In contrast to cases showing 2 different IgH subtypes, cases characterized by 2 different IgL peaks can be considered as truly biclonal, because no molecular mechanism for changing light chain expression within the same myeloma clone has been described so far. Biclonal myeloma cases expressing both kappa and lambda are not exceptional, although its frequency has been estimated to be only around 1% to 2%. This low frequency has led to difficulty in interpreting the clinical characteristics of these patients; some authors having found no difference in the clinical characteristics and prognosis, while others suggest a poor response to therapy. Two cases expressing cytoplasmic Igk and Igλ but secreting only IgG have been described, suggesting that it is possible to produce both light chain isotypes. This observation can be explained by the fact that the Igk light chain was unable to assemble with the Ig heavy chain and illustrates how a functional IgH- IgL assembly may be one of the mechanisms leading to allelic exclusion and mono specificity [5].

Occurrence of isotype switch and appearance of abnormal protein bands have, however been reported in myeloma patients after high dose therapy. This appears to be related to recovery of normal immunoglobulin production rather than alteration in disease biology. This change is also associated with increased survival [6].

Mono- and biclonal gammopathy were also reported in two immunocompetent individuals caused by acute infection with Bartonella henselae resulting in cat-scratch disease (CSD). Bartonella henselae has been shown to induce host cell production of the vascular endothelial growth factor (VEGF) in vitro, resulting in proliferation of endothelial cells and thus representing a potential novel bacteria-dependent mechanism of tumor growth. Furthermore, it has been demonstrated that bacterial eradication by antibiotic treatment results in complete regression of the angiomatosus tumors. Bartonella henselae is also capable of inducing the production of proinflammatory cytokines such as tumor necrosis factor alpha, interleukin (IL) 1β, IL-2, IL-6, IL-8, and IL-10. While IL-10 is an important differentiation factor for plasma cell formation and immunoglobulin secretion, IL-6 constitutes a major growth factor for myeloma and plasma cells, induces immunoglobulin production, and is an active factor in B-cell differentiation. The eradication of CSD following antibiotic treatment led to the termination of gammopathy [7].

CONCLUSION

Biclonal multiple myeloma accounts for only 1% of chemotherapy due to poor drug compliance by the fast degenerating general physical condition.
all myelomas. This was the first case reported in our institution where so far 600 electrophoresis have been done. Clinical presentation and response to therapy is like other cases of multiple myeloma.

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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES