

A Rare Case of Multiple Myeloma with Biclonal Gammopathy

ABHIK BANERJEE¹, KSHAMA PIMPALGAONKAR², ALAP LUKIYAS CHRISTY³

ABSTRACT

Multiple myeloma is a debilitating malignancy arising from plasma cells. These malignant plasma cells called myeloma cells proliferate and infiltrate the bone marrow. The disease is characterized by the presence of a monoclonal protein in plasma and/or the urine.

In this report, we present a case of biclonal multiple myeloma which showed two M bands on serum protein electrophoresis. The patient had elevated serum IgA and IgG levels. To reveal the nature of M bands or clonality, serum Immunofixation study was performed which revealed IgA with Lambda and IgG with Kappa light chains. Such pattern is very rare if we consider the various immunofixation patterns observed in different gammopathies.

Keywords: Immunofixation electrophoresis, Neoplastic clonal disease, Serum protein electrophoresis

CASE REPORT

A 64-year-old female patient presented with anaemia, fatigue and lower back pain since one month. Routine Laboratory investigations were done following a thorough clinical assessment. Haemoglobin was 10.8 g/dL, ESR was 101mm/1st hr. Serum albumin was 3.37g/dL (Reference range: 3.2-4.6 g/dl), whereas, serum calcium and creatinine were within normal limits. X-ray dorsal spine showed a lytic lesion in the body of D8 vertebra. X-ray lumbar spine showed evidence of degenerative changes at L4 and L5 level. The bone marrow aspiration showed 21% plasma cells including some binucleate forms. All these features were compatible with plasma cell dyscrasia suggestive of multiple myeloma.

Serum protein electrophoresis and immunofixation electrophoresis were done. Serum protein electrophoresis on agarose gel revealed two sharp discrete bands in the gamma globulin region [Table/Fig-1]. Densitometric analysis of monoclonal components revealed M spike 1= 1.14 g/dl and M spike 2= 0.79 g/dl. On Immunofixation Electrophoresis (Sebia), serum revealed IgA lambda and IgG kappa gammopathy [Table/Fig-2].

Serum β_2 microglobulin measured by chemiluminescence was 8251.3ng/ml (Reference range: 609-2366ng/ml). Serum Immunoglobulin and free light chains levels were measured by nephelometry. IgG level was 18.20gm/L (Reference range: 6.5-16.4gm/L), IgM level was 0.92gm/L (Reference range: 0.39-3.38gm/L) whereas IgA level was 9.95 gm/L (Reference range: 0.90-

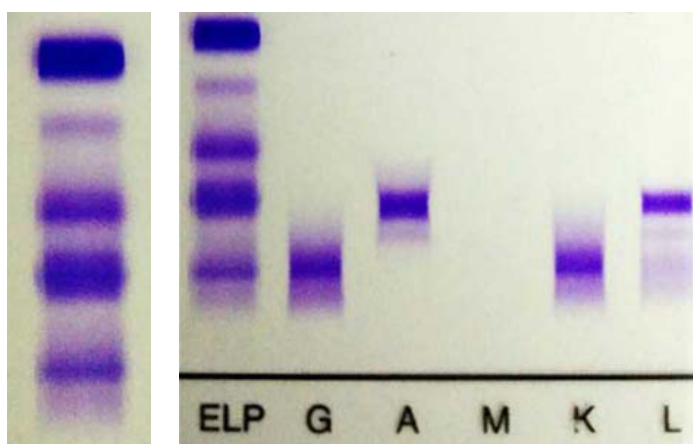
5.32 gm/L). The free kappa chain level was 55.60mg/L (Reference range: 3.30-19.40mg/L) and the free lambda chains level was 63.70 mg/L (Reference range: 5.71-26.30mg/L) with a free kappa/lambda light chain ratio of 0.87 (Reference range: 0.26-1.65). Urine Bence-Jones protein was positive with heat coagulation test.

Thus a final diagnosis of Biclonal multiple myeloma was made. Unfortunately, patient could not be tracked to know regarding her treatment and subsequent follow-up.

DISCUSSION

Multiple myeloma is a neoplastic clonal disease characterised morphologically by plasma cell infiltration of the medullary space and involvement of extraosseous tissues in a multi-focal fashion [1]. Monoclonal gammopathy is a group of B cell disorders which is known for production of a specific and unique M component. However, biclonal gammopathies are defined by simultaneous appearance of different M components, two distinct or different monoclonal proteins [2]. Biclonal gammopathy is relatively rare in M proteinemia and accounts for approximately 1-5% of all myelomas [3]. The most commonly encountered combination is IgG and IgA (53%), followed by IgM and IgG (24%) as per literature [2,3]. According to different literature, either one monoclonal cell clone in a monoclonal gammopathy may give rise to biclonal gammopathy or else, the same may arise from two different monoclonal cell clones. Hence, biclonal gammopathy may arise either due to independent proliferation of two separate clones of plasma cells where each clone gives rise to an unrelated monoclonal immunoglobulin or this may result from a single clone of plasma cells producing two different monoclonal proteins [4].

Biclonal gammopathies are more symptomatic than its monoclonal counterpart. However, no significant difference has been reported with monoclonal gammopathy in respect to clinical features, presentations or response to therapy. About 40% of the patients with biclonal gammopathies present with suggestive clinical signs and symptoms. A significant percentage of the symptomatic patients have underlying lymphoproliferative disease most commonly waldenstrom macroglobulinaemia. Nafia Al-Riyami et al., had recently described a rare occurrence of biclonal gammopathy in a patient with Chronic Lymphocytic Leukemia (CLL) [5]. Rest of the symptomatic patients either have multiple myeloma or have some underlying non-haematological disorder. Nae Yu Kim et al., described a rare case of biclonal gammopathy accompanied by prostate



[Table/Fig-1]: Serum protein electrophoresis. [Table/Fig-2]: Serum immunofixation electrophoresis.

cancer [4]. In our study, patient presented with anaemia, fatigue and low back pain. However, no underlying disorders were found other than multiple myeloma.

Ideal biclonal cases show two different Ig Light chain rather than two different Ig Heavy chain subtypes because most commonly a single myeloma clone can express a single type of light chain only. Hence, such true biclonal myeloma cases expressing both kappa and lambda are extremely rare. Between 1966 and 1979, a study was conducted on 57 patients detected with biclonal gammopathy. Out of these 57 patients, 53% patients had IgG, IgA components whereas 26% had IgG, IgM components. Of the 115 light chains, 70% were kappa and 63% were both kappa and lambda [3]. A large study comprising of 1027 plasma cell myeloma patients showed only 2% cases of biclonal gammopathy on serum protein electrophoresis [6]. However, there was no mention regarding the combinations of biclonal M-proteins detected in the study. There are few other reports where combinations of IgG/IgM, IgA/IgG, and kappa/lambda light chain biclonal gammopathies have been described [7–10]. Study of Nafia Al-Riyami et al., described a rare case of biclonal gammopathy with CLL which showed biclonal immunoglobulin A (IgA) kappa and IgA lambda in serum immunofixation electrophoresis [5]. Mala Mahto et al., described a similar case of IgG Kappa and IgA Lambda type biclonal gammopathy detected by appearance of two bands in the gamma region on serum protein electrophoresis [11]. Bakta and Sutarka reported a rare case of biclonal gammopathy with IgA and IgM in a 48-year-old male patient [12].

CONCLUSION

Biclonal multiple myeloma accounts for only 1-5% of all myelomas. In the case presented above, we have reported IgA Lambda and

IgG Kappa type of biclonal gammopathy detected by appearance of two bands in the gamma region on serum protein electrophoresis. The classes IgA Lambda and IgG Kappa were further confirmed by immunofixation.

REFERENCES

- [1] Osterborg A, Hansson LO, Mellstedt H. Immunoglobulins in multiple myeloma. In: Garhton G, Durie B(eds). Multiple myeloma. 1st ed. London: Oxford University Press 1996;36-50.
- [2] Osterborg A, Mellstedt H. Monoclonal and biclonal immunoglobulin producing disorders. *Eur J.* 1989;43(51):11-18.
- [3] Kyle RA, Robinson R, Katzman J. The clinical aspects of biclonal gammopathies. *Am J Med.* 1981;71:999-1006.
- [4] Kim NY, Gong SJ, Kim J, Youn SM, Lee JA. Multiple myeloma with biclonal gammopathy accompanied by prostate cancer. *Korean J Lab Med.* 2011;31(4):285-89.
- [5] Al-Riyami N, Al-Farsi K, Al-Amrani K, Al-Harrasi S, Al-Huneini M, Al-Kindi S. Biclonal gammopathy in chronic lymphocytic leukemia: case report and review of the literature. *Oman Medical Journal.* 2015;30(3):216-18.
- [6] Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clinic Proceedings.* 2003;78(1):21-33.
- [7] Juge-Morineau N, Heirman C, Bakkus M, Van Camp B, Malfait R, Harousseau JL, et al., Immunoglobulins D and M multiple myeloma variants are heavily mutated. *Clinical Cancer Research.* 1997;3(12):2501-06.
- [8] Huppmann AR, Liu ML, Nava VE. Concurrent diagnoses of Hodgkin lymphoma and biclonal myeloma in the bone marrow. *Annals of Diagnostic Pathology.* 2010;14(4):268-72.
- [9] Franck P, Petitpain N, Guerci AP, Denisart S, Jacob C, Gueant JL. Myeloma with two monoclonal IgG and IgD in serum: a case report. *Acta Haematologica.* 1994;92(3):144-47.
- [10] Tharp AM, Woodruff RD, Shihabi ZK. IgD-Kappa myeloma: an unusual case. *Annals of Clinical and Laboratory Science.* 2003;33(1):97-100.
- [11] Mahto M, Balakrishnan P, Koner BC Lali P, Mishra. TK, Saxena A. *Rare case of biclonal gammopathy.* IJCRI. 2011;2(2):11-14.
- [12] Bakta IM, Sutarka IN. Biclonal gammopathy in multiple myeloma: a case report. *Gan To Kagaku Ryoh.* 2000;27(2):544-88.

PARTICULARS OF CONTRIBUTORS:

1. Pathologist, Department of Clinical Chemistry and Immunoassays, SRL Central Clinical Reference Laboratory, Mumbai, Maharashtra, India.
2. Biochemist, Department of Clinical Chemistry and Immunoassays, SRL Central Clinical Reference Laboratory, Mumbai, Maharashtra, India.
3. Biochemist, Department of Clinical Chemistry and Immunoassays, SRL Central Clinical Reference Laboratory, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Kshama Pimpalgaonkar,
Biochemist, Department of Clinical Chemistry and Immunoassays, SRL Central Clinical Reference Laboratory,
Mumbai-400062, Maharashtra, India.
E-mail: kshamapp@rediffmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jun 30, 2016**

Date of Peer Review: **Jul 26, 2016**

Date of Acceptance: **Sep 22, 2016**

Date of Publishing: **Dec 01, 2016**