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Biclonal Gammopathy: A case report

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Abstract: *Biclonal gammopathies are characterized by simultaneous production of two different monoclonal proteins. They are rare disease entities and represent only 1-5% of all gammopathies. The composition of the monoclonal proteins can vary and combinations of IgG-IgA, IgG-IgM, IgA-IgA with kappa and lambda chains have been reported in literature. Here we report one such atypical case of multiple myeloma with biclonal gammopathy corresponding to IgG-IgA/Lambda.*

Keywords: *Multiple Myeloma, Biclonal Gammopathy, Serum Protein Electrophoresis, Serum Immunofixation electrophoresis.*

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I. Introduction:

Multiple myeloma is the second most common hematological malignancy and accounts for 1% of all cancers[1].It is characterized by the abnormal clonal proliferation of malignant plasma cells resulting in the production of monoclonal proteins of a single isotype. The monoclonal (M) proteins can be the entire immunoglobulin, light chain only, or, rarely, heavy chain only. This M-protein can be detected by Serum or Urine Protein electrophoresis(SPEP and UPEP respectively), where it appears as a single distinct band on agarose gel and a discrete peak on densitometric tracing. Further confirmation and characterization of the M-protein band regarding its heavy and light chain composition is done by Immunofixation electrophoresis (IFE) which has higher sensitivity than protein electrophoresis [2].Very rarely, SPEP and serum IFE might show the concurrent presence of two distinct M-bands. This condition is known as biclonal gammopathy and is seen in only 1-5% of all cases. In this report, we describe a case of biclonal gammopathy with IgG-IgA/Lambda.

II. Case Report:

A 56year old male presented with fatigue and persistent back pain for past 6 months. Physical examination revealed pallor and localized tenderness and swelling on lower back. The patient was found to be anemic with a hemoglobin level of 7.7 g/dL. Serum creatinine was raised to 2.3 mg/dl. There was hyperproteinemia (Serum total protein = 10.9 g/dL) and hypoalbuminemia (Serum albumin : 2.73 g/dL) with a reversal of albumin/globulin ratio to 0.33. Routine urine examination revealed moderate proteinuria(++).

A lytic lesion was found in the body of D10 vertebra on X-ray of dorsal spine. X-ray lumbar spine showed evidence of degenerative changes at L4 and L5 level. The bone marrow aspiration detected 21% plasma cells including some binucleate forms.

The serum protein electrophoresis performed on Sebia HYDRASYS 2 SCAN FOCUSING system revealed two distinct bands (M bands of 5.01g/dL and 0.21g/dL) in gamma globulin region.(*Figure 1*)

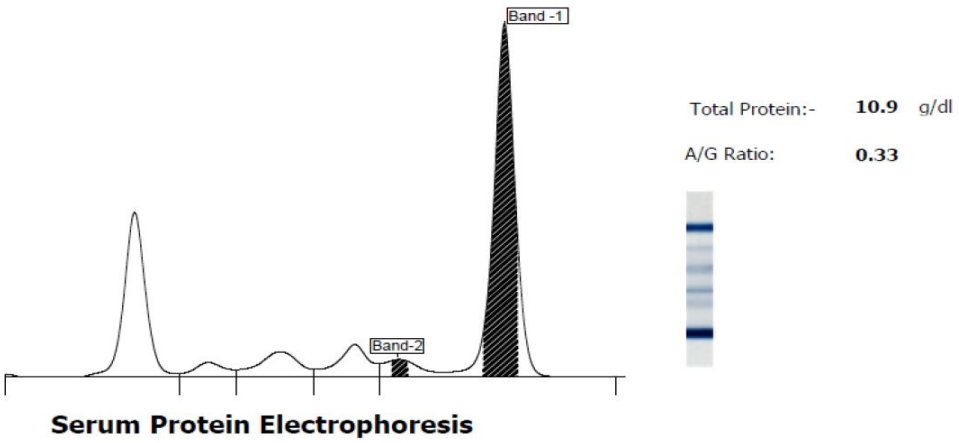

Figure 1: Serum protein electrophoresis showing two monoclonal bands in gamma region.

SIFE was also performed in the Sebia HYDRASYS 2 SCAN FOCUSING system. The proteins, separated by electrophoresis on alkaline buffered agarose gels, were incubated with individual antisera against IgG, IgA, IgM heavy chains and kappa, lambda light chains. The two bands detected by SPEP were characterised as IgG Lambda and IgA Lambda respectively.(*Figure 2*)

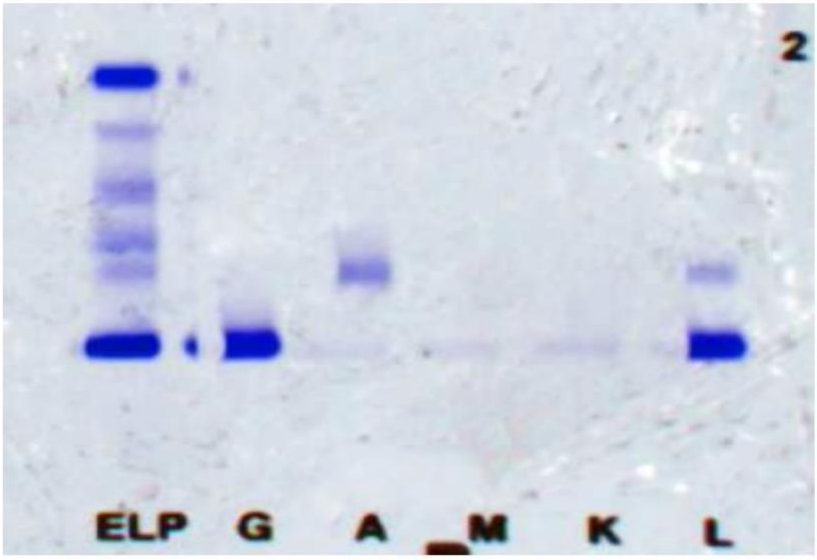

Figure 2: Serum Immunofixation electrophoresis depicting IgG-Lambda and IgA-Lambda.

Further work-up revealed a high β2 microglobulin level of 5460 ng/mL (Reference range: 700- 1800 ng/mL). Both serum IgG and serum IgA were raised, their levels being 50 g/L(Reference range: 7- 16 g/L) and 5.24 g/L (Reference range: 0.7-4.0 g/L), respectively. Serum IgM was low at <0.17g/L(Reference range: 0.4-2.3 g/L). All of these were measured nephelometrically on Siemens Dade Behring II analyser.

Serum Free light chain levels were measured using Freelite assay from The Binding site on the Optilite analyser platform.Free Kappa: Lambda Ratio was found to be 0.09(Reference range:0.26-1.65) while free Kappa light chain was 10.8 mg/L(Reference range: 3.3–19.4 mg/L) and free Lambda light chain was 120 mg/L(Reference range:5.71–26.3 mg/L).

Based on these findings, a diagnosis of Multiple myeloma with biclonal gammopathy was made.

III. Discussion:

Multiple myeloma is a hematological malignancy caused by clonal proliferation of plasma cells. The tumor, its products, and the host response to it can manifest in multiple organ dysfunctions and symptoms like bone pain/fracture, renal failure, susceptibility to infection, anemia, hypercalcemia, and occasionally clotting abnormalities, neurologic symptoms, and manifestations of hyperviscosity. It is associated with expansion of a single clone of immunoglobulin (Ig) secreting plasma cells that results in the secretion of a unique homogeneous monoclonal protein (M component) [3].

However, in a rare 1-5% of cases of multiple myeloma, instead of a single monoclonal band, biclonal gammopathy, defined by simultaneous appearance of two distinct monoclonal protein, is found [4]. This can result from either a proliferation of two clones of plasma cells with each producing an unrelated monoclonal spike or from the production of two monoclonal spikes by a single clone of plasma cells [5].

Various composition of these monoclonal proteins have been described in previous literature. Ghammad et al reported that the most frequent isotype was IgG-IgM with a slight predominance of the Kappa light chain whereas Garcia et al found that the most prevalent composition corresponded to IgG-IgG [6,7].On the other hand, two different studies proclaimed the most common combination to be IgG-IgA [8,9].

Despite the variable electrophoretic picture, no difference in clinical outcome has yet been reported between biclonal and monoclonal gammopathies [4].

IV. Conclusion:

Biclonal gammopathies are rare entities occurring in 1-5% of all gammopathies. Both monoclonal and biclonal gammopathies have been reported to have similar clinical presentations and disease outcome. However, recognition and measurement of both clonal proteins during follow up helps in assessing treatment response and deciding furthercourse of action.

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