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Case Report

Biclonal Gammopathy of IgA Kappa variants - A Case Report

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Abstract

Multiple myeloma is a clonal malignant neoplasm of plasma cells and is characterized by the secretion of monoclonal protein in plasma. Here, we report a case of biclonal multiple myeloma having two spikes on serum protein electrophoresis, one being in Beta-2 region and the other in gamma region. Further on immunofixation, both peaks were found to be of IgA-kappa variant. Biclonal gammopathy is a rare case, which accounts for only 1% of all myelomas but biclonal gammopathy of IgA kappa variant has not been described in the literature so far.
Keywords: Monoclonal gammopathy, Immunofixation, Serum protein electrophoresis, Biclonal gammopathy.

1. Introduction

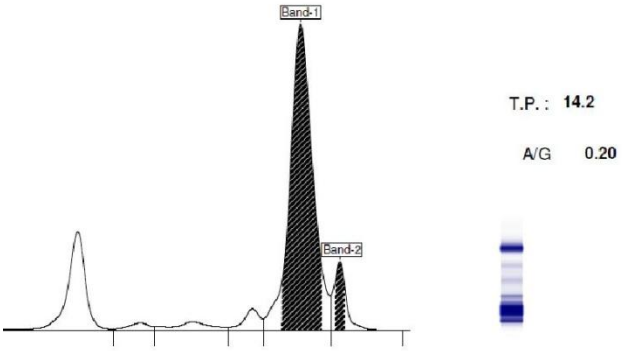
Multiple myeloma is a plasma cell neoplasm characterized by involvement of skeleton at multiple sites. Although bony disease dominates, it can also spread to lymph nodes and extra-nodal sites such as skin. The proliferation and survival of myeloma cells are dependent on several cytokines, most notably IL-6. High IL-6 levels are associated with poor prognosis. Factors produced by neoplastic plasma cells also mediate bone destruction, the major pathologic feature of multiple myeloma.[1] Multiple myeloma presents most often as multifocal destructive bone tumors composed of plasma cells (plasmacytomas) throughout the skeletal system. Bones in the axial skeleton are affected most commonly. The peak age of incidence of multiple myeloma is between 50 and 60 years. The dominant presenting complaints are weakness, fatigue and weight loss – all non specific symptoms. Anemia caused by marrow infiltration is often present and can be exacerbated by autoimmune hemolysis, which is seen in about 10% of patients.

The monoclonal immunoglobulin identified in the blood is referred as 'M' component, in reference to myeloma. Unlike normal plasma cells, in which production and coupling of heavy(H) and light(L) chains are tightly balanced, neoplastic plasma cells often synthesize excess 'L' or 'H' chains along with complete immunoglobulins, the detection of which is done by serum or urine protein electrophoresis and immunofixation.[1] Approximately, 1-2% of patients with multiple myeloma have biclonal gammopathy.[2]

2. Case history

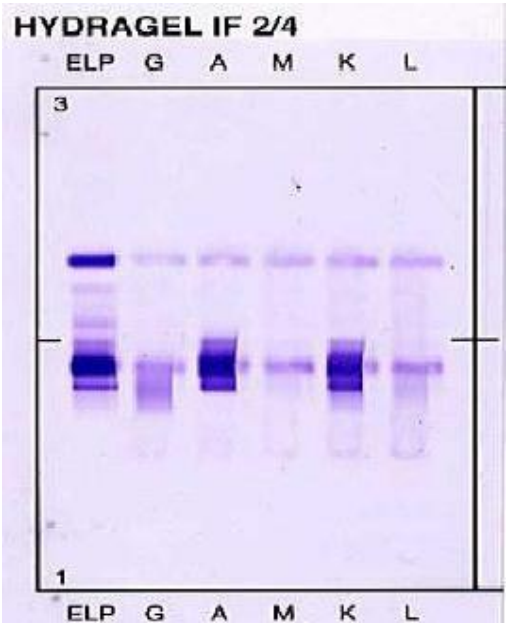
A 50-year-old male, farmer by occupation, presented with the complaints of low backache, weight loss (10 kg) since three months, associated with decreased appetite. On examination, tenderness over the spine is noted. Complete blood picture revealed Hb concentration 7.5 g/dL, RBC count – 2.53million/cumm, MCV – 88fl, MCH - 30pg, MCHC - 34 g/dL, WBC - 6,200/cumm, Platelets - 2.42 lac/cumm. Peripheral smear shows anisocytosis, normocytic hypochromic with prominent rouleaux formation. Serum creatinine level is 2.8mg/dL. MRI spine shows patchy signal intensity involving D1/D2/D4/D9 which is suggestive of? Metastasis /? Tuberculosis /? Myeloma. Bone marrow cytology smears revealed prominence of plasma cells accounting 60-65%, few binucleate and multinucleate forms along with plasma blasts constituting about 4-5% in focal areas. These features are suggestive of plasma cell dyscrasia. These findings are correlated with bone marrow biopsy. Serum protein electrophoresis showed two bands. Band-1 (8.62 gm%) is seen in Beta 2 region and Band-2 (0.74 gm%) is seen in gamma region.(figure-1).

Figure 1: Serum protein electrophoresis shows Band-1 in beta2 region and Band-2 in gamma region



On subjecting to immunoelectrophoresis, it is found that both bands are of IgA –kappa (figure-2). Nephelometric measurement of serum immunoglobulins unveiled IgA level of 9910 mg/dL (Ref Range: 70 – 400 mg/dL), IgG level of 552 mg/dL (Ref Range : 700-1600 mg/dL), IgM level of 43 mg/dL (Ref Range : 40 – 230 mg/dL), Free kappa light chain level of 680 mg/L (Ref Range : 3.3 -19.4 mg/L), Free lambda light chain level of 11.6 (Ref Range : 5.71-26.3 mg/L) and free kappa/free Lambda ratio is 58.62 (0.37 – 3.1).

Figure 2: Immunoelectrophoresis with two bands of IgA-Kappa



3. Discussion

Multiple myeloma is a malignant disease of plasma cells that manifests as disease in the bone marrow, monoclonal protein in the blood and/or urine, and evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder.[3] Multiple myeloma is the second most common form of hematological malignancy after Non-Hodgkin lymphoma.[2]

Monoclonal gammopathy is a group of B-Cell disorders which result in production of a specific and unique monoclonal immunoglobulin (M-Component). Biclonal gammopathy is characterized by the simultaneous appearance of two different M-components. The presence of two monoclonal proteins may be because of the proliferation of two clones of plasma cells, each producing an unrelated monoclonal immunoglobulin, or it may result from the production of two monoclonal proteins by a single clone of plasma cells.[4,5] The most common combination is IgG and IgA (33%) and followed by IgM and IgG combination (24%).[6] Kyle *et al* reported that out of the 57 patients, 30 (53%) had IgG and IgA components, 15 (26%) had IgG and IgM, six had two IgG components, three had IgA and IgM, one (2%) had IgA proteins, one had IgA and IgE and 1 had triclonal gammopathy. Although the clinical features of biclonal gammopathy and its response to therapy are similar to those of monoclonal gammopathy, this subject is of importance because of the lack of clinical data in the literature.[4] Bakta and Sutarka reported a rare case of biclonal gammopathy with IgA and IgM . In their case, a 48 year old male was diagnosed with biclonal gammopathy of IgA and IgM components and his clinical response was good after two series of conventional chemotherapy.[7] Riddell *et al* reported that 2.5% of 1,135 patients with monoclonal gammopathy had biclonal gammopathy. They postulated that in some patients complete class switching in a single plasma cell clone resulted in the production of two M proteins, but in others the M proteins arose from two separate plasma cell clones.[8]

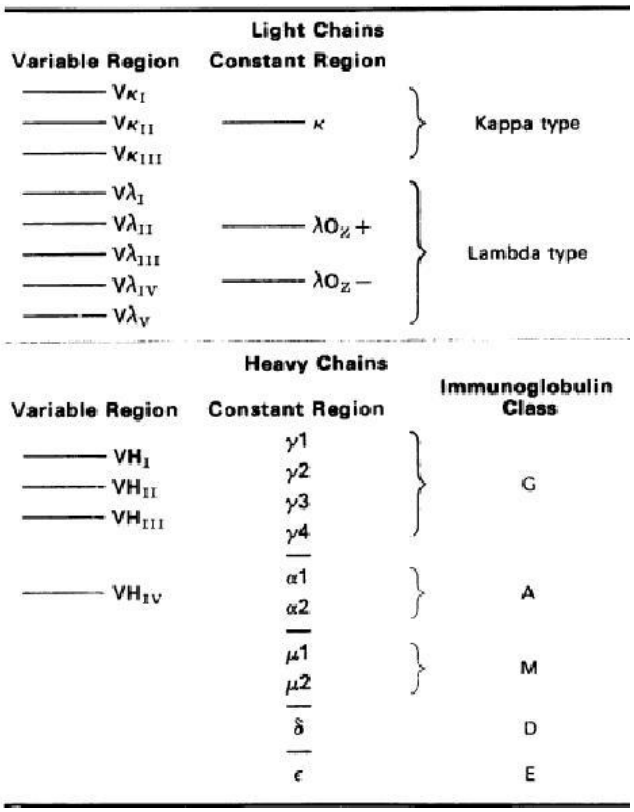
The diagnosis of myeloma requires 10% or more clonal plasma cells on bone marrow examination or a biopsy proven plasmacytoma, evidence of end organ damage (hypercalcemia, renal insufficiency, anemia or bone lesions) that felt to be underlying plasma cell disorders and presence of serum and/or urinary monoclonal protein (except in patients with true non secretory multiple myeloma).[3]

IgA appears selectively in seromucous secretion, tears, nasal secretions, saliva, and gastrointestinal secretions. In these secretions it is present as a dimer with an additional secretory component synthesized by the local secretory epithelium. IgA is also present in the serum. The two subclasses of IgA are differentiated immunochemically and called IgA1 and IgA2. Structurally these subclasses are quite different; IgA2 lacks the interchain disulphide bonds linking the heavy and light chains which are characteristic of all other immunoglobulins. Because of this, the subclasses can be differentiated by electrophoresis by suitable conditions which dissociate the heavy and light chains of IgA2. Normally human serum consists of approximately 90% IgA1 molecules.[9] Donald R. Hoffman reported one case with 17 g/dL of paraprotein. Electrophoretogram of that patient showed a huge peak in the beta region and with a small peak in the gamma. Both peaks were typed as IgA-kappa. Both polymers and charge variants are seen with IgA variants.[10] Muhammad Younas *et al* reported a case of biclonal gammopathy of IgA-lambda in a 53 year old male.[11] Sarma *et al* (1971) have suggested four possible models of the immunoglobulin molecule based on four ways of joining the Fab regions to the Fc.[12]

A study of amino-acid sequences reveals that although there is one kappa chain C type, the V region sequence can be divided into at least three main subgroups (Milstein, 1967), each of which probably originates from a separate gene or group. Present sequence data increases the number and when more data is available, this number may well rise to 20 or more (figure 3).[9] Figure 3 shows possible combinations of light and heavy chains in variable and constant region.[9]

Clinical presentation and response to the therapy is similar to the other cases of multiple myelomas. This is the rare case of biclonal gammopathy with IgA-kappa variant. This case is important because of its rare incidence and the lack of clinical data in the literature.

Figure 3: Shows possible combinations of light and heavy chains in variable and constant region



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