Multiple Myeloma: A Case of Atypical Presentation on Protein Electrophoresis

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Abstract Multiple myeloma is a group of B-cell disorders resulting in the secretion of a specific and unique monoclonal immunoglobulin (M-protein). Protein electrophoresis is advised whenever multiple myeloma is suspected. The monoclonal protein migrates as a single entity in the electric field and is detected by the non-specific protein stain as a more intensely stained band superimposed on the usual protein pattern. The M-protein usually migrates in the gamma or beta region of the normal protein pattern; very rarely it may appear in the α_2 or even in α_1 region. Here we have given an atypical case presentation where the patient with multiple myeloma presented with two M-spike one each in α_2 and β -globulin region on agarose gel protein electrophoresis with hypoglobulinemia but with reversed A:G ratio.

Keywords Multiple myeloma · M-protein · Agarose gel protein electrophoresis · Immunofixation electrophoresis · Biclinal gammopathy

Introduction

Multiple myeloma is a malignant disorder characterized by proliferation of single clone of plasma cells derived from B-cells in the bone marrow. The median age at diagnosis of multiple myeloma is 70 years, and the occurrence increases with age [1].

The M-protein is a tumor marker specific for monoclonal gammopathies because it reflects the clonal proliferation of immunoglobulin. The best method for detecting M-protein (monoclonal Protein) is high resolution agarose gel electrophoresis. M-protein is generally observed as a localized band which is frequently seen on γ or β globulin region, it may also be seen on α_2 globulin region but this situation is very rare [2, 3]. Immunofixation electrophoresis is used to identify the clonality (type) of M-proteins observed on agarose gel electrophoresis.

Case Report

An 80 years old male was referred to Apollo Hospital, Bhubaneswar in May 2011 with symptoms of bone pain and fatigue. On physical examination there was severe anemia. Laboratory investigations including X-ray were carried out. On investigation hemoglobin 5.3 gm%, hematocrit 16.4%, RBC 2.4 million/cu.mm, WBC 3100/cu.mm, platelets 2,50,000/cu.mm, ESR 123 mm/1st hour with rouleaux formation was observed on the smear. Serum protein was 10.0 g/dl and albumin 2.77 g/dl with A:G ratio 0.38. Serum beta 2 microglobulin was 18,599 μ g/(normal 670–1,310 μ g/l) and serum calcium was 8.4 mg/dl. Serum Urea and creatinine was 19 and 0.8 mg/dl respectively. GFR by MDRD calculator was 109 ml/min/1.73 m².

Agarose gel protein electrophoresis was done on Helena Bioscience, Europe using SAS-MX SP-10 SB kit. On Agarose gel protein electrophoresis total protein: 10.0 g/dl, albumin: 2.77 g/dl, alpha-1: 0.15 g/dl, alpha-2: 3.34 g/dl, beta: 3.47 g/dl, gamma: 0.28 g/dl (Fig. 1). There were two sharp peaks corresponding to α_2 globulin and β globulin region. The above findings were confirmed on immunofixation electrophoresis (IFE) Gel no. 64597 using

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Scan Index: 1

Scan Image

Scan Trace

Fig. 1 Agarose gel protein electrophoresis shows hypoalbuminemia with gross increase in alpha-2 and beta globulins. The two spikes seen in the scan corresponds to alpha-2 and beta globulins regions

SAX-MX IFE-1 kit. The results were analysed using Helena software PT version 3.0. The two peaks were seen as two separate IgA- κ bands (Fig. 2).

Bone marrow aspiration showed normocellular comparing patient's age. M:E ratio = 1:2. The plasma cells were increased in number (14%). Many of the plasma cells were having large nucleus with nucleoli (immature plasma cells). Binucleated plasma cells were seen.

In the bidirectional cranium X-ray graphy, five lytic lesions, the biggest one being 5 mm in diameter were detected. In dorsal and lumbar vertebra direct X-ray graphs, collapse fractures were seen on L2–L3 and L4–L5. The patient was diagnosed as Stage-3 according to The International Staging System.

Test Results

Index	Band	Rel.Area	Conc. (gm/dl)	Range (gm/dl)
1	Albumin	27.70%	2.77 L	3.50 ... 5.00
2	Alpha 1	1.47%	0.15	0.11 ... 0.40
3	Alpha 2	33.39%	3.34 H	0.43 ... 1.03
4	Beta	34.65%	3.47 H	0.53 ... 1.40
5	Gamma	2.79%	0.28 L	0.71 ... 1.54
Total			10.00	
Ratio		0.38		

Discussion

Multiple myeloma is an uncommon malignancy accounting for approximately 10% of all haematological malignancies. Serum electrophoresis can be routinely used for the diagnosis of multiple myeloma and is well correlated with biochemical, radiological and pathological findings. The conventional technique serum electrophoresis is still widely used for the demonstration of M-Protein in the myeloma patient and it remains a gold standard. Multiple myeloma arises from plasma cell dyscrasia. These malignant plasma cells synthesize monoclonal antibody and release it to the circulation. As a result high concentration of monoclonal antibodies is present in bone marrow as well as in serum [4].

Fig. 2 Immunofixation electrophoresis reveals two dense bands in SP region. The two bands immunologically correspond to two IgA- κ bands

The circulating M-protein may consist of an intact immunoglobulin, the light chain only, or (rarely) the heavy chain only. The heavy chain is from one of the five immunoglobulin classes G, A, M, D or E, while the light chain is either κ (kappa) or λ (lambda) in type. It occurs as intense, narrow band most often found with the gamma-globulins, then in a diminishing frequency between γ and the β -globulin and rarely in the β and α_2 regions. Generally IgA, IgG and IgM proteins are not observed on the α_2 fractions. These proteins compose β -1, β -2, and γ fractions [5]. However, in IgG multiple myeloma immunoglobulins may rarely migrate from γ fraction to α_2 fraction [6]. M-protein that is seen on the α_2 band is just reported in a few numbers of IgA multiple myeloma cases. Very rarely, biclonal gammopathies (accounts for 1% of all monoclonal gammopathies) or triclonal gammopathy can be observed in multiple myeloma.

In our patient most of the biochemical results were suggestive of the pattern found in multiple myeloma. The patient was having normal serum calcium level at time of diagnosis. Hypercalcemia is found initially in 22–30% patient with multiple myeloma [7, 8], the exact cause of which is unknown. The patient was not in renal failure as evident from GFR and renal function test. Renal failure, defined as a serum creatinine ≥ 2 mg/dl at the time of diagnosis, is seen in 21% of patients [9]. In the patient, the M band on the α_2 region and β region was shown to be bound to IgA. A biclonal gammopathy is suspected when there are two proteins with different mobilities comprising two different monoclonal heavy chains with their respective monoclonal light chains [10]. A biclonal gammopathy may also consist of two heavy chains of the same class and monoclonal light chains of the same type. In this setting, one must be careful to exclude monomers and aggregates as well as monomers and polymers of an M-protein. This is the first case of biclonal gammopathy reported in our

Hospital where more than 200 electrophoresis have been done in the last 1 year. Clinical presentation and response to therapy is like other cases of multiple myeloma.

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