

Research Article

CASE STUDY: RARE CASE BICLONAL GAMMOPATHY ON ELECTROPHORETOGRAM

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ABSTRACT

Multiple myeloma is a cancer of plasma cells, normally responsible for producing antibodies. It is a group of B-cell disorders resulting in the secretion of a specific and unique monoclonal immunoglobulin (M-protein). Protein electrophoresis serves as a gold standard for the diagnosis of multiple myeloma. The protein fraction migrates under the influence of electric field according to the mass of individual fraction. The M-protein usually migrates in the gamma or beta region of the normal protein pattern; very rarely it may appear in the beta region. Here we have given an atypical case presentation where the patient with multiple myeloma presented with two M-spikes one each in beta and gamma - globulin region on agarose gel protein electrophoresis with hypoglobulinemia but with reversed A:G ratio.

Keywords: *Multiple Myeloma, M-Protein, Agarose Gel Protein Electrophoresis, Biclonal Gammopathy*

INTRODUCTION

Multiple myeloma, also known as plasma cell myeloma is a cancer of plasma cells, normally responsible for producing antibodies. In multiple myeloma, collections of abnormal plasma cells accumulate in the bone marrow, where they interfere with the production of normal blood cells. Multiple myeloma is a blood disorder related to lymphoma and leukemia, because it usually arises in the bone marrow. Most cases of myeloma also feature the production of a paraprotein—an abnormal antibody which can cause kidney problems. As multiple myeloma progresses, plasma cells begin to spill out of the bone marrow and deposit elsewhere in the body, causing further organ damage bone lesions and hypercalcemia are also often encountered.

Myeloma is diagnosed with blood tests (serum protein electrophoresis, serum free kappa/lambda light chain assay), bone marrow examination, urine protein electrophoresis, and X-rays of commonly involved bones. 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 gamma or beta globulin region, it may also be seen on alpha-2 globulin region but this situation is very rare (Kyle *et al.*, 2004; Longo, 1998).

In theory, multiple myeloma can produce all classes of immunoglobulin, but IgG paraproteins are most common, followed by IgA and IgM. IgD and IgE myeloma are very rare. In addition, light and or heavy chains (the building blocks of antibodies) may be secreted in isolation: κ - or λ -light chains or any of the five types of heavy chains (α -, γ -, δ -, ϵ - or μ -heavy chains).

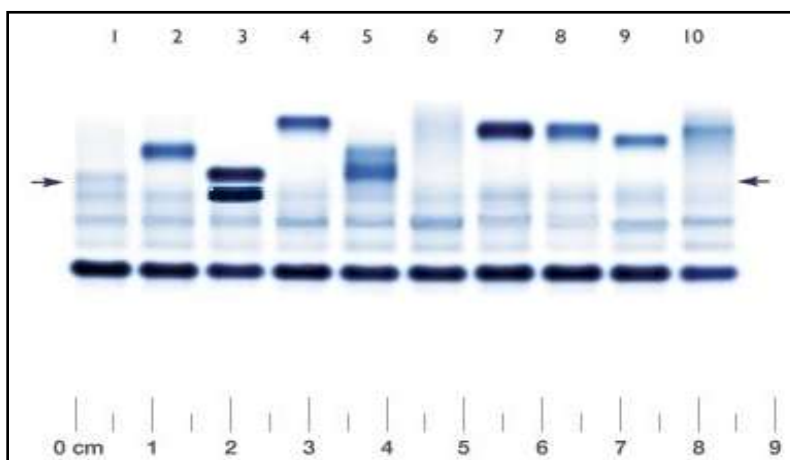
CASES

A 73 years old male was seen in private clinic at Kochi, Kerala for complaints of general weakness and bone pain in July 2013. On physical examination there was severe anemia. The patient was referred to DDRC-SRL Diagnostic Ltd, Kochi branch for laboratory investigation. Laboratory investigations including X-ray were carried out. On investigation hemoglobin 7.2 gm%, hematocrit 18.4%, RBC 3.2 million/cu.mm, WBC 4000/cu.mm, platelets 1,75,000/cu.mm, ESR 79 mm/1st hour with rouleaux formation was observed on the smear. Serum protein was 12.7 g/dl and albumin 2.65 g/dl with A:G ratio 0.26, serum calcium was 9.8 mg/dl. Serum Urea and creatinine was 15 and 1.0 mg/dl respectively. Beta-2 microglobulin level was found to be 8.7 mg/L.

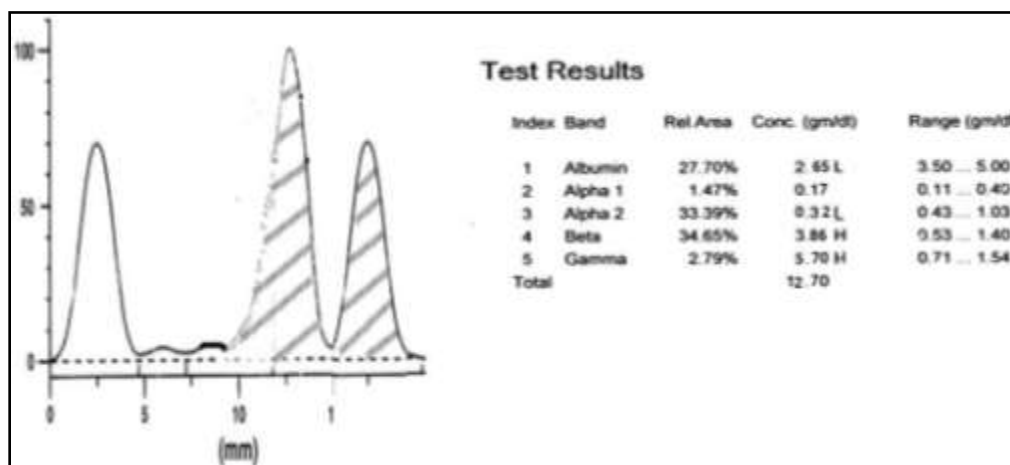
Patient's serum and urine was subjected for protein electrophoresis. The electrophoresis was performed on

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Helena Bioscience, Europe. Agarose gel protein electrophoresis total protein: 12.7 g/dl, albumin: 2.65 g/dl, alpha-1: 0.17 g/dl, alpha-2: 0.32 g/dl, beta: 3.86 g/dl, gamma: 5.7 g/dl. There were two spike seen on slide one each in region corresponding to beta and gamma region. No band was seen on urine electrophoresis. The sample was send to referral centre for confirmation by immunofixation. Bone marrow was normocellular. M:E ratio = 1:2. There was increased in plasma cell number (19%) as well as increased in nucleus and nucleolus size. X ray cranium showed 3 lytic lesions. In vertebral X ray collapse fracture was seen in L4-L5 vertebra. The patient was categorized into stage III according to the International Staging System.



Agarose Electrophoresis Slide Showing Two 'M' Band One Each In Beta Region And Gamma Region



Electrophoretogram Showing Hypoalbuminemia With Two Prominent Spikes In Beta And Gamma Region

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 (Durie and Salmon, 1975). The circulating M-protein may consist of an intact immunoglobulin, the light chain only, or (rarely) the

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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 j (kappa) or k (lambda) in type. It occurs as intense, narrow band most often found with the gamma-globulins, then in a diminishing frequency between gamma and the beta-globulin and rarely in the beta and alpha-2 regions. Generally IgA, IgG and IgM proteins are not observed on the alpha-2 fractions. These proteins compose beta-1, beta-2, and gamma fractions (O'Connell *et al.*, 2005). However, in IgG multiple myeloma immunoglobulins may rarely migrate from c fraction to alpha-2 fraction (Kyle and Rajkumar, 2004). M-protein that is seen on the alpha-2 band is just reported in a few numbers of IgA multiple myeloma cases. IgA, IgM, and sometimes IgG, along with complement proteins, also can be identified in the beta fraction. IgA is the one most commonly found in the beta region, but any type can be found there. Two paraproteins found in the same patient are generally considered to be produced by different clones, hence the name diclonal (oligoclonal) gammopathies (Imhof *et al.*, 1966). Very rarely, biclonal gammopathies (accounts for 1% of all monoclonal gammopathies) or triclinal gammopathy can be observed in multiple myeloma.

The clonal plasma cells cause an overproduction of Interleukin 6 (IL-6) (also known as osteoclast activating factor or OAF) resulting in osteoclast activation and subsequent bone destruction. These areas of bone destruction, known as lytic lesions, can lead to fractures of long bones such as arms and legs, or even more commonly, to fractures of the vertebral bodies which constitute the spine. The same process which causes bone loss, causes calcium to be removed from bone, and can cause hypercalcemia (Esteve and Roodman, 2007). 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 (Bakkus *et al.*, 2000). A biclonal gammopathy may also consist of two heavy chains of 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 first case of biclonal gammopathy reported in our diagnostic centre where nearly 300 electrophoresis are done every month.

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