

## Atypical M-Protein Localization in Protein Electrophoresis in a Patient With Multiple Myeloma

*Multipl Miyelomlu Bir Olguda Protein Elektroforezinde Atipik M-Proteini*

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Monoclonal gammopathy is a group of B-cell disorders resulting in the secretion of a specific and unique monoclonal immunoglobulin (M-component). The best method for detecting a monoclonal protein is high resolution agarose gel electrophoresis. This test detects abnormalities in the migration of the proteins on electrophoresis and can be performed with samples of serum or urine. An M-protein is usually visible as a localized band on agarose gel electrophoretic peak in the beta, gamma, or rarely in the alpha-2 globulin region of the densitometer tracing. Here, we presented a multiple myeloma patient with IgA kappa paraprotein showing an M spike in the alpha-2 globulin region in agarose gel electrophoresis.

**Key Words:** Blood protein electrophoresis; multiple myeloma; paraproteinemias.

Monoklonal gamopati, belirli bir monoklonal immünglobulin (M-protein) sekresyonuna yol açan B-hücre bozukluklarının bir grubudur. Monoklonal bir proteinin belirlenmesinde en iyi yöntem, yüksek çözünürlüklü agaroz jel elektroforezidir. Bu test elektroforezde proteinlerin migrasyon anormalliklerini gösterir ve serum ya da idrar örnekleri üzerinde uygulanabilir. M-proteini genellikle, agaroz jel elektroforezi densitometre kayıtlarında gama, beta bölgelerinde, nadiren de alfa-2 globulin bölgesinde bir bant şeklinde görülebilir. Bu yazıda, agaroz jel elektroforezinde, alfa-2 globulin bölgesinde M bandına sahip IgA kappa paraproteinemili bir multipl miyelom olgusu sunuldu.

**Anahtar Sözcükler:** Protein elektroforezi; multipl miyelom; paraproteinemi.

Among the methods of protein electrophoresis; agarose gel electrophoresis is much more sensitive than cellulose acetate method. In order to determine the immunoglobulin subtype and ensure the presence of M-protein in all patients with local M band detected in protein elec-

trophoresis, serum and urine immunofixation procedure must surely be performed as further investigation. M-protein is generally observed as a localized band which is frequently seen on gamma or beta region, it may also be seen on alpha-2 globulin region but this situation is very

rare.<sup>[1,2]</sup> Sometimes, IgG multiple myeloma may extend to the alpha-2 globulin area, because IgG M-protein may range from the slow gamma to the alpha-2 globulin region.<sup>[3]</sup> Here, we presented an adult patient diagnosed as IgA kappa type multiple myeloma, who had an M band on alpha-2 globulin region on the protein electrophoresis performed by agarose gel electrophoresis.

### CASE REPORT

Seventy-eight-year-old woman referred to our hematology clinic with symptoms of fatigue and back pain in November 2005. In the physical examination, there was no pathological finding other than paleness of the skin and conjunctiva. In the laboratory examinations performed, the following values were found; erythrocyte sedimentation rate: 120 mm/hour, Hb: 7.1 g/dl, Htc: 21.3%, leucocyte count: 6100/mm<sup>3</sup>, platelet count: 361.000/mm<sup>3</sup>, reticulocyte: 0.9% and rouleaux formation was observed on the blood smear. Serum ferritin: 314 ng/ml, BUN: 41 mg/dl, creatinin: 4.3 mg/dl, uric acid: 7.6 mg/dl, calcium: 12.6 mg/dl, lactic dehydrogenase: 490 U/L, alkaline phosphatase: 83 U/L, on protein electrophoresis: total protein: 9.0 g/dl, albumin: 3.4 g/dl, alpha-1: 0.4 g/dl, alpha-2: 3.8 g/dl (M spike was 3.7 g/dl), beta: 1.0 g/dl, gamma: 0.5 g/dl (Fig. 1). In the serum immunofixation electrophoresis: IgA: 3280 mg/dl (68-425), IgM: 17 mg/dl (50-196), IgG: 367 mg/dl (844-1912), kappa: 1780 mg/dl (170-370), lambda: 30 mg/dl (90-210). The bone marrow aspirate showed infiltration with plasma cells by 56%. In the bidirectional cranium X-ray graphy, five lytic lesions, the biggest one being 5 mm in diameter were detected. In dorsal and lomber vertebra direct X-ray graphs, collapse fractures were seen on L2-L3 and L4-L5. Beta-2 microglobulin level was 21.4 mg/dl (0.0-2.5) and creatinine clearance was found to be 18.1 ml/hour. Urinary system ultrasonography was normal. The patient was diagnosed as Stage-IIIB multiple myeloma according to Salmon-Durie staging criteria. The patient received melphalan 10 mg/day prednisolone 60 mg/day, four days per cycles, every six weeks due to renal failure. Because of patient's bone lesions and hypercalcemia,

biphosphonate (zoledronic acid) treatment was added. Also, transfusion was given to patient once per month with a single unit erythrocyte suspension. Regarding L2-3 and L4-5 lumbar vertebra collapse fracture, the patient also received radiotherapy (a total of 30 Gys) to the lumbar region. Although the patient's back pains were subsided, no hematological respond was obtained from the four cycles of melphelan and prednisolone therapy. Blood count values were found as: Hb: 7.0 g/dl, Htc: 20.3%, leucocyte count: 3400/mm<sup>3</sup>, platelet count: 113.000/mm<sup>3</sup>. On protein electrophoresis; total protein: 7.0 g/dl, albumin: 3.0 g/dl, alpha-1: 0.3 g/dl, alpha-2: 2.3 g/dl, beta: 0.8 g/dl, gamma: 0.6 g/dl (Fig. 2). Thalidomid 200 mg/day plus dexamethasone 20 mg/day four days per month were initiated. This therapy was well-tolerated by the patient and all symptoms were diminished in the third month of treatment. Hb was 10 g/dl and Htc was 31%. M band on the alpha-2 region on the protein electrophoresis had disappeared (Fig. 3). When the patient was last seen in October 2006, her clinical and laboratory findings were stable with Thalidomid plus dexamethasone therapy.

### DISCUSSION

Monoclonal gammopathies are a group of disorders that is characterized by homogeneous monoclonal M-protein production, as a result of a single plasma cell clone proliferation. Each

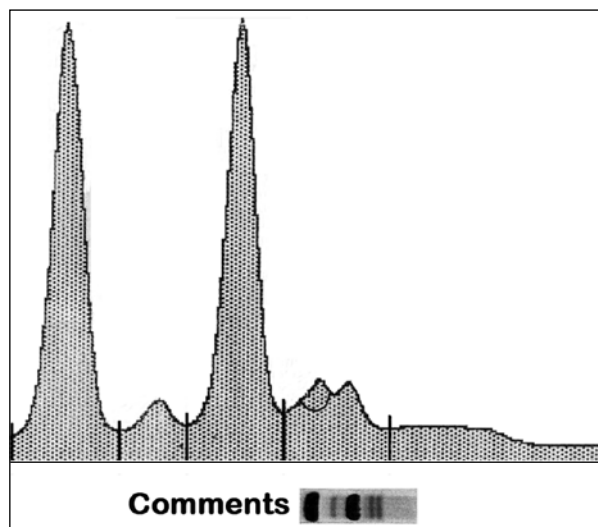
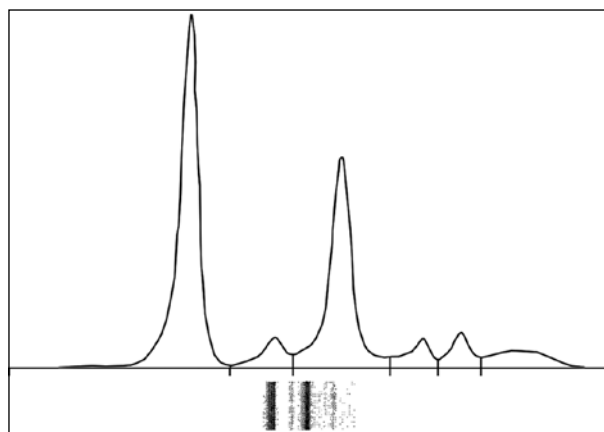
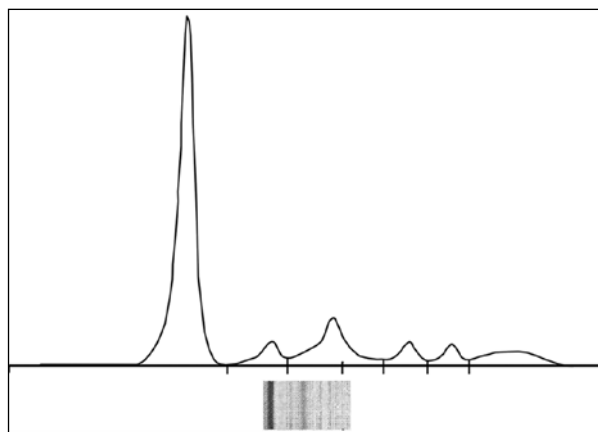


Fig. 1- M spike on alpha-2 region is seen on the protein electrophoresis in duration of the diagnosis.



**Fig. 2-** The finding of electrophoresis after therapy of alkeran plus prednol with four cure.



**Fig. 3-** The view of electrophoresis after administration of thalidomide plus dexamethasone on third month.

M-protein is composed of two heavy polypeptide chains from two of the same classes and subclasses, and from same type of light polypeptide chains. Polyclonal immunoglobulins are produced by several plasma cell clones. Heavy and light chains included in the polyclonal immunoglobulin population are heterogeneous and usually increase in reactive and inflammatory events, whereas, monoclonal elevation of immunoglobulins is observed in malign and potentially malign situations.<sup>[1]</sup> Very rarely, biclonal gammopathies (accounts for 1% of all monoclonal gammopathies) or triclonal gammopathy can be observed in multiple myeloma and other plasma cell dyscrasia. Ceruloplasmin, alpha-2 macroglobulin and haptoglobulin constitute the alpha-2 fraction of the protein electrophoresis and the alpha-2 component increases as an acute phase reactant. Generally IgA, IgG and IgM proteins are not observed on the alpha-2 fractions. These proteins compose beta-1, beta-2, and gamma fractions.<sup>[4]</sup> However, in IgG multiple myeloma immunoglobulins may rarely migrate from gamma fraction to alpha-2 fraction.<sup>[3]</sup> M-protein that is seen on the alpha-2 band is just reported in a few numbers of IgA multiple myeloma cases in literature. Mseddi-Hdiji et al.<sup>[5]</sup> reported that in electrophoresis that is performed by agarose gel method 78% of the 242 monoclonal gammopathy cases had M band on gamma region whereas 22% of the cases had band on beta region and none of the cases had it on alpha-2 region. Bakta and Sutarka<sup>[6]</sup> observed

two separate M bands on the beta-2 and alpha-2 regions in the serum protein electrophoresis of a patient that they considered to have multiple myeloma. From the serum immunofixations, these were reported to be IgM and IgA immunoglobulins. In our patient, the M band on the alpha-2 region was shown to be bound to IgA. In a study conducted by Tunstall et al.,<sup>[7]</sup> when the relation between alpha-2 macroglobulin and various diseases on humans and mice were investigated; in humans, alpha-2 macroglobulin was reported to be decreased by 50% in IgG myeloma, decreased in light-chain myelomas and IgD myelomas, and increased or normal in IgA myelomas. Again, Caterini et al.,<sup>[8]</sup> reported that in alpha-2 electrophoretic migration in IgA myeloma patients, very rarely, dense viscosity and elevated myelomatosis paraprotein migrate to alpha-2 without hyperviscosity syndrome. As a result, we wanted to remind that, M band on alpha-2 region in serum protein electrophoresis can rarely be seen in IgA myeloma patients.

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