

Case Report: IgD-Kappa Myeloma: An Unusual Case

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Abstract. A rare case of biclonal IgD-K and IgG-K myeloma is described. The patient initially presented with anemia, renal insufficiency, and proteinuria. The IgD-K, initially, was overlooked as a light chain; however, it decreased in serum concentration after treatment by ~90%, in contrast to the IgG-K that decreased in serum by ~40 % over a 9-yr period. Clinically, the patient responded well to treatment and improved greatly during this period. Practical recommendations are suggested in order to detect such cases. (received 10 September 2002; accepted 19 September 2002)

Keywords: myeloma, IgD, immunoglobulins, immunofixation, light chains

Introduction

IgD immunoglobulins are expressed on the membranes of B lymphocyte in many species including humans. Their function is not well understood but is thought to enhance the activity of the humoral response [1]. The serum level of this immunoglobulin is very low (10-110 mg/L) in comparison to IgG, IgA, or IgM [2,3].

IgD myeloma is a rare entity, accounting for 1-2% of reported cases of myeloma [5]. It typically has a poor prognosis [4]. Most cases (60-90%) are of the λ type [6]. Biclinal gammopathies involving IgD are even more rare, since biclonal bands in general constitute only 3-4% of all myelomas [7]. Patients with IgD myeloma often present with renal failure, associated with Bence-Jones proteinuria [8]. Since immunofixation for Ig D is not routinely performed, many of these cases are either missed or are misclassified as light chains.

We report a rare case of biclonal IgG-K and IgD-K myeloma. This case presents several interesting findings regarding diagnosis and prognosis. We discuss some practical steps for detecting such cases.

Case Report

Because he was becoming dizzy on standing, a 68-yr-old man consulted his physician in November 1993. Laboratory tests showed a blood hemoglobin concentration of 8.9 g/dl (reference range, 14-18 g/dl), serum creatinine concentration of 2.5 mg/dl (reference range, 0.5-1.5 mg/dl), and urine protein excretion of 15 g/24 hr. X-rays of the skull showed two possibly lytic lesions of bone. The diagnosis of myeloma was made at a community hospital, based on a bone marrow biopsy that revealed a K-positive malignant plasmacytoma, which comprised more than half of the biopsy specimen (53 % plasma cells). Immunofixation (at the community hospital) showed that the patient had IgG-K and light chains in the serum and light chains in the urine. He was treated with melphalan and prednisone.

Because of the severity of the myeloma, the patient was referred to our institution in May 1994. Bone marrow examination confirmed the diagnosis of myeloma. Serum electrophoresis and serum immunofixation showed again the presence of both an IgG-K gammopathy and "free-K light chains" (Fig. 1). The IgG-K band was estimated as 0.76 g/dl and the "free-K" band was estimated as 2.02 g/dl; urine immunofixation was not performed. The patient received a 12-mo cycle of chemotherapy with

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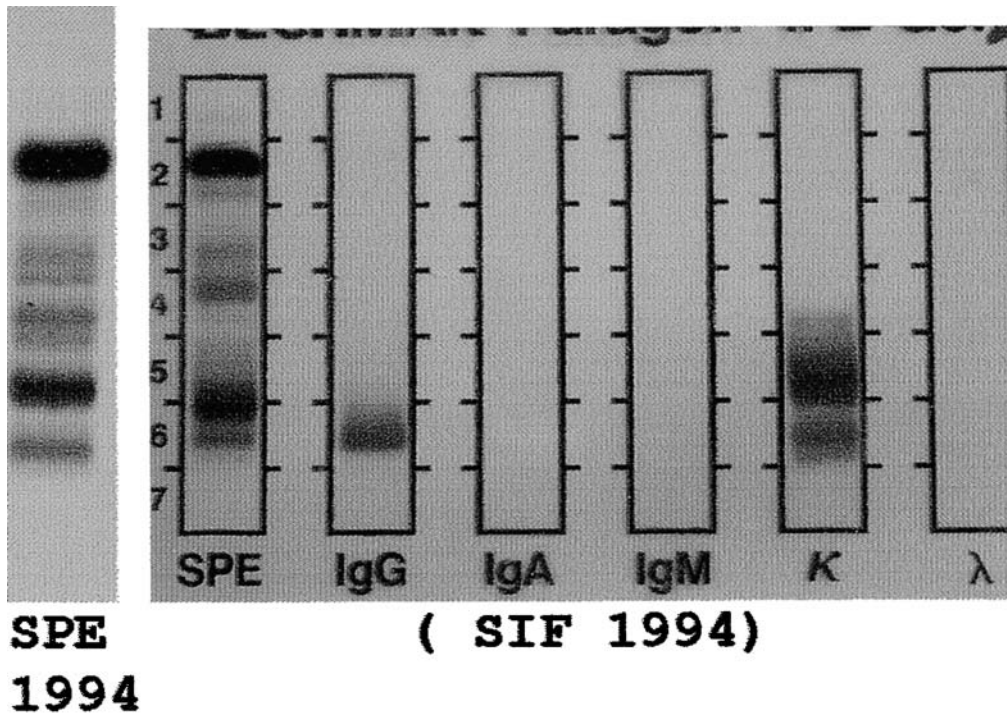


Fig. 1. Serum electrophoresis (SPE) and serum immunofixation (SIF) performed on the patient's serum in September 1994.

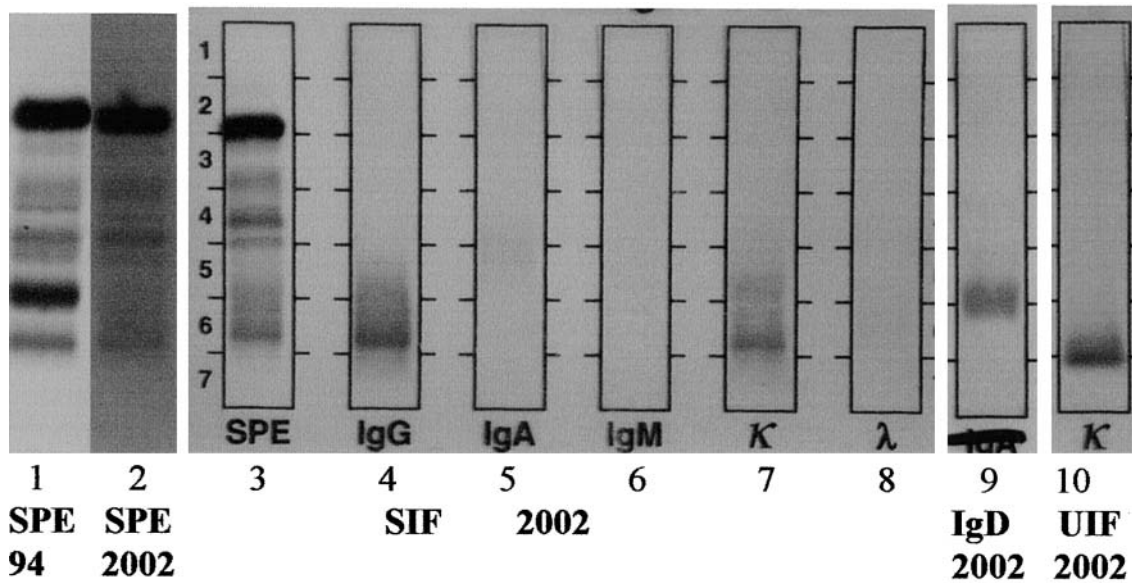


Fig. 2. Protein electrophoresis (SPE) of the patient's serum in 2002 (contrasted to that in 1994); immunofixation (SIF) of the patient's serum in 2002 (including an extra lane for IgD) and immunofixation (UIF) of the patient's urine in 2002.

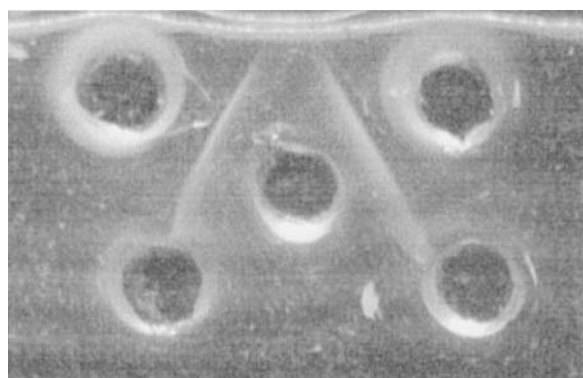


Fig. 3. Ouchterlony plate analysis for IgD in the patient's serum (top 2 wells) and in negative control serum (bottom 2 wells).

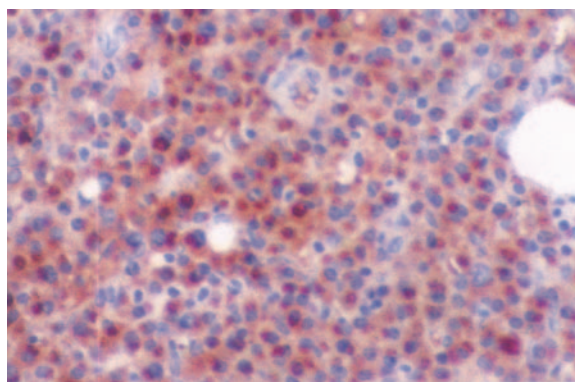


Fig. 4. Bone marrow sample from the patient in May 1994, with immunostaining for IgD (aminoethylcarbazole chromogen, hematoxylin counterstain, original magnification x132).

cytoxan, vincristine, alkeran, and prednisone. His serum creatinine concentration declined from 2.5 to 2.1 mg/dl; urine protein concentration declined to 0.9 g/24 hr (reference range 0-0.2 g/24 hr); and the M-peak in the urine electrophoresis pattern was 0.6 g/24 hr. After this original cycle of chemotherapy, he was treated with interferon and occasionally with prednisone for renal insufficiency. Over the ensuing years, the patient has been followed regularly and has shown steady improvement of his serum creatinine and urine protein levels.

In February 2002, the patient made a routine visit to his physician. His blood hemoglobin concentration was 13.5 g/dl (reference range 14-18) and the serum creatinine level was 1.8 mg/dl. Serum electrolyte concentrations were within normal limits. Urine protein excretion was 0.29 g/24 hr. Serum protein electrophoresis revealed an M-spike at the cathodal end of the γ -region (previously identified as the IgG-K band), estimated as 0.42 g/dl (Fig. 2). An additional light band, previously identified as "free-K light chain," was also seen and estimated as 0.2 g/dl. This represented about 40% decrease in IgG-K and 90% decrease in what was thought to be "free light chains" from the initial diagnosis in May 1994.

Since a great decrease in the protein synthesis of one clone but not other was quite apparent but

puzzling, immunofixation studies of both urine and serum were performed. Again, the serum gammopathy appeared to be composed of IgG-K and free-K light chains. However, examination of the urine revealed only one band of light chains (corresponding to the migration of the IgG) and nothing corresponding to the migration of the so called serum "free-K light chains" (Fig 2). On review, the concentration of the serum free-K light chains (ie, 2.1 g/dl, as reported early in 1994) seemed to be much higher than expected. This prompted a check for the presence of serum IgD.

Ouchterlony immunoassay for serum IgD showed the presence of large amounts of IgD in the patient's serum, when compared to serum from a normal subject (Fig. 3). Immunofixation was performed a second time with an added lane of anti-IgD (Fig. 2). The results proved that the small mid-gamma band, previously thought to be free-K light chain, was actually an IgD-K gammopathy. A new immunostaining of the bone marrow biopsy from May 1994 showed strong positive staining for IgD-K, with focal staining for IgG, IgM, and IgA, while staining for λ was negative (Fig. 4).

At the present time (August 2002), despite slightly elevated concentrations of serum creatinine 1.5-1.9 mg/dl (normal range, 0.5-1.5 mg/dl), the patient feels well and is asymptomatic.

Discussion

This case is unique in several ways. First, and most important, the patient is doing well clinically almost 9 yr after the original diagnosis. IgD myelomas tend to have poor prognosis; in one study, the median survival time was 12 mo following diagnosis [6]. IgD myelomas typically have an aggressive course, with severe anemia, extramedullary involvement, lymphadenopathy, amyloidosis, and splenomegaly [5]. Second, contrary to expectation, the chemotherapeutic regimen appeared more effective in decreasing the synthesis of IgD, compared to that of IgG. The serum level of IgD-*K* γ -globulin decreased from 2.02 g/L to 0.52 g/L, with little change in the IgG-*K* complex during 8 yr. Third, neoplastic B-cells that secrete IgD tend to possess a λ -chain, not *K*; thus 60-90% of IgD myelomas are of the λ type. This is attributed either to inhibition of the assembly of IgD-*K* or rapid intracellular catabolism prior to secretion [9], but the majority of the cell-bound IgDs are *K* type [10], while 90% of monoclonal IgDs in serum are λ type [9]. Finally, the patient has a biclonal gammopathy, which accounts for only 3-4% of all multiple myelomas [7]. Possibly, patients with a biclonal gammopathy with IgD-*K* (instead of λ) have a better prognosis than typical IgD myelomas. Curiously, the IgD clone responded better to therapy than the IgG clone.

This case shows how easy it is to overlook the diagnosis of IgD. However, it is important to point out that this patient with "missed" IgD myeloma was treated appropriately and responded well to the treatment. IgD myeloma is rare and usually mimics a light chain. It would be expensive to perform routine immunofixation tests on every light chain to rule out IgD. The presence in the serum of IgG-*K* and what seemed to be light chains was sufficient to diagnose myeloma in this case, but the exact diagnosis was missed. Certain features, as seen here, can suggest that IgD is present: (a) higher than usual concentration of free light chains in serum, (b) urine free light chains that migrate on electrophoresis to a point different from that seen with the serum, and (c) two related clones of cells that respond differently to chemotherapy.

An alternative to the expensive immunofixation test is use of the Ochterlony plate, as demonstrated here. These is a more cost-effective method to detect IgD. Furthermore, several samples can be studied at the same time. This case shows that a keen eye and a high level of suspicion are important elements for diagnosing cases of IgD myeloma.

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