Two cases of IgD multiple myeloma

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Abstract

The authors describe two clinical cases of IgD lambda chain multiple myeloma, both diagnosed in an Internal Medicine Department in 1995. Some considerations are made concerning such uncommon form of myeloma.

Key words: multiple myeloma, IgD.

Introduction

Multiple myeloma (MM) accounts for 1% of all malignant diseases,[1,2,3] and is more common amongst Black people (2%). [2,4] The incidence increases with age; its peak is reached at around 70 years, and diagnosis is often established at around 62 years.[5]

The monoclonal proliferation of lymphocytes results in the production of molecules or sub-units of immunoglobulins (Igs) that look like abnormal bands on electrophoresis, or even lymphokines. These abnormal Igs are known as paraproteins. The lymphoproliferative diseases associated with the proliferation of paraproteins are varied. In a study carried out by the Mayo Clinic in 1990, involving 856 patients with monoclonal gammopathy, the following distribution was found: monoclonal gammopathy of undetermined significance (63%), MM (12%), amyloidosis (9%), lymphoma (5%), solitary or extramedullary myeloma (4%), chronic lymphocytic leukaemia (3%), indolent myeloma (2%), and macroglobulinaemia (2%).[1]

The frequency of the various types of MM reflects the physiological concentrations of the various immunoglobulins.[2,5,6,7,8] Therefore, immunoglobulin D MM (IgD MM) accounts for 1% to 2%, [8,9,10,11] and was described for the first time in 1965 by Rowe and Fahey.[6,11]

Attempts have been made to attribute particular characteristics to the various subtypes of MM. Thus, in respect to IgD MM, it appears to be prevalent in males aged under 60 years;[5] the concentration of the monoclonal peak on electrophoresis is low or undeterminable, and Bence-Jones proteinuria occurs in almost all cases. Hepatosplenomegaly, lymphadenopathy, extra-osseous lesions and amyloidosis are common manifestations.[5,6,12]

Clinical cases

Case 1

JMC (PU no. 290100222), male, 66 years, Caucasian. On the 19th March 1995, the patient went to the Emergency Department due to intense anorexia accompanied by nausea and vomiting, reporting oliguria and obstipation, for which he was hospitalized with a diagnosis of renal insufficiency and anaemia. Personal history includes renal lithiasis and a car accident in 1987, which resulted in paraplegia. Objective examination revealed mucocutaneous pallor and absence of visceromegaly. Due to the paraplegia, it was difficult to assess the patient's functional state.

Routine biochemical tests revealed renal insufficiency, hyperuricaemia and hypocholesterolaemia (*Table I*), with normal hepatic function. Hematological tests revealed macrocytic anaemia (*Table II*).

Given the patient's complaints, an upper gastrointestinal endoscopy was performed, which revealed an atrophic gastritis of the body and fundus, and erosive bulbitis. In the urine culture, Pseudomonas aeruginosa and Streptococcus agactiae were identified.

Serum protein electrophoresis (PEP) revealed a monoclonal peak in the gamma globulin fraction (*Fig. 1*). Immunoelectrophoresis (IEP) determined a monoclonal IgD I gammopathy accompanied by hypoglobulinaemia G, M and A (*Table III*). Urine

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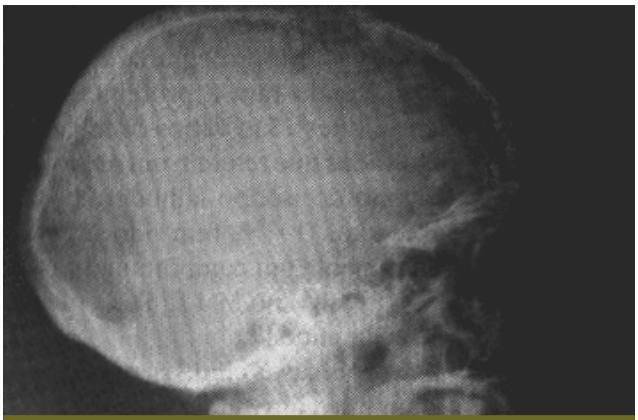
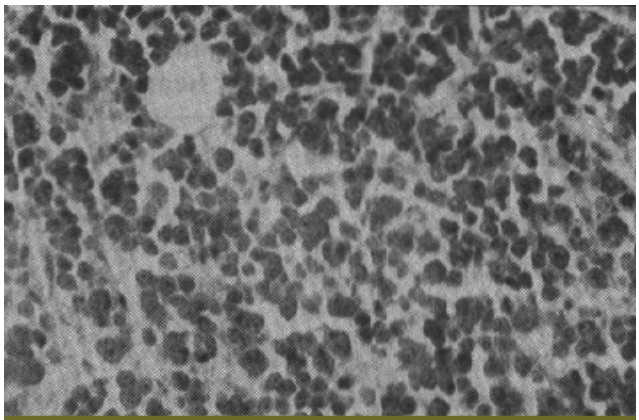


Bone biopsy: invasion of the marrow by moderately differentiated plasma cells

FIG. 1



Skull with osteolytic, punched-out lesions.

FIG. 2

IEP identified a large amount of l-type light-chain proteins (74.30 g/L) in comparison to the k-type (0.1 g/L). Myelogram showed 60% of plasma cells, many of which were atypical (*Table III*).

Skeleton X-ray revealed osteopenia, without evidence of osteolytic lesions and also old fractures from the car accident in which the patient was involved.

The patient began therapy with prednisolone (2 mg/kg/day) and melphalan (0.25 mg/kg/day) for four days every six weeks, according to the Alexanian dose regimen followed by the Department. Besides chemotherapy, a H2 receptor antagonist (cimetidine), a xanthine-oxidase inhibitor (alopurinol) and antibiotics (norfloxacin and co-trimoxazole) were prescribed based on the antibiogram.

In July of the same year, the patient was readmitted to hospital with febrile syndrome, abdominal pain, and poor general state. He underwent another upper gastrointestinal endoscopy and biopsies, which detected a gastric ulcer. Blood cultures were negative and urine culture identified Pseudomonas aeruginosa. At this point, an improvement was observed in the laboratory parameters. Key findings were improved anaemia (Hb – 11.1 g/dL with MGV – 100fL) and renal function (creatinine - 1.4 mg/dL and ureic nitrogen - 3.2 mg/dL; uric acid - 2.7 mg/dL), and unaltered hypocholesterolaemia and ESR > 105 mm on the 1st hour. In the serum PEP, the monoclonal peak (*Fig. 1*) showed

TABLE I

Biochemical parameters

		Case 1 (Age/Sex)	Case 2 (Age/Sex)
		66/male	56/female
Creatinine (mg/dL)	0.6-0.11	2.3	1.7
Urea (mg/dL)	6-22	23	35
Calcium (mg/dL)	8.1-10.4	9.4	11.4
Uric acid (mg/dL)	3.0-7.0	10.9	11.4
LDH (U/L)	230-470	525	420
Cholesterol (mg/dL)	140-240	86	196

TABLE II

Hematological parameters

		Case 1	Case 2
Leukocytes (G/l)	4.5-11.0	4.1	10.6
Hb (g/L)	12-16	7.6	8.5
MGV (fL)	86-98	100	88.4
MCHC (g/dL)	32-36	36	33
ESR (mm 1st H)	< 20	> 105	92
% bone marrow plasma cells	< 4	60	57

TABLE III

Biochemical parameters

		Case 1	Case 2
Protein (g/dL)	6.2-8.1	7.4	6.3
Albumin (g/dL)	3.5-5.6	3.1	4.0
IgG (g/L)	6.94-16.18	4.39	5.44
IgA (g/L)	0.68-3.78	0.50	0.60
IgM (g/L)	060-2.63	0.22	0.31
Ig D (g/L)	0.000-0.140	24.200	2.960
Serum l-type chain proteins (g/L)	2.69-6.38	23.00	3.58
Serum k-type chain proteins (g/L)	5.74-12.76	2.65	4.15
b2-microglob. (mg/dl)	< 2.10	28.93	5.6
Plasma viscosity (cp)	1.50-1.72	1.82	—

a marked reduction in gammaglobulins, with IgD of 2.060 g/L and l-type light-chain proteins of 6.26 g/L, accompanied only by a reduction in IgG.

The patient died in outpatient care six months after the diagnosis, and after completing three cycles of chemotherapy.

Case 2

IJD (PU no. 390500428), female, 56 years, Caucasian. On June 26, 1995, the patient was referred to the Emergency Department from her local hospital, due to acute respiratory insufficiency, following therapy with analgesics for "renal pain". The patient was admitted to the Medicine Service to investigate normocytic normochromic anaemia and renal insufficiency, which were detected in the analytical test on admission. Personal history included low back pain with mechanical characteristics for the past few months, and asthenia, weight loss and anorexia with one month of evolution. Objective examination revealed mucocutaneous pallor, absence of visceromegaly, and difficulty walking without support. Her functional score, according to the Eastern Cooperative Oncology Group (ECOG) scale, was 213.

Routine biochemical tests confirmed renal insufficiency, hyperuricaemia, hypercalcemia and low HDL cholesterol (*Table I*), with normal hepatic function. Hematological tests confirmed normocytic normochromic anaemia (*Table II*). During hospitalization, pre-renal insufficiency and hypercalcemia were resolved with oral hydration; the last serum nitrogen levels were 23 mg/dL, creatinine 1.0 mg/dL and calcium 9.2 mg/dL.

Serum PEP revealed a monoclonal peak in the gamma globulin fraction (*Fig. 2*). Serum immunoelectrophoresis determined a monoclonal IgD I gammopathy accompanied by hypoglobulinaemia G, M and A (*Table III*). Urine IEP identified a larger amount of l-type light-chain proteins (40.80 g/L) in comparison to the k-type (3.16 g/L). Myelogram showed 59% of plasma cells, many of which were atypical (*Table III*). Bone biopsy revealed massive invasion of the marrow by plasma cells (*Fig. 3*).

X-ray of the skeleton revealed intense osteopenia and multiple osteolytic images distributed through the cranial vault (*Fig 4*) and neck of the femur. Computed axial tomography of the spine revealed structural changes in several vertebrae, without medullary involvement.

The patient was given the same therapy as that reported for the previous case, but had only two cycles of chemotherapy. Because the patient migrated to the USA, she was not observed again by us, and as far as we know she was alive in December 1995.

Comments

IgD is found in extremely small amounts in the serum, and is highly susceptible to proteolysis.[4] Its functions are still not clear; however, it is known that it is initially detected in the surface of B cells associated with IgM, and indicative of mature or "virgin" B cells.[9] These two immunoglobulins are important antigen receptors.[2]

As a rule, patients with IgD MM have a low or undetermined monoclonal (M) peak on serum electrophoresis[5,10,11,13] and are associated with almost all cases of Bence-Jones proteinuria, with Bence-Jones proteinaemia being rare.[5] There are several published papers that report a clear predominance of the lambda isotype (± 90%) over kappa (k).[5,6,9] Clinically, a less aggressive behavior in the k-type IgD MM has been suggested in relation to the I-subtype.[10]

In both clinical cases described above, a high elevation of the M component was observed, particularly in case 1 (Fig. 1). Both cases had Bence-Jones proteinuria with I-type light-chain protein. In case 1, Bence-Jones proteinaemia was observed.

Regarding the distribution by gender and age, most of the published case series report a higher prevalence among males, and two thirds of the patients are under 60 years; therefore, the disease affects younger patients.[5,6]

These myelomas are thought to have a shorter survival, of around 14 months,[5] perhaps associated with a late diagnosis, given the electrophoretic characteristics described above[12] and/or more aggressive behaviour.[10] Nevertheless, other competing factors may exist, which to date, are unknown. Paraproteinaemia levels do not seem to be important, neither does renal involvement.[6,14]

The incidence of renal insufficiency in IgD MM is high (67%),[6,9] which may be due to the association of these myelomas with light-chain proteins.[5,9] The occurrence of renal amyloidosis is also more frequently observed in IgD myelomas than in the remaining types, 44% over 6-24%, respectively,[9] in which l-type light-chain proteins are sometimes present, regardless the type of MM.[8] Amyloid substance was not investigated in any of the cases.

Shimamoto and colleagues carried out a retrospective trial of 165 cases of IgD MM and concluded that of all the variables listed in the Durie and Salmon or the British Medical Research Council staging system, the only predicting factors seem to be just the subtype of light-chain proteins and leukocyte count.[11]

In regard to the occurrence of osteolytic lesions, some authors report a frequency similar to that found for light-chain MM, which is more common than IgG and IgA.[6]

Of course, all these considerations about IgD MM are relative, considering the small number of case series. The authors, for this study, had the chance to review five case series. Thus, by way of example, the Mayo Clinic [10] carried out a retrospective trial involving 53 patients with IgD MM diagnosed between the 1st January 1996 and 31st December 1992, and obtained the following results: bone-related complaints 72%; fatigue 36%; loss of weight 32%; plasmacytoma 19%; amyloidosis 19%; renal insufficiency 33%; hypercalcemia 22%; M peak 66%; and Bence-Jones proteinuria 96%; I-type chain 60% and K-type 38%, with 2% of undetermined types; average survival time, 21 months. ■

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