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A Case of IgE Myeloma: Methodology and Review of the Literature

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A 56-year-old man presented with a one-year history of progressive weakness predominantly affecting his extremities and persistent low back pain. Ouchterlony immunodiffusion of the concentrated urine detected a marked increase in lambda light chains. A sternal bone marrow documented a diagnosis of multiple myeloma. Screening high resolution agarose gel electrophoresis revealed diffuse hypogammaglobulinemia and, retrospectively, an equivocal, faint band which migrated in the fast gamma region. By using a combination of immunoelectrophoresis and immunofixation electrophoresis, this questionable band was determined to represent an IgE lambda monoclonal protein. Radioimmunoassay for IgE documented a serum concentration of 50.6 mg/dl. No intact IgE was found in the urine. Following chemotherapy, the patient's serum IgE level decreased significantly, and he is presently asymptomatic.

Features of special interest in this case include the low serum IgE level on presentation, which was difficult to detect on the screening electrophoretogram, and the use of immunofixation electrophoresis in the detection and characterization of these "difficult" gammopathies.

IgE myeloma is the rarest and most recently described among the plasma cell dyscrasias. This rarity undoubtedly reflects the low level of IgE normally found in serum (1) and thus the small number of IgE producing cells present (2). Since the initial observation by Johansson and Bennich in 1967, only 19 cases have been reported (3-21), including a case of benign monoclonal IgE gammopathy (22) and several other reports where monoclonal IgE was associated with other disorders (23-26).

The purpose of this paper is to describe the clinical and immunochemical features of this new case of IgE myeloma and to compare them with the previously reported cases. In addition, the methodology used to resolve serum paraproteins present in low concentration will be briefly discussed.

Case Report

A 56-year-old Caucasian man presented in March, 1983 complaining of a one-year history of progressive weakness and tiredness with persistent low back pain, pain in both legs and arms, and difficulty in chewing due to extreme jaw weakness.

His past medical history was remarkable for bilateral carpal tunnel syndrome in 1981. There was no history of asthma, hay fever, or food allergy. The patient was not taking any medication.

Physical examination was unremarkable except for prominent, firm temporal and antecubital superficial veins bilaterally and mild hepatosplenomegaly.

Laboratory data included a white blood cell count of 7,700/mm^3 (71% neutrophils, 26% lymphocytes, 2% monocytes, 1% basophils), and a hemoglobin level of 14.2 g/dl. The platelet count was 416,000/mm^3. The peripheral blood smear showed mild anisocytosis without rouleau. Blood urea nitrogen was 16 mg/dl, and the creatinine level was 1.1 mg/dl. The calcium level was 9.8 mg/dl, uric acid was 6.1 mg/dl. The total protein level was decreased (6.1 g/dl) with the albumin level 4.1 g/dl. The urinalysis was unremarkable. The creatinine clearance was 138 ml/min. Twenty-four-hour urine protein was markedly elevated (5.4 g/vol). Metastatic bone survey was negative. A sternal bone marrow aspirate disclosed normal cellularity with 19% mature plasma cells and 4.5% proplasmacytes. No amyloid was identified. Rectal and left deltoid biopsies were also negative for amyloid. Serum protein electrophoresis revealed an equivocal band in the gamma region which later proved to be monoclonal IgE.

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The patient was started on chemotherapy including vincristine, 1,3-bis-(2-chloroethyl)-1-nitrosourea (BCNU), adriamycin, cyclophosphamide, melphalan, and prednisone with gradual improvement. Two months following treatment, his urine protein and serum IgE level had decreased significantly (Table I). The patient is presently asymptomatic and is being followed on an outpatient basis.

Materials, Methods, and Results

Protein studies

Rate nephelometric quantitation of serum immunoglobulins using a Beckman nephelometer documented diffuse hypogammaglobulinemia with an IgG level of 586 mg/dl, IgM 34 mg/dl, and IgA 29 mg/dl.

High resolution agarose gel electrophoresis (HRAGE) of serum and concentrated urine was performed on Panagel slides (Worthington) consisting of 1% agarose on plastic supports in barbital buffer (pH 8.6) at 200 volts for 45 minutes. After electrophoresis was completed, the agarose gel was fixed in picric acid solution for ten minutes, rinsed in 95% ethanol, and stained in Amido Black. Serum protein electrophoresis showed a total protein level of 6.4 g/dl, albumin 4.2 g/dl, alpha-1 globulin 0.3 g/dl, alpha-2 globulin 0.68 g/dl, beta globulin 0.79 g/dl, and gamma globulin 0.48 g/dl. Retrospectively, a faint, equivocal band was present in the fast gamma region (Fig. 1a).

Double immunodiffusion in agar was performed according to the method of Ouchterlony (27). The concentrated urine revealed markedly increased free lambda light chains with a trace of IgG and negative IgM and IgA. Double immunodiffusion of the serum for IgE was positive up to a dilution of 1:256.

Immunofixation electrophoresis (IFE) was performed by a modified method of Ritchie and Smith (28). The patient's serum and pooled human control sera were diluted with barbital buffer (pH 8.6) to obtain a final protein concentration of 5 μg/10 μl. Three to five microliters of the diluted sample were applied to the Panagel slides, and the proteins were separated as described above by HRAGE (Panagel Electrophoresis Reagent Kit and Migration Unit, Worthington DR0047601 and DR0047602). After the electrophoresis run was completed, the gel was removed, and one Whatman #1 filter paper strip was laid over the cathodal portion of each sample. Approximately 100-150 μl of antiserum against IgG, IgA, IgM, IgD, IgE, lambda, and kappa was evenly applied along the center length of each strip, and the gel was incubated with the antiserum in a humidity chamber for one hour at room temperature. The gel was removed, rinsed with saline, and pressed for 10 minutes using drying blotter pads. Following further washes with saline and deionized water and repressing between wash cycles, the slide was dried at 50°C for 10 to 15 minutes and stained in Amido Black for 10 minutes. The slide was then destained in reagent grade water until the background was clear, blotted, and air dried. The serum demonstrated a broad monoclonal IgE band in the fast gamma region with a lambda light chain band which had the same migration. A second, darker staining lambda band, which migrated in the beta region and was obscured by the C-3 component of complement in the HRAGE, represented free monoclonal lambda light chains (Fig. 1b).

Immunoelectrophoresis (IEP) of the serum and urine was carried out on agarose plates (Paragon, Beckman) by a modification of Scheidegger's method (29). The urine IEP demonstrated a heavy arc corresponding to markedly elevated lambda light chains (Fig. 2a). The serum displayed two abnormal arcs joined by a line of

TABLE I

Patient's Response to Chemotherapy

	Total Urine Protein (g/vol)	Total Serum Protein (g/dl)	Serum IgE (mg/dl)	Immunoglobulins (mg/dl) IgG	IgM	IgA	Bone Marrow Plasmacytosis (%)
Pretherapy	5.4	6.1	50.6 (230,000 U/ml)	586	34	29	23.5
2 Months Post-Therapy	0.6	6.3	19.8 (90,000)	457	30	23	9
Normal Range	0-0.1	6.8-8.5	0-0.05 (0-250)	600-1700	50-250	60-300	0-1

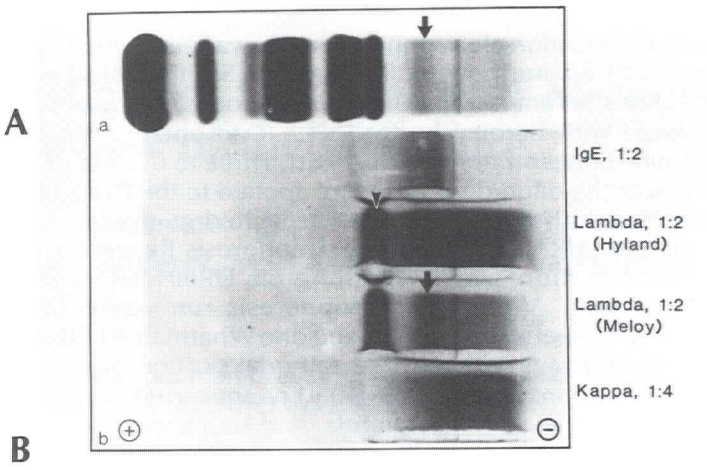

Fig. 1

A. High resolution agarose gel electrophoresis of serum demonstrates a faint, equivocal band (arrow) in the fast gamma region associated with a reduction of gammaglobulins.

B. Serum immunofixation electrophoresis in agarose gel shows a broad monoclonal IgE band (arrow) associated with a monoclonal lambda spike (arrow) which has the same migration. A second lambda band (arrowhead) migrates in the region and is masked in the screening serum electrophoretogram by the C-3 component of complement. Staining with free and bound anti-kappa sera reveals diffuse polyclonal kappa light chains.

identity; one arc signified free lambda light chains, and the other possibly indicated monoclonal lambda chains associated with the IgE moiety or polyclonal lambda chains associated with the IgG immunoglobulin (Fig. 2b). The serum also documented an abnormal arc precipitating with anti-IgE antiserum (Fig. 2b); the normal serum failed to form a precipitin line with this antiserum because of the normally low level of IgE. No intact immunoglobulins were present in the urine by either IEP or fractional separation by Sephadex G-75 chromatography (Pharmacia Fine Chemicals). The total serum IgE level as measured by solid-phase radioimmunoassay (30) was 230,000 U/m,l (50.6 mg/dl).

Immunohistochemistry

Immunohistochemical localization of IgE, kappa, or lambda in lymphocytes was accomplished using a direct immunoperoxidase staining technique. Cytospin slide preparations of Ficoll/Hypaque mononuclear cell suspensions prepared from bone marrow aspirate were used. A negative reagent control (primary antibody replaced with a 1:20 dilution of Horseradish-peroxidase-15 mg/10 ml PBS) and a positive tissue control slide were included in the evaluation.

The bone marrow plasma cells displayed intracytoplasmic positivity for both IgE and lambda light chains (Figs. 3a,b, and c).

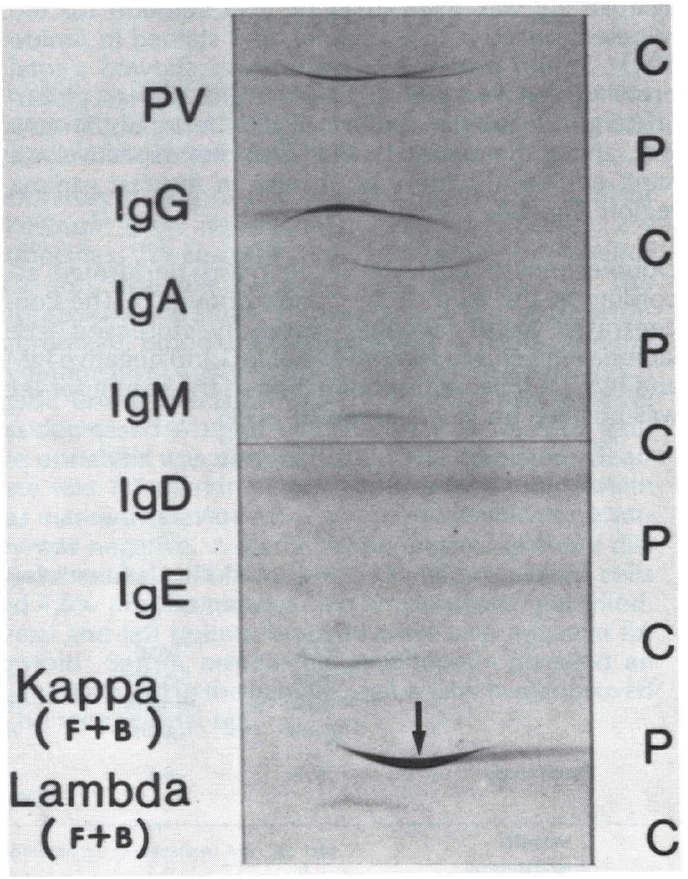

Fig. 2a
Urine immunoelectrophoresis with free monoclonal lambda light chains (arrow).

Discussion

The clinical and immunochemical features of 20 cases of IgE myeloma are summarized in Tables II and III.

The first two cases (3,4) were characterized by plasma cell leukemia, monoclonal light chains of the lambda type, and absence of bone lesions; however, subsequent reports showed a much greater heterogeneity associated with this entity. The mean age at presentation in this study was 61.7 years with a range of 48 to 77. No significant differences in age were present between men and women. Male to female ratio was almost equal (11:9) approximating that of IgG and IgA myeloma (31).

The clinical features were similar to other types of multiple myeloma except for a higher frequency of hepatosplenomegaly (35%), which is fairly uncommon in myeloma (32). Bone lesions were predominantly lytic (50%); however, two cases (10%) showed osteosclerosis, a feature which, when unrelated to therapy or pathological fracture, occurs in no more than 3% of

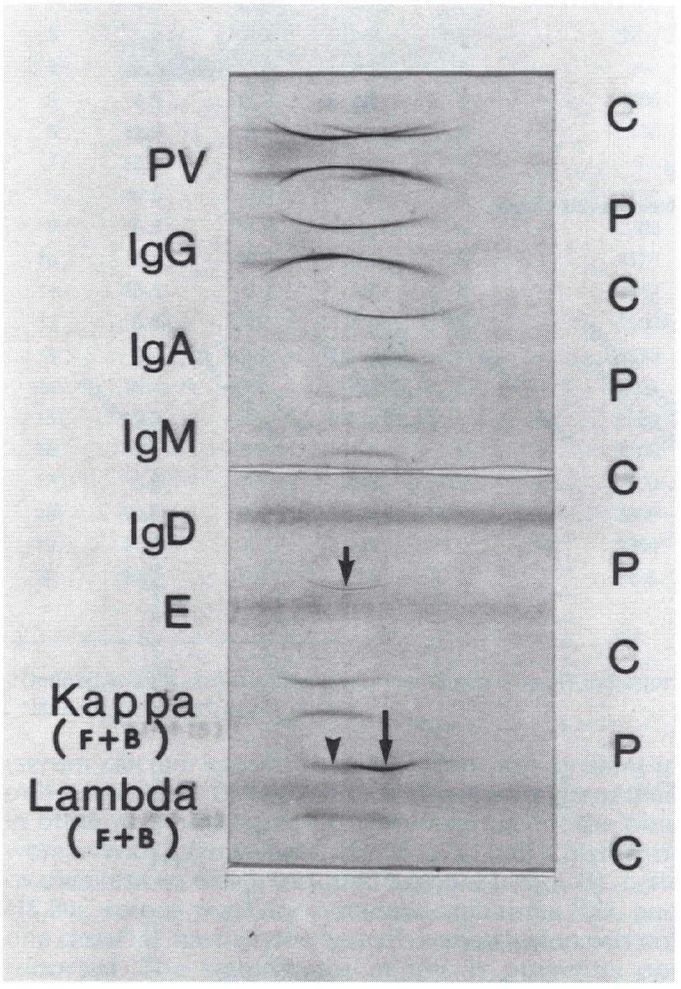

Fig. 2b

The serum immunoelectrophoresis shows two abnormal arcs with the anti-lambda antiserum joined together by a line of identity. One of these arcs signifies free monoclonal light chains (arrow); the other signifies either monoclonal lambda chains bound to IgE or polyclonal lambda chains bound to IgG immunoglobulin (arrowhead). Also note the abnormal arc precipitating with anti-IgE antiserum (arrow).

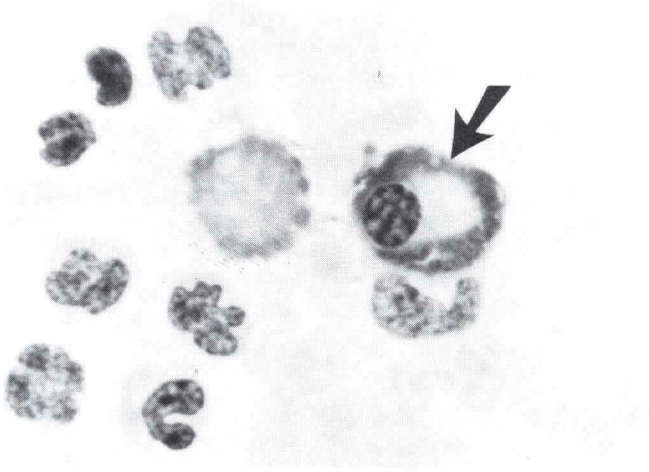

Fig. 3a

Direct immunoperoxidase staining of bone marrow plasma cells for intracytoplasmic a) IgE, b) lambda and c) kappa immunoglobulins confirming IgEλ myeloma. Monoclonality is supported by the positive intracytoplasmic reaction to lambda light chain antiserum and negative kappa light chain study (direct immunoperoxidase, X 1250).

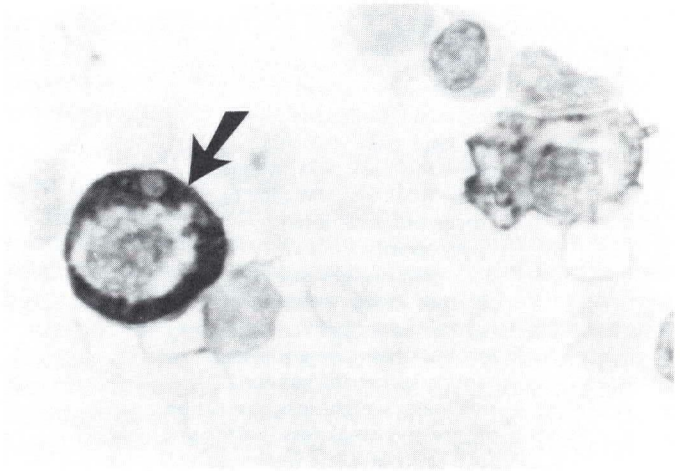

Fig. 3b

patients with non-IgE type of myeloma (33-35). In this respect, one of the reported cases (5) remains questionable (20) because of the appearance of the sclerotic lesions following melphalan therapy (36). Plasma cell leukemia was reported in five patients (25%), four of whom were men. This feature has been cited in only 1.5 to 2% of reviewed myeloma cases (37,38) and to date appears to be the most characteristic feature of IgE myeloma (20,21). Anemia, with a hemoglobin level of less than 12 g/dl, was detected in 18 patients (90%) and appears to be more common and severe than in other myeloma types (32).

Severe renal failure (BUN greater than 80 mg/dl) was found in three cases (15%). This compares to a similar frequency in IgG and IgA myeloma but is less than half as common as in light chain disease (39). Hypercalcemia

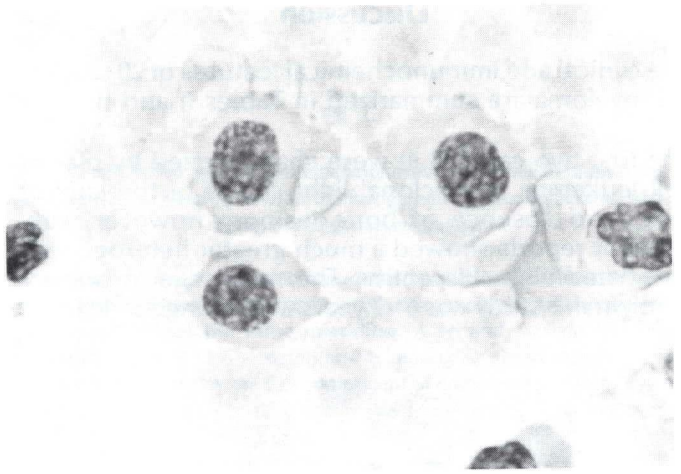

Fig. 3c

TABLE II

Clinical Features of IgE Myeloma (20 Cases)

Case No.	Age (yr) at Diagnosis and Sex	Clinical Features	Hepatosplenomegaly	Lytic or Sclerotic Bone Lesions	Severe Renal Failure	Plasma Cell Leukemia (% Plasma Cells)	Survival from Diagnosis (months)	Reference
1	50,M	chest and low back pain	—	—	—	+(61)	42	3
2	60,M	fatigability, poor vision	+	—	—	+(65)	12	4
3	65,F	weakness, fatigue, nosebleed	+	L,S	—	—	11	5
4	51,M	bone pain	+	L	—	—	> 2.5	6
5	48,F	bone pain	—	L	—	—	> 6	7
6	59,M	back pain	—	L	—	—	>16	8
7	57,M	weakness, headaches, blurred vision	+	—	+	—	1.3	9
8	69,F	hip and back pain	—	L	—	—	2	10
9	54,M	pathological fracture, weakness, weight loss, pain	+	L	+	+(27)	17	11
10	69,M	anorexia, nausea/vomiting, weight loss	—	L,S	+	—	6	12
11	64,F	back and rib pain, weight loss	—	L	—	—	> 7	13
12	65,F	weakness, weight loss epistaxis, pollinosis	+	L	—	—	NR	14
13	55,F	low back pain, asthenia	—	—	+	+(12)	13	15
14	60,F	chest and back pain, weight loss, weakness, fatigability, recurrent infections	—	L	—	—	6	16
15	77,M	"pyonephritis"	—	—	—	—	50	17
16	68,M	back pain, weight loss Herpes Zoster infection	—	—	—	—	>24	18
17	71,F	right shoulder pain	—	L	—	—	>11	19
18	69,F	low back pain, weight loss, anorexia, nausea/vomiting	—	L	—	—	> 4	20
19	67,M	weakness, weight loss, confusion	—	—	+	+(20)	9	21
20	56,M	progressive weakness, back pain, extremity and jaw weakness	+	—	—	—	> 2	present case

NR — Not reported

TABLE III

Biochemical and Immunochemical Features of IgE Myeloma (20 Cases)

Case Number	Hemoglobin (g/dl)	Total Serum Protein (g/dl)	Urine Protein (g/vol)	Light Chain Type (Kappa/Lambda)	Bence Jones Proteinuria*	Serum IgE (mg/dl)	M-Protein Electrophoresis Mobility	Serum Calcium (mg/dl)	Serum Creatinine (mg/dl)	Percent Plasma Cells in Bone Marrow at Diagnosis	Reference
1	10.2	9.5	NR	L	+	4500	fast-γ	NR	1.1	"Numerous"	3
2	4.0	12.5	3.18	L	+	7500	γ	9.6	4.4	"Almost total replacement"	4
3	5.0	8.4	NR	K	–	2700	mid-γ	9.5	1.2	"Heavy Infiltration"	5
4	7.0	10.1	NL	K	–	180	α	NR	NR	50.2	6
5	6.5	11.3	NR	K	–	6300	γ	12	1.9	50	7
6	12.9	8.4	0.05 (g/L)	K	–	2100	γ	NL	NL	"Considerable Excess"	8
7	10.1	5.1	15.1	K	+	60	γ-β	8.1	NR	39	9
8	10.5	9.5	NR	K	–	2100	β-2	9.9	1.2	60-100	10
9	6.3	11.0	16 (g/L)	K	+	2700	fast-γ	13.4	1.8	58.3	11
10	8.1	10.7	3.0	K	+	4170	mid-γ	NL	2.6-10	>50	12
11	10.5	8.1	NR	K	–	2417	β	10.9	1.2	>90	13
12	<8.0	NR	1.35 (g/L)	K	–	5500	NR	NR	NR	"Blastic Forms"	14
13	8.0	9.9	1.1 (g/L)	K	–	4550	fast-γ	9.2	1.0-9.0	53	15
14	10	9.2	NR	L	+	3800	β	NR	NR	22 and 33	16
15	10.5	8.1	0.8 (g/L)	L	NR	1600	fast-γ	NR	2.6	5	17
16	9.4	8.0	8.6	K	+	3100	γ	8.6	0.9	72.4	18
17	8.3	7.6	NR	K	–	1500	fast-γ	8.1	1.2	53.6	19
18	10.6	9.5	1.5 (g/L)	K	+	3500	fast-γ	5.1	1.1	37	20
19	11.0	10.3	NR	L	NR	2800	α	NR	6.2	90	21
20	14.2	6.1	5.4	L	–	50.6	fast-γ	9.8	1.1	23.5	present case

*Defined as light chains present in urine detected by pH indicator colorimetric screening methods, heat test, and sulfosalicylic acid test. NR = not reported, NL = normal.

(serum calcium greater than 11 mg/dl) was present in only two (14.3%) of 14 patients and is less frequent than in other myeloma types (40). Interestingly, of the nine women with IgE myeloma, five (55.6%) had a history of ovarian lesions which included Brenner tumor (5), cysts (15,20), serous papillary cystadenocarcinoma (10), and one case (14) in which the type of ovarian lesion was not reported. The significance of this is presently not known.

None of the reported cases showed any evidence of amyloidosis, although our case presented with symptomatology suggestive of this disorder. The light chains were typed as kappa in almost three quarters of patients with IgE myeloma as compared to two thirds of patients with IgG and IgA myeloma and only one tenth of those with IgD myeloma (18,39,40). The M-protein migrated predominantly in the fast gamma region on zone electrophoresis. The serum IgE concentration ranged from 50.6 to 7500 mg/dl with a mean of 3056 mg/dl. Marrow plasmacytosis exceeded 50% in 9 of 15 cases (60%) where such information was documented.

The mean survival time from diagnosis in 11 patients who died was 15.4 months with a range of 1.3 to 50 months. Survival time from diagnosis was less than 24 months in 9 patients. Despite a reported favorable initial response to chemotherapy in many patients, the average survival time is shorter than for IgG and IgA myeloma but longer than for IgD myeloma and light chain disease of the lambda type (31,32). Well-recognized features denoting a relatively poor prognosis are similar to those of other types of myeloma (41,42) and include renal failure, severe anemia, extensive skeletal involvement, and Bence Jones proteinuria (16).

The present case is of interest because of the low level of M-protein in the serum (50.6 mg/dl) which was not initially appreciated as an M-spike on the screening electrophoretogram. This, coupled with the markedly elevated lambda light chains found in the urine, led to an initial consideration of light chain disease even though features commonly present in this disorder, such as hypercalcemia, Bence Jones proteinuria, renal failure, amyloidosis, and lytic bone lesions were absent (43). It is quite conceivable that some patients with IgE myeloma have been typed as light chain disease in the past (16).

This leads to a discussion on the evaluation of monoclonal proteins when present in low concentration. Traditionally, monoclonal proteins (MPs) in serum or urine have been studied by a combination of zone electrophoresis and classical IEP (44,45). Recent improvement in the average survival of patients with multiple myeloma has been dependent on earlier diagnosis and thus less tumor cell burden and decreased serum MP concentration (46). It may be difficult, on the basis of IEP analysis alone, to detect a small serum MP due to the limited resolving power of this technique (47). Other paraprotein isolation and purification methods are time consuming and laborious. We use HRAGE with IFE in conjunction with IEP when studying difficult monoclonal gammopathies. IFE consistently appears to be superior to both IEP and routine protein electrophoresis for the detection and characterization of MPs, particularly at concentrations of less than 1000 mg/dl (48-55). IFE offers several advantages over other techniques including decreased performance time, so that diffusion leading to band broadening is kept to a minimum with resulting increased resolution, reduced reagent consumption, and its easy interpretation and comparison to the agarose electrophoretic pattern (56). Closely apposed bands are easily resolved by IFE but may be completely lost in IEP (55-57).

In conclusion, we have presented the clinical and immunochemical features of a new case of IgE myeloma with a review of the literature. This entity appears to be associated with an increased frequency of severe anemia, less hypercalcemia and amyloidosis, a tendency to plasma cell leukemia and gammopathy of the kappa light chain type, and a shorter survival. Additional information awaits further documented cases. We have suggested the use of the more sensitive technique of immunofixation electrophoresis to study these monoclonal gammopathies in hope that earlier diagnosis and increased survival rates will be attained.

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References

1. Hobbs JR. Monoclonal immunoglobulins from random mutations. Br J Cancer 1969;22:717-9.
2. Bergsagel DE. Plasma cell myeloma. In: Williams WJ, Beutler E, Erslev AJ, Rundles RW, eds. Hematology. New York: McGraw-Hill Book Co., 1977:1099.
3. Johansson SGO, Bennich H. Immunological studies of an atypical (myeloma) immunoglobulin. Immunology 1967;13:381-94.
4. Ogawa M, Kochwa S, Smith C, Ishizaka K, McIntyre OR. Clinical aspects of IgE myeloma. N Engl J Med 1969;281:1217-20.
5. Fishkin BG, Orloff N, Scaduto LE, Borucki DT, Spiegelberg HL. IgE multiple myeloma: A report of the third case. Blood 1972;39: 361-7.
6. Stefani DV, Mokeeva RA. Two rare cases of myeloma disease (Type D and E). Probl Haemat Blood Transf USSR 1972;6:44-7.
7. Knedel M, Fateh-Moghadam A, Edel H, Bartl R, Neumeier D. Multiples myelom mit moroklonaler IgE-gammopathie. Dtsch Med Wochenschr 1976;101:496-9.
8. Mills RJ, Fahie-Wilson MN, Carter PM, Hobbs JR. IgE myelomatosis. Clin Exp Immunol 1976;23:228-32.
9. Vladutiu AO, Kohli RK, Prezyna AP. Monoclonal IgE with renal failure. Am J Med 1976;61:957-62.
10. Weiner E, Dicamelli R, Showel J, Osmand AP, Sassetti RJ, Gewurz H. IgE myeloma presenting with classical myeloma features. J Allergy Clin Immunol 1976;58:373-80.
11. Yoshitake J, Hiramatsu S, Komatsubara Y, et al. A case of IgE myeloma. Acta Haematol Jap 1976;39:862-75.
12. Rogers JS, Spahr J, Judge DM, Varano LA, Eyster ME. IgE myeloma with osteoblastic lesions. Blood 1977;49:295-9.
13. Bouvier M, Creyssel R, Lejeune E, Coeur P, Daumont A. Aspect clinique du myeloma IgE. A propos d'une observation personnelle et d'une revue de la litterature. Rev Rhum Mal Osteoartic 1978;45:185-92.
14. Zavazal V, Sach J, Rozprimova L, Brumelova V. An unusual case of IgE myeloma. Allergol Immunopathol 1978;6:423-6.
15. Vaerman JP. A new case of IgE myeloma (Des) ending with renal failure. J Clin Lab Immunol 1979;2:343-8.
16. Dammacco F, Miglietta A, Tribalto M, Mandelli F, Bonomo L. The expanding spectrum of clinical and laboratory features of IgE myeloma. Ric Clin Lab 1980;10:583-90.
17. Bomchil G, Becherini JO. Mieloma IgE de evolucion prolongada. Sangre 1980;25:503-6.

18. Endo T, Okumura H, Kikuchi K, et al. Immunoglobulin E (IgE) multiple myeloma. A case report and review of the literature. Am J Med 1981;70:1127-32.
19. Kimura J, Suzuki N, Tomioka H, Takahashi H. A case of IgE myeloma. Rinsho Ketsueki 1981;22:1469-77.
20. Sala P,Tonutti E, Ruscio M, Colle R, Antonutto G, Falconieri G. IgE myeloma. Report of a new case and review of the literature. Haematologica 1981;66:787-95.
21. West NC, Smith AM, Ward R. IgE myeloma associated with plasma cell leukemia. Postgrad Med J 1983;59:784-5.
22. Ludwig H, Vormittag W. "Benign" monoclonal IgE gammopathy. Br Med J 1980;281:539-40.
23. Baenkler HW. Monoclonal gammopathy of IgA and IgE type in a case of chronic lymphatic leukemia. Acta Haematol 1976;56: 189-92.
24. Shirakura T, Takekoshi K, Umi M, et al. Waldenström's macroglobulinemia with IgE M-component. Scand J Haematol 1978; 21:292-8.
25. Cornwell GG, Michaelson TE, Sanders WH. Comparative studies on a monoclonal IgGλ and two IgE K components from an individual patient: Evidence for shared idiotypic determinants between the two IgE proteins but not the IgG protein. Immunology 1980;39:511-7.
26. Brown GL, Corby DG, Lima JE, DiBella NJ, Nelson JK, Gray MR. IgE-IgM kappa gammopathy associated with lymphocytic lymphoma: Immunological evaluation. Milit Med 1977;142:921-5.
27. Ouchterlony O. Diffusion-in-gel methods for immunological analysis. Prog Allergy 1962;6:30-154.
28. Ritchie RF, Smith R. Immunofixation. 1. General principles and application to agarose gel electrophoresis. Clin Chem 1976; 22:497-9.
29. Scheidegger JJ. Une-micro-methode de l'immunoelectrophorese. Int Arch Allergy 1955;7:103-10.
30. Ceska M, Lundkvist U. A new and simple radioimmunoassay method for the determination of IgE. Immunochem 1972;9: 1021-30.
31. Jancelewicz Z, Takatsuki K, Sugai S, Pruzanski W. IgD multiple myeloma. Arch Intern Med 1975;135:87-93.
32. Kyle RA. Multiple myeloma. Review of 869 cases. Mayo Clin Proc 1975;50:29-40.
33. Langley GR, Sabean HB, Sorger K. Sclerotic lesions of bone in myeloma. Can Med Assoc J 1966;94:940-6.
34. Evison G, Evans KT. Bone sclerosis in multiple myeloma. Br J Radiol 1967;40:81-9.
35. Lowbeer L. Occurrence of osteosclerosis in multiple myeloma. Lab Med Bull Pathol 1969;10:397.
36. Rodriguez LH, Bernett Finkelstein J, Schullen Berger CC, Alexanian R. Bone healing in multiple myeloma with Melphalan chemotherapy. Ann Intern Med 1972;76:551-6.
37. Pruzanski W, Platts ME, Ogryzlo MA. Leukemic form of immunocytic dyscrasia (plasma cell leukemia). Am J Med 1969;47:60-74.
38. Kyle RA, Maldonado JE, Bayrd ED. Plasma cell leukemia: Report on 17 cases. Arch Intern Med 1974;133:813-8.
39. Hobbs JR. Immunochemical classes of myelomatosis: Including data for a therapeutic trial conducted by a medical research council working party. Br J Haematol 1969;16:599-606.
40. Hobbs JR, Corbett AA. Younger age of presentation and extraosseous tumor in IgD myelomatosis. Br Med J 1969;1:412-4.
41. Witts LJ, Blackburn EK, Callender ST, et al. Report on the first myelomatosis trial: Part 1. Analysis of presenting features of prognostic importance. Br J Haematol 1973;24:123-39.
42. Hobbs JR. Monitoring myelomatosis. Arch Intern Med 1975;135: 125-30.
43. Stone MJ, Frenkel EP. The clinical spectrum of light chain myeloma: A study of 35 patients with special reference to the occurrence of amyloidosis. Am J Med 1975;58:601-19.
44. Zawadzki ZA, Edwards GA, Adams RV. M-components in immunoproliferative disorders. Electrophoretic and immunologic analysis of 200 cases. Am J Clin Pathol 1967;48:418-30.
45. Kyle RA. In: Rose NR, Friedman H, eds. Manual of clinical immunology. American Society for Microbiology 1976:734.
46. Alexanian R, Balcerzak S, Bonnet D, et al. Prognostic factors in multiple myeloma. Cancer 1975;36:1192-201.
47. Axelsen NH, Harboe M, Jonsson V, Videbaek A. u-chain disease in a case of chronic lymphocytic leukemia and malignant histiocytoma. II. Immunochemical studies. Scand J Haematol 1976;16:218-25.
48. Pascali E. Pezzoli A, Chiarandini A. Immunofixation: Application to the identification of "difficult" monoclonal components. Clin Chem 1982;28:1404-5.
49. Marshall MO. Comparison of immunofixation and immunoelectrophoresis methods in the identification of monoclonal immunoglobulins in serum. Clin Chim Acta 1980;104:1-9.
50. Pizzolato MA, Goni FR, Salvarezza RC. Immunofixation on cellulose acetate: An improved screening method for monoclonal immunoglobulins. J Immunol Methods 1979;26:365-8.
51. Pedersen NS, Axelsen NH. Detection of M-components by an easy immunofixation procedure: Comparison with agarose gel electrophoresis and classical immunoelectrophoresis. J Immunol Methods 1979;30:257-62.
52. Whicher JT, Hawkins L, Higginson J. Clinical applications of immunofixation: A more sensitive technique for the detection of Bence Jones protein. J Clin Pathol 1980;33:779-80.
53. Keshgegian AA, Peiffer P. Immunofixation as an adjunct to immunoelectrophoresis in characterization of serum monoclonal immunoglobulins. Clin Chim Acta 1981;110:337-40.
54. Pudek MR. Investigation of monoclonal gammopathies by immunoelectrophoresis and immunofixation. Clin Chem 1982;28:1231-2.
55. Sun T, Lien YY, Degnan T. Study of gammopathies with immunofixation electrophoresis. Am J Clin Pathol 1979;72:5-11.
56. Ritchie RF, Smith R. Immunofixation. III. Application to the study of monoclonal proteins. Clin Chem 1976;22:1982-5.
57. Cawley LP, Minard BJ, Tourtellotte WW, Ma BI, Chelle C. Immunofixation electrophoretic techniques applied to identification of proteins in serum and cerebrospinal fluid. Clin Chem 1976;22:1262-8.