A 71-Year-Old Woman with Multiple Myeloma Status after Stem Cell Transplantation

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CASE

A 71-year-old woman with a 9-year history of monoclonal gammopathy of undetermined significance presented with anemia [hemoglobin, 11.6 g/dL (116 g/L); reference interval (RI), 12–15.5 g/dL (120–155 g/L)], an increased serum calcium concentration [10.2 mg/dL (2.55 mmol/L); RI, 8.9–10.1 mg/dL (2.22–2.52 mmol/L)], and a 4800 mg/dL (48 g/L) monoclonal protein band (M-spike) after serum protein electrophoresis (SPEP). Immunofixation electrophoresis (IFE) revealed a monoclonal IgA κ protein. Her IgA concentration was markedly increased to 4720 mg/dL [47.2 g/L; RI, 61–356 mg/dL (0.61–3.56 g/L)], and the serum immunoglobulin free light chain (FLC) κ/λ ratio was 7 (RI, 0.26–1.65). A bone marrow biopsy confirmed 40% involvement by monoclonal κ-restricted plasma cells with a plasma cell labeling index of 0.4% (intermediate). A bone survey revealed diffuse osteopenia, multiple small lytic lesions throughout the skeleton, and a lesion consistent with a plasmacytoma at T7. A diagnosis of multiple myeloma (MM) (Durie–Salmon stage IIIA, international stage 2) was confirmed. The patient was initially treated medically and then underwent successful autologous stem cell transplantation. The patient was asymptomatic, with negative results in serum and urine protein electrophoresis and IFE evaluations for 1.5 years.

A follow-up SPEP evaluation 2 years after the patient received her transplant revealed an M-spike of 3920 mg/dL (39.2 g/L) and an IgA concentration of 3810 mg/dL (38.1 g/L). A bone marrow biopsy showed 60%–70% involvement by monoclonal plasma cells. The results of a urine IFE test were negative. The patient was treated with a regimen of 25 mg Revlimid daily on days 1–21 and 20 mg dexamethasone weekly. The patient's M-spike decreased to 1100 mg/dL (11 g/L) by 1 month after treatment, and her IgA concentration was reduced to 1260 mg/dL (12.6 g/L). Two months into treatment, the patient had detectable monoclonal protein but no measurable M-spike, and her IgA concentration was 402 mg/dL (4.02 g/L). The dexamethasone dosage was reduced to 10 mg weekly for the third month, and her serum IgA concentration decreased further, to 340 mg/dL (3.4 g/L), which is within the RI.

The patient was maintained on pamidronate monthly and with 25 mg Revlimid daily as a single agent. Bimonthly monitoring by SPEP and IFE testing and measurement of her IgA concentration were continued for 1 year. Follow-up SPEP and IFE results were normal (Fig. 1); however, the serum IgA concentration steadily increased above the upper reference limit, even in the presence of normal IFE results and normal serum FLC ratios (Table 1). Because of the patient's history of IgA disease, her hematologist felt this increase in IgA might be a sign of relapsed disease.

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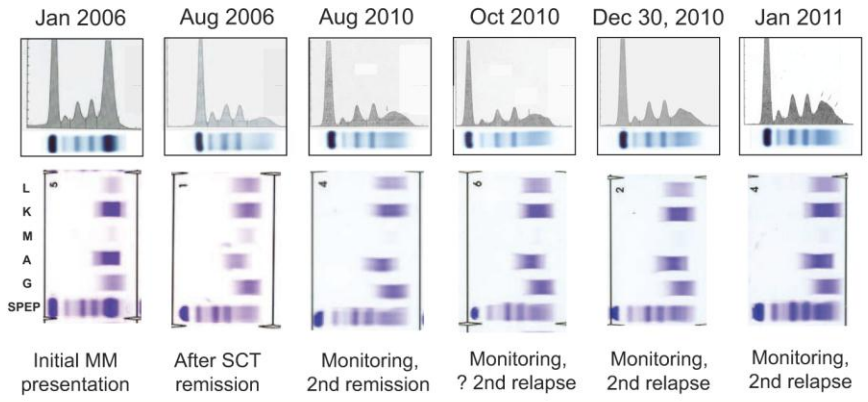

Fig. 1. SPEP and IFE analysis at various times throughout the course of disease.
The patient's broad M protein spike was typed as IgA κ at presentation. Monitoring of the second remission shows increased restriction in the A and K lanes in only the most recent examinations. SCT, stem cell transplantation.

Table 1. Laboratory results for IFE interpretation, immunoglobulin FLC ratio, IgA HLC pair quantification ratio (IgA κ/IgA λ), and IgA quantification at various times throughout the course of the disease.

Date	IgA,g/L[a]	IFE	FLC κ/λ	IgA κ/IgA λ	Clinical comments
RI	0.61–3.56	Negative	0.26–1.65	0.7–2.2	
Jan 8, 2008	38.1[b]	M-spike (3920 mg/dL)[a,b]	10.3[b]	463[b]	First relapse
Aug 13, 2008	3.28	Negative	1.9[b]	3.7[b]	After relapse, 25 mg Rev[c] daily, 10 mg Dex weekly
Apr 22, 2009	4.34[b]	Negative	1.14	2.9[b]	Increased Dex to 20 mg weekly because of IgA
Nov 4, 2009	4.28[b]	Negative	1.06	2.8[b]	Dex removed owing to side effects
Jun 23, 2010	6.58[b]	Negative	1.21	4.1[b]	Single-agent Rev
Aug 25, 2010	7.67[b]	Negative	1.08	5.6[b]	Single-agent Rev
Oct 27, 2010	9.14[b]	Negative	1.36	5.6[b]	Add 10 mg Dex weekly
Dec 1, 2010	8.04[b]	Negative	1.38	8.2[b]	Bony disease progression, radiation to ilium
Dec 30, 2010	8.80[b]	Restricted migration[b]	2.07[b]	13[b]	Disease relapse, increase Dex to 20 mg weekly
Jan 20, 2011	12.20[b]	Restricted migration[b]	4.75[b]	24.8[b]	Will switch to alternative regimen

[a] The factor for converting the IgA and M-spike concentrations in the traditional unit of measure (milligrams per deciliter) to SI units (grams per liter) is ×0.01.
[b] Abnormal result.
[c] Rev, Revlimid; Dex, dexamethasone.

Questions to Consider
• What are the potential causes of a steadily increasing immunoglobulin in an MM patient in remission?
• What are the criteria for laboratory detection of MM relapse?
• What tests can be used to determine the clonality of serum immunoglobulins?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the December 2011 issue of *Clinical Chemistry*. To view the case and comments online,

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go to http://www.clinchem.org/content/vol57/issue12 and follow the link to the Clinical Case Study and Commentaries.

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