Clinical Case Study

Sharply Increased Serum Free Light-Chain Concentrations after Treatment for Multiple Myeloma

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CASE DESCRIPTION

CASE

A 53-year-old woman presented to the orthopedic department with severe diffuse muscular and bone pain. An x-ray of her right upper extremity revealed a lytic destructive lesion in the right humerus. Computed tomography scans showed multiple lytic lesions in the spine and pelvis, and a biopsy confirmed the presence of 70% plasma cells, which were κ light chain restricted. The patient was referred to a hematologist. Although no monoclonal protein was detected in the serum by protein electrophoresis or by immunofixation electrophoresis (IFE),[3] the κ free light chain (FLC) was increased at 47.2 mg/L (reference interval, 3.3–19.4 mg/L), with a κ / λ FLC ratio of 23 (reference interval, 0.26 –1.65). Serum concentrations of β_2- microglobulin and albumin were 248 nmol/L (reference interval, 59.5–153 nmol/L) and 37 g/L (reference interval, 34–47 g/L), respectively. The urine protein concentration was not increased, but protein electrophoresis revealed a small M (monoclonal) spike in the γ region (32 mg/24 h). In addition, IFE identified a monoclonal κ light chain (Bence Jones protein). On the basis of these findings, the patient was informed that she had stage I (International Staging System) oligosecretory/ nonsecretory multiple myeloma (MM).

The patient underwent surgical repair of her right humerus and was evaluated 1 month after her surgery. At that point, a second serum FLC measurement showed a κ FLC concentration of 68.2 mg/L. The patient's hematologist recommended close observation in lieu of initiating therapy because of her lack of symptoms. The patient's serum κ FLC concentration was monitored monthly and remained <50 mg/L for the next 3 months. Five months after diagnosis, the patient began to complain of mild fatigue, shortness of breath, and palpitations. A 10-fold increase in the urinary M protein to 333 mg/24 h was noted, along with a decrease in the blood hemoglobin concentration to 79 g/L (reference interval, 120–155 g/L) and an increase in the calcium concentration to 2.80 mmol/L (reference interval, 2.22–2.52 mmol/L). Her hematologist recommended initiation of treatment, and the patient was enrolled in a clinical trial protocol consisting of lenalidomide (25 mg/day) and dexamethasone (40 mg/ day) administered for 21 days of a 28-day cycle. At 1 month after initiation of treatment, the patient was noted to be tolerating the regimen well, with an increase in her hemoglobin to 91 g/L, a minimal decrease in serum IgG from a pretreatment value of 2.95 g/L to 2.71 g/L (reference interval, 6.00 –15.00 g/L), and a reduction in her serum creatinine concentration from 115 μmol/L to 88

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μmol/L (reference interval, 62–106 μ mol/L). The patient also stated that she felt less fatigued. Her serum κ FLC concentration, however, was inexplicably increased to 2180 mg/L (Fig. 1). By her next follow-up appointment a month later, the patient had completed 2 full cycles of the lenalidomide and dexamethasone regimen and showed evidence of continued response, as evidenced by a rise in the hemoglobin concentration to 105 g/L and a decrease in urinary protein excretion to 132 mg/24 h. The patient's serum κ FLC concentration remained increased at 1500 mg/L, however.

Questions to Consider
• Why was the patient's high serum FLC initially not detected by IFE?
• What are the potential causes of increases FLC after treatment?
• How can light-chain escape be differentiated from FLC antigen excess?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the January 2009 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol56/issue 1 and follow the link to the Clinical Case Study and Commentaries.

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