A Rapidly Deteriorating Patient with Gross Increase in Serum Free Light Chains

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CASE DESCRIPTION

A 71-year-old man presented with increasing confusion after dialysis. He was admitted for progressive decline in functional status over a 1-month period including delirium, a fall, and difficulty with pain, speaking, and walking. Four years ago, he was diagnosed with stage IIIB multiple myeloma with IgAκ M-protein and corresponding κ free light chain (FLC).[3] He was treated with combination chemotherapy of cyclophosphamide, bortezomib, and dexamethasone, and he achieved partial remission. Medical history was significant for myeloma-related end-stage renal failure, hypertension, osteonecrosis of the jaw secondary to bisphosphonate, and recent onset of squamous cell carcinoma.

At presentation, physical examination was unremarkable. The patient was alert and oriented, with a Glasgow coma scale of 15. Laboratory findings included hemoglobin concentration of 10.4 g/dL [reference interval (RI), 13.5–17.0 g/dL] and mean red cell volume of 114 fL (RI, 82–98 fL). Additional test results included a plasma total protein concentration of 6.5 g/dL (RI, 6.0–8.0 g/dL), albumin concentration of 4.2 g/dL (RI, 3.5–4.8 g/dL), total calcium concentration of 12.4 mg/dL (RI, 8.7–10.3 mg/dL; 3.11 mmol/L; RI, 2.18 –2.58 mmol/L), ionized calcium concentration of 6.12 mg/dL (RI, 4.68 –5.16 mg/dL; 1.53 mmol/L; RI, 1.17–1.29 mmol/L), phosphorus concentration of 7.3 mg/dL (RI, 2.5–5.0 mg/dL; 2.36 mmol/L; RI, 0.80 –1.60 mmol/L), alkaline phosphatase concentration of 75 U/L (RI, 30–105 U/L), creatinine concentration of 10.2 mg/dL (RI, 0.68 –1.13 mg/dL; 903 μmol/L; RI, 60–100 μmol/L), and blood urea nitrogen concentration of 69 mg/dL (RI, 7–22 mg/dL; 24.6 mmol/L; RI, 2.5– 8.0 mmol/L).

Serum protein electrophoresis (SPE) (Fig. 1, A and C) showed hypogammaglobulinemia, with a β region of 1.0 g/dL. Immunofixation electrophoresis identified the presence of IgAκ M-protein in the β region. Serum κ and λ FLCs concentrations were 4490.00 mg/dL (RI, 0.33–1.94 mg/dL) and 1.12 mg/dL (RI, 0.57–2.63 mg/dL), respectively, with a κ/λ FLC ratio of 4009.00 (RI, 0.26 –1.65).

Three weeks later, a second SPE (Fig. 1, B and C) showed hypogammaglobulinemia but with an increased β region of 1.4 g/dL. In the β region, immunofixation electrophoresis identified an IgAκ M-protein along with a κ FLC band. The plasma total protein and albumin concentrations were 5.7 g/dL and 3.4 g/dL, respectively. Serum κ and λ FLC concentrations were 7830.00 mg/dL and 0.99 mg/dL, respectively, with a κ/λ FLC ratio of 7909.00. No urine specimens were submitted. Of note, the κ FLC and total protein concentrations were highly discordant, with the κ FLC concentration (7830.00 mg/dL or 7.83 g/dL) exceeding the total protein concentration (5.7 g/dL).

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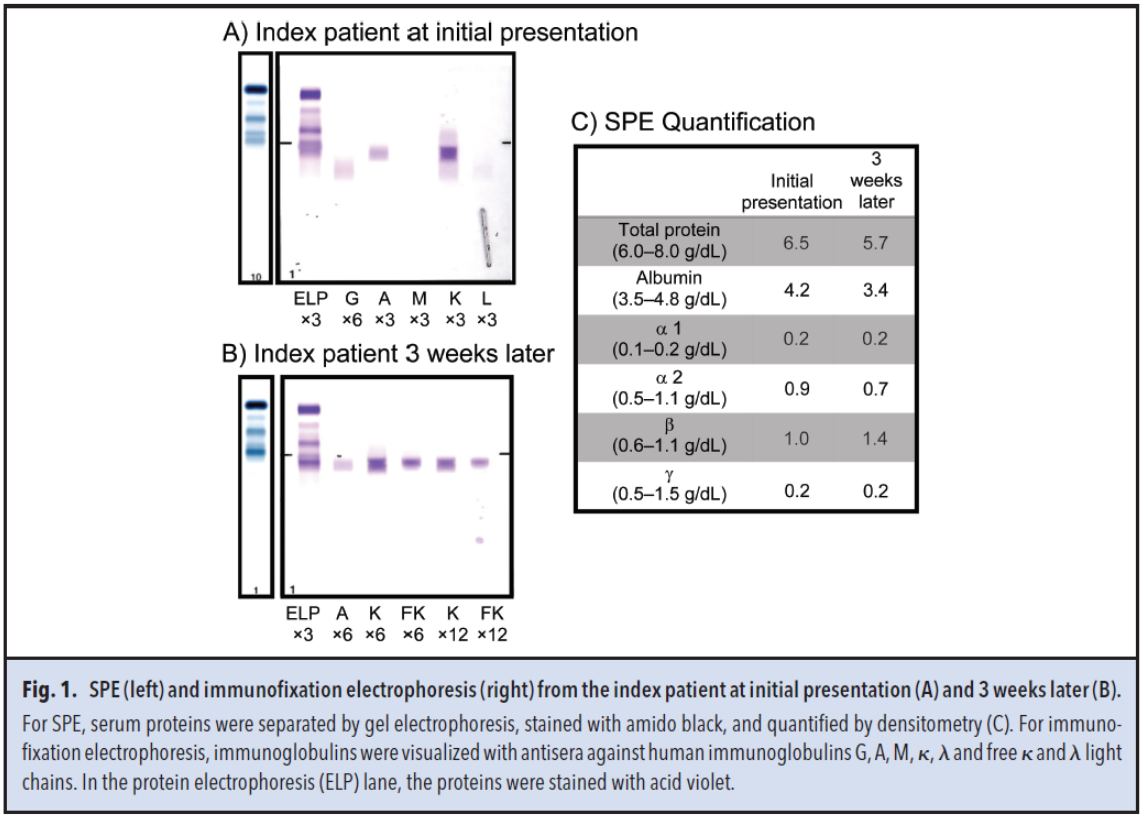
[3] Nonstandard abbreviations: FLC, free light chain

QUESTIONS TO CONSIDER
• What are causes of discordance between total protein and serum FLC quantification?
• What are limitations of serum FLC assays?
• What strategies can be used to clarify suspected inaccurate FLC results?



	Initial presentation	3 weeks later
Total protein (6.0–8.0 g/dL)	6.5	5.7
Albumin (3.5–4.8 g/dL)	4.2	3.4
α 1 (0.1–0.2 g/dL)	0.2	0.2
α 2 (0.5–1.1 g/dL)	0.9	0.7
β (0.6–1.1 g/dL)	1.0	1.4
γ (0.5–1.5 g/dL)	0.2	0.2

Fig. 1. SPE (left) and immunofixation electrophoresis (right) from the index patient at initial presentation (A) and 3 weeks later (B).
For SPE, serum proteins were separated by gel electrophoresis, stained with amido black, and quantified by densitometry (C). For immunofixation electrophoresis, immunoglobulins were visualized with antisera against human immunoglobulins G, A, M, κ, λ and free κ and λ light chains. In the protein electrophoresis (ELP) lane, the proteins were stained with acid violet.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the September 2019 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol65/issue9 and follow the link to the Clinical Case Study and Commentaries.

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