Clinical Case Study

Unusual Increased β-Globulins in an Elderly Patient

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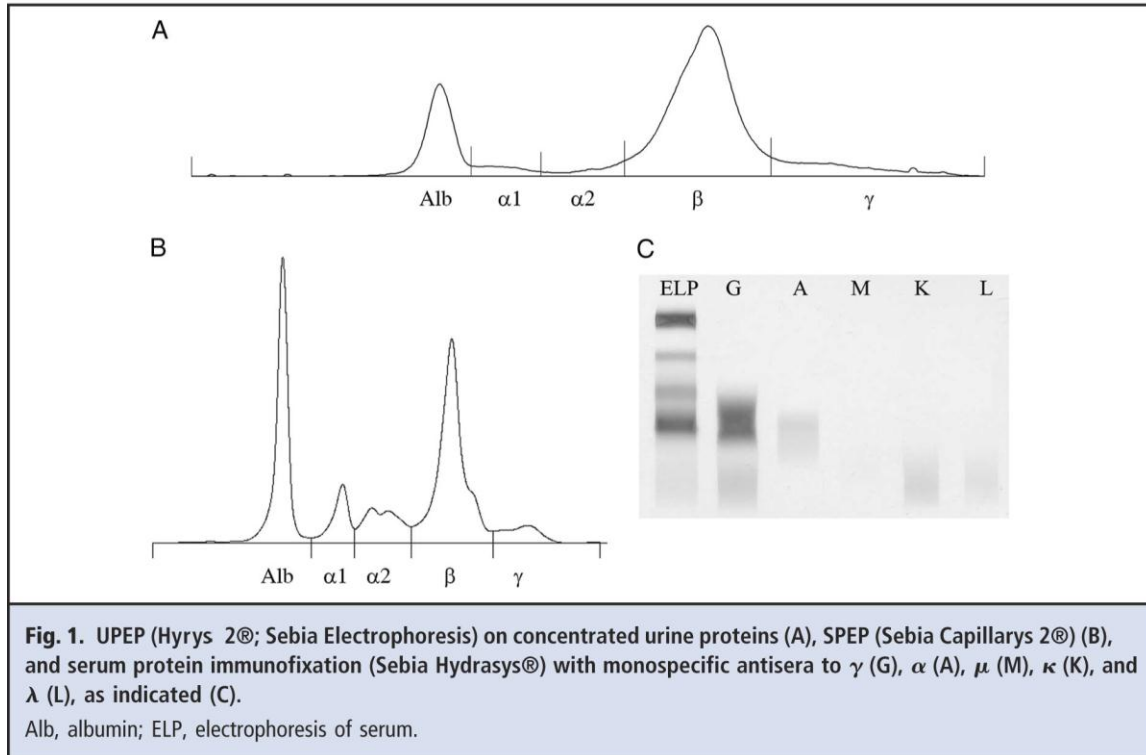
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CASE

A 90-year-old man who had a history of transurethral prostate resection for benign prostatic hyperplasia was admitted for left hip pain. A hip radiography examination revealed a large osteolytic lesion in the left greater trochanter, and a bone scintigraphy evaluation showed increased activity in the same area. Because of the patient's history, metastasis from prostate carcinoma was suspected, and bone biopsies were performed the same week. Ten days later, the patient was hospitalized in the emergency department after a fall that fractured the femoral neck. At admission, plasma sodium, chloride, and potassium concentrations were all within their respective reference intervals. The plasma concentration of total protein was 5.0 g/dL (50 g/L) [reference interval, 6.0–8.0 g/dL (60–80 g/L)], and that of albumin was 1.5 g/dL (15 g/L) [reference interval, 3.0–4.5 g/dL (30–45 g/L)]. The albumin-corrected calcium concentration was 10.8 mg/dL (2.69 mmol/L) [reference interval, 9.0–10.6 mg/dL (2.25–2.65 mmol/L)]. Hematology tests showed mild normocytic (mean corpuscular volume, 95.1 fL; reference interval, 80–97 fL]), aregenerative [reticulocyte count, $54 \times 10^3/\mu L$ ($54 \times 10^9/L$); reference interval, $25–80 \times 10^3/\mu L$ ($25–80 \times 10^9/L$)] anemia, with a low hemoglobin concentration [9.9 g/dL (99 g/L); reference interval, 13.0–17.0 g/dL (130–170 g/L)] and leukopenia [$2.5 \times 10^3/\mu L$ ($2.5 \times 10^9/L$); reference interval, $4.0–10.0 \times 10^3/\mu L$ ($4.0–10.0 \times 10^9/L$)]. The plasma creatinine value was 1.1 mg/dL (97 μmol/L) [reference interval, 0.71–1.20 mg/dL (62–106 μmol/L)], and the urea nitrogen concentration was 35.0 mg/dL (12.5 mmol/L) [reference interval, 7.8–19.6 mg/dL (2.8–7.0 mmol/L)]. The urine protein value was 540 mg/24 h (reference interval, 0–150 mg/24 h). Urine protein electrophoresis (UPEP) showed the presence of an unusual spike in the β region (Fig. 1A). We measured an increased urine concentration of free κ light chain [1.4 mg/dL (14 mg/L); reference interval, 0–0.2 mg/dL (0–2 mg/L)], along with a normal concentration of urine β_2-microglobulin.

The patient underwent surgical repair of his left femur. In the meantime, our laboratory asked for serum to complete the investigation of the abnormal UPEP pattern. Investigations of the serum sample revealed a decreased albumin concentration [1.45 g/dL (14.5 g/L); reference interval, 3.0–4.5 g/dL (30–45 g/L)]. Immunoglobulin quantification revealed an increased IgG value [2950 mg/dL (29.5 g/L); reference interval, 700–1000 mg/dL (7–10 g/L)]. IgA and IgM were within their respective reference intervals. Serum protein electrophoresis (SPEP) showed an increased α1 region, along with decreased albumin and γ regions. Moreover, we found an increased β region

(19.1 g/L, quantified from the electrophoresis trace and the total protein concentration), along with a loss of separation between the β1 and β2 regions because of a narrow spike (Fig. 1B). With a normal concentration of β-globulins of approximately 300 mg/dL (3 g/L), we estimated the monoclonal protein concentration at approximately 1600 mg/dL (16 g/L). Serum immunofixation was performed with antibodies specific for heavy chains (G, A, M) and light chains (κ, λ). A band was present in the IgG lane with a β electrophoretic mobility, with no corresponding band for the light chain (Fig. 1C). Serum free light chains included a decreased free κ chain [0.06 mg/dL (0.6 mg/L); reference interval, 0.33–1.94 mg/dL (3.3–19.4 mg/L)], a decreased free λ chain [0.045 mg/dL (0.45 mg/L); reference interval, 0.57–2.63 mg/dL (5.7–26.3 mg/L)], and a normal κ/λ ratio of 1.33 (reference interval, 0.26–1.65). The results of IgG subclass quantification were as follows: IgG1, 768 mg/dL (7.68 g/L) [reference interval, 500–800 mg/dL (5–8 g/L)]; IgG2,<9.0 mg/dL (<0.09 g/L) [reference interval, 90–300 mg/dL (0.9–3 g/L)]; IgG3, 23.0 mg/dL (0.23 g/L) [reference interval, 10–80 mg/dL (0.1–0.8 g/L)]; and IgG4, 1.0 mg/dL (0.01 g/L) [reference interval, 10–60 mg/dL (0.1–0.6 g/L)].

Fig. 1. UPEP (Hyrys 2®; Sebia Electrophoresis) on concentrated urine proteins (A), SPEP (Sebia Capillarys 2®) (B), and serum protein immunofixation (Sebia Hydrasys®) with monospecific antisera to γ (G), α (A), μ (M), κ (K), and λ (L), as indicated (C).
Alb, albumin; ELP, electrophoresis of serum.

Questions to Consider
• What are the potential causes of increased β-globulins?
• What can explain the discrepancy between the presence of κ light chains in the urine and the presence of a monoclonal IgG without light chains in the serum?
• What investigations should be performed to characterize the protein responsible for the spike in the β region of the UPEP results?
• What can explain the observation that the sum of the 4 IgG subclasses [<800 mg/dL (<8 g/L)] was not equal to the total IgG concentration [2950 mg/dL (29.5 g/L)]?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the July 2011 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol57/issue7 and follow the link to the Clinical Case Study and Commentaries.

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