Problematic Proteins: A Patient with a High Paraprotein Concentration

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CASE DESCRIPTION

A 60-year-old man presented to his primary care provider with progressive exercise intolerance and fatigue for the past year. An exercise stress test was normal in January of 2023. However, laboratory studies showed increased serum globulins. He was referred to a hematologist for suspected multiple myeloma. Monoclonal immunoglobulin (Ig) G lambda protein was found in serum. Bone marrow biopsy in May 2023 found 40% clonal plasma cells with high-risk cytogenetic findings (1q21 gain). Positron emission tomography scans showed diffusely increased metabolic activity throughout the skeletal system, limiting evaluation of myelomatous lesions. Laboratory studies to monitor progression included a comprehensive metabolic profile, quantitative immunoglobulins, serum protein electrophoresis (SPE), and immunofixation electrophoresis (IFE).

Blood samples for chemistries were collected in a lithium heparin plasma separator tube, and a specimen for electrophoresis was collected at the same time in a serum separator tube. Testing used primary collection tubes. An Abbott Alinity C analyzer yielded extremely high total protein and IgG concentrations, and low albumin and sodium concentrations (Table 1). Electrolytes were measured by indirect ion-selective electrode methods. Plasma creatinine and urea concentrations were within reference intervals. IgA and IgM were decreased. Agarose gel SPE (Helena SPIFE Touch) yielded a markedly higher albumin concentration than the automated chemistry analysis, gamma-globulins of 2.6 g/dL (26 g/L), and an M-spike of 2.1 g/dL (21 g/L) protein (indicated by a green arrow in Fig. 1A), contrasting with a measured IgG concentration of nearly 8 g/dL (80 g/L). IFE showed that the paraprotein was IgG lambda (Fig. 1B). Specimens were not hemolyzed or lipemic. No problems with other patient specimens or quality controls occurred. The large difference in results from chemistry analysis vs SPE raised the question of which method was correct. Similar discrepancies had been obtained for chemistries and SPE for the same patient 10 days before, raising questions from clinicians about the reliability of the laboratory analyses.

Testing on the Alinity analyzer was repeated 5 days later using the plasma specimen, which had been stored capped and refrigerated to maintain stability. The repeat chemistry analyses showed substantial differences vs the initial analysis and raised additional questions about the consistency of the chemistry results (Table 1). Determining the true value of paraprotein concentration was important for initiating treatment and qualification for clinical trials. There was also a question about whether the patient was truly hyponatremic, considering the substantial difference between initial and repeat sodium concentrations.

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QUESTIONS TO CONSIDER	
1.	What caused the large difference between the quantitative IgG result and the quantitation of the M-spike on SPE?
2.	Why was serum albumin on the chemistry analyzer much lower than on SPE?
3.	What effect does increased total protein concentration have on serum sodium measurement?
4.	What other tests could help distinguish between pseudohyponatremia and true hyponatremia?

Table 1. Values from SPE and automated chemistries.

SPE			Automated chemistries			
Fraction	g/dL	Ref. range		Initial	Repeat	Ref. range
Total protein	12.3	(6.6–8.7)	Total protein	12.4	8.7	(6.8–8.7 g/dL)
Gamma	2.65	(0.5–1.6)	IgG	7998	3139	(700–1600 mg/dL)
• (M-spike 2.11 in gamma)			IgA	42	51	(70–400 mg/dL)
Beta	1.90	(0.6–1.3)	IgM	46	61	(40–230 mg/dL)
Alpha-2	1.44	(0.4–1.0)	Albumin	2.9	3.6	(3.5–5.2 g/dL)
Alpha 1	0.48	(0.1–0.4)	BUN	16	17	(6–23 mg/dL)
Albumin	5.92	(3.3–5.0)	Creatinine	0.9	1.1	(0.7–1.3 mg/dL)
			Sodium	121	137	(135–145 mmol/L)
			Potassium	3.7	4.5	(4.5–5.1 mmol/L)
			Chloride	101	106	(96–107 mmol/L)
			CO_2	21	20	(22–30 mmol/L)

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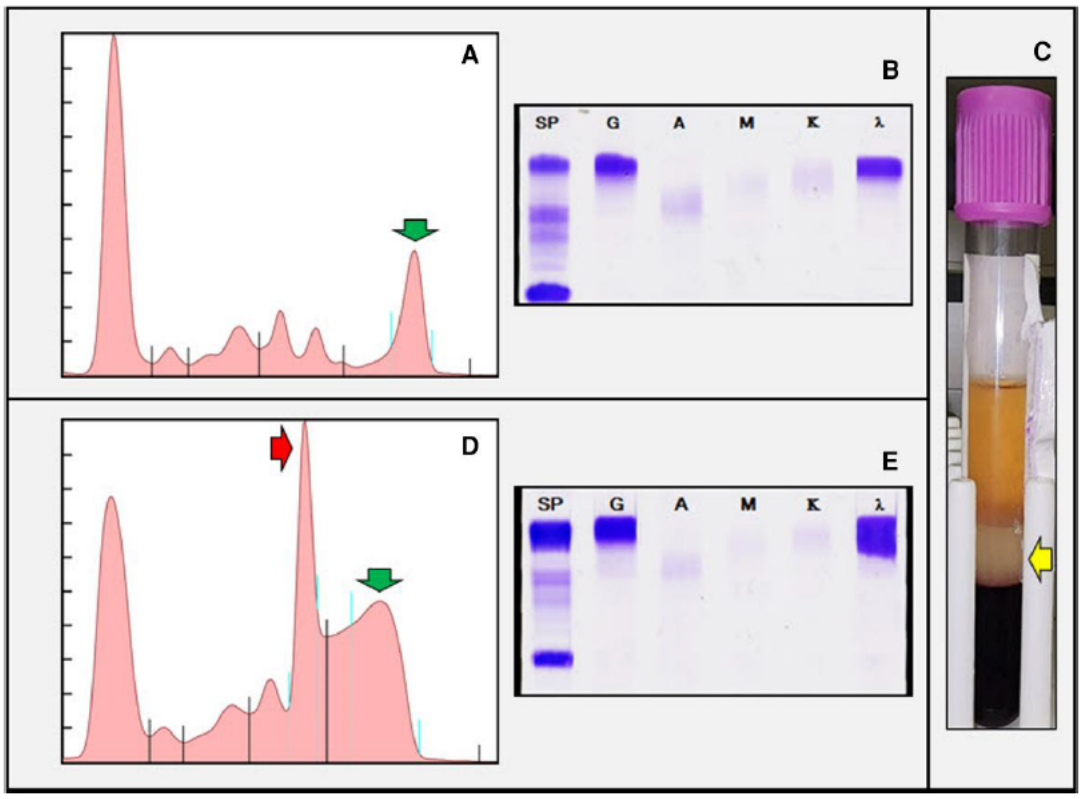

Fig. 1. Serum analysis. (A), Initial SPE scan; (B), Immunofixation electrophoresis (IFE) with lanes for total protein (SP), IgG, IgA, IgM, kappa, and lambda; (C), Photograph of EDTA collection tube with arrow indicating cryoprecipitate; (D), SPE after warming of specimen; (E), IFE of warmed specimen.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the July 2024 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/70/7 and follow the link to the Clinical Case Study and Commentaries.

Educational Centers

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