Complex Hyponatremia in a Cancer Patient with Hypercholesterolemia

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CASE DESCRIPTION

A 76-year-old male with a past medical history of type 2 diabetes mellitus, hyperlipidemia, and coronary artery disease presented for outpatient endoscopic retrograde cholangiopancreatography (ERCP) due to painless jaundice which was suggestive of malignancy. Biopsies and stenting were performed during the procedure, and the patient was promptly admitted to the medical intensive care unit (ICU) due to severe hyponatremia (plasma sodium 111 mEq/L).

In the days leading up to his procedure, both the patient and his wife noted some increased confusion but the patient had no other neurologic symptoms. He did not drink alcohol or use illicit substances. Over concerns of new malignancy, the patient had adopted a “hypernutrition” diet for the past 2 weeks consisting of one pound of spinach daily in smoothies mixed with fruit, chia, and flax seeds. He also consumed one gallon of water daily and followed an online program to “rid him of toxins.” He was not taking any medications associated with hyponatremia and had not had any changes to his medications other than recent discontinuation of atorvastatin and gemfibrozil due to liver dysfunction.

Physical examination revealed jaundice, scleral icterus, and dry mucous membranes, but was otherwise unremarkable. No neurologic deficits or focal neurologic signs were observed. Liver function tests were notable for elevations in alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, and prothrombin time/international normalized ratio (PT/INR) (Table 1).

Upon admission to the ICU, plasma and whole blood sodium were measured, confirming the low values at 114 mEq/L and 125 mEq/L, respectively. Plasma and urine osmolality were also low at 268 mOsm/kg and 207 mOsm/kg, respectively, and urine sodium was 31 mEq/L. Concern for pseudohyponatremia prompted a lipid panel, which revealed extremely elevated total cholesterol (964 mg/dL or 25.0 mmol/L, desirable <200 mg/dL or <5.2 mmol/L) and low-density lipoprotein cholesterol (LDL-C) estimated via the Friedewald equation (925 mg/dL or 24.0 mmol/L, desirable ≤130 mg/dL or ≤3.4 mmol/L), with low high-density lipoprotein cholesterol (HDL-C) (6 mg/dL or 0.2 mmol/L, desirable ≥40 mg/dL or ≥1 mmol/L) and slightly elevated triglycerides (166 mg/dL or 1.9 mmol/L, desirable <150 mg/dL or <1.7 mmol/L).

Nephrology was consulted for suspicion of mixed elements of both pseudohyponatremia and true hyponatremia. The patient was initially volume-resuscitated with normal saline boluses, then treated with water restriction and restoration of biliary flow. Sodium increased as the patient’s condition normalized over a 4-day hospital stay. Biopsy from ERCP eventually revealed pancreatic adenocarcinoma.

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QUESTIONS TO CONSIDER	
1.	How should extreme elevations in total cholesterol be clinically approached?
2.	Could the elevated cholesterol impact sodium and in which direction?
3.	What strategies can the clinical laboratory use to investigate potential electrolyte exclusion effects?
4.	In what scenarios might routine lipid measurements be unreliable?

Table 1. Relevant laboratory results prior to and during hospital admission.[a]

	Reference interval	Outpatient pre-procedure	Day 1	Day 2	Day 3	Day 4
Sodium	135–145 mEq/L	111	114	117	120	125
Sodium—whole blood	135–145 mEq/L		125	128	132	134
Potassium	3.5–5.0 mEq/L	4.0		3.8	3.6	3.6
Chloride	95–107 mEq/L	77		86	91	95
CO2	22–29 mEq/L	22		22	20	18
BUN[b]	10–20 mg/dL	11		12	10	13
Creatinine[c]	0.67–1.17 mg/dL	0.91		0.90	0.72	0.81
Glucose[d]	65–139 mg/dL			147	166	200
Calcium[e]	8.5–10.5 mg/dL			8.5	8.6	8.9
Albumin[f]	3.4–4.8 g/dL			2.8	2.8	2.9
ALP	40–129 U/L	1709		1255	1076	910
ALT	0–41 U/L	157		90	65	56
AST	0–40 U/L	115		50	32	28
Direct bilirubin[g]	0–0.2 mg/dL	13.6		5.3	4.1	3.7
Total bilirubin[g]	0–1.2 mg/dL	18.7		7.6	6.2	5.9
Total protein	6.0–8.0 g/dL			5.4	5.8	6.0
PT—citrate plasma	9–12 s	13		14		15
INR—citrate plasma	<4.0	1.2		1.3		1.5
Osmolality	280–300 mOsm/kg		268	269	288	
Osmolality—urine	350–1050 mOsm/kg		207	338	592	646
Sodium—urine	mEq/L		31	44		

Abbreviations: BUN, blood urea nitrogen; CO2, carbon dioxide; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT, prothrombin time; INR, international normalized ratio.
[a]Unless otherwise specified, tests were performed on lithium heparin plasma.
[b]BUN mg/dL to mmol/L x0.357.
[c]Creatinine mg/dL to μmol/L x88.4.
[d]Glucose mg/dL to mmol/L x0.0555.
[e]Calcium mg/dL to mmol/L x0.25.
[f]Albumin and total protein g/dL to g/L x10.
[g]Direct and total bilirubin mg/dL to μmol/L x17.1.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the September 2025 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/71/9 and follow the link to the Clinical Case Study and Commentaries.

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