

Electrolyte Derangements when Ectopic Cushing's Is Included in Dual Paraneoplastic Syndrome



To the Editor:

Although ectopic adrenocorticotrophic hormone (ACTH) syndrome is typically characterized by hypokalemia, which may be refractory to treatment, as in the recently reported case,¹ the occasional patient presents with concurrent hyponatremia, as depicted in several case studies.²⁻⁵ This biochemical association is attributable to the rarely reported paraneoplastic syndrome of coexistence of ectopic ACTH secretion and syndrome of inappropriate antidiuretic hormone secretion.²⁻⁴ The underlying cause was small-cell lung cancer in all 11 fully investigated cases.²⁻⁴ Among patients with this syndrome (the so-called “dual paraneoplastic syndrome”), plasma ACTH levels have ranged from “high normal”² to 851 pg/mL.⁴ In the 91-year-old patient who presented with hyponatremia and hypokalemia (the latter easily reversed by administration of triamterene),⁵ hyponatremia was initially incorrectly attributed to triggering of inappropriate secretion of antidiuretic hormone by congestive heart failure (because chest radiography showed cardiomegaly and pulmonary congestion).⁵ When the provisional diagnosis was subsequently revised (again incorrectly) to hypoadrenalism-related hyponatremia, a short synacthen test was performed, which yielded the following results:

Basal (9 am) plasma cortisol, 310.7 mcg/dL
Plasma cortisol 30 minutes after a 250-mcg dose of intravenous 1-24 tetracosactrin amounted to 464 mcg/dL

Additionally, plasma osmolality was documented as 259 mOsm/kg, but there was no evaluation of plasma vasopressin or urine osmolality.

On the afternoon of the short synacthen test, the patient underwent abdominal computed tomography, which revealed bilateral adrenal hyperplasia and hepatic metastases. These findings prompted a revision of the diagnosis to ectopic

ACTH syndrome. This time, plasma ACTH was measured, and this registered a level of 64 pg/mL with concurrent plasma cortisol of 609 mcg/dL. The corresponding plasma ACTH precursor level amounted to 2704 pmol/L (reference range 5-34 pmol/L). Repeat chest radiography showed mediastinal lymphadenopathy. She died the following day. No autopsy was performed.

COMMENTS

- 1) The coexistence of hypokalemia and hyponatremia should raise the index of suspicion for the possibility of dual paraneoplastic syndrome.
- 2) A high ACTH precursor/ACTH ratio of approximately 48 or more supports a diagnosis of ectopic Cushing's⁶ if plasma ACTH is only modestly elevated.

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<https://doi.org/10.1016/j.amjmed.2019.11.009>

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Funding: None.

Conflict of Interest: None.

Authorship: The author is solely responsible for the content of this manuscript.

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