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CASE REPORT PEER REVIEWED | OPEN ACCESS

Severe hyponatremia in the setting of mediastinal neuroblastoma in an elderly male

Alexander Black, Nishant Gohel, Sankarabharan Kanikireddy

ABSTRACT

Introduction: Neuroblastomas are rare neoplasms with the potential to express paraneoplastic syndromes.

Case Report: We report the case of a 77-year-old male with biopsy-confirmed unresectable anterior mediastinal neuroblastoma with symptomatic hyponatremia likely due to paraneoplastic syndrome of inappropriate antidiuretic hormone (SIADH). He had multiple inpatient admissions for symptomatic hyponatremia over the 3-year period that we examined, with a paucity of admissions during chemoreduction with adjuvant radiation therapy. Due to the rarity of this tumor, there is no standard treatment protocol and the literature regarding these neoplasms exists primarily as case reports.

Conclusion: This case report adds to the existing literature detailing paraneoplastic SIADH in the setting of mediastinal neuroblastoma in adults and highlights the importance for oncologists to be cognizant of this syndrome as a complication of a particular rare malignancy.

Keywords: Hyponatremia, Neuroblastoma, Oncology, Paraneoplastic syndrome

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INTRODUCTION

Neuroblastomas are neoplasms of neural crest cell origin and are classically thought of as childhood tumors. They are associated with amplification of the n-MYC oncogene and have an association with Beckwith–Weidemann syndrome and opsoclonus-myoclonus ataxia syndrome [1]. According to the Surveillance, Epidemiology, and End-Results cancer database the overall incidence in adults is 0.12 cases per million per year from 1998 to 2002 [2]. Herein, we detail a case of an anterior mediastinal neuroblastoma in an adult with likely paraneoplastic syndrome of inappropriate antidiuretic hormone (SIADH).

CASE REPORT

A 77-year-old male with past medical history of hypertension, type II diabetes, coronary artery disease, atrial fibrillation, and anterior mediastinal neuroblastoma presented to the emergency department (ED) with a chief complaint of confusion. He is status-post mediastinoscopy/thoracotomy with anterior Chamberlain procedure (Lvl. 5, left) in 2018 after discovery of a large anterior mediastinal mass involving the pericardium at the left cardiac apex extending to regional lymph nodes. Computed tomography (CT) images taken in 2018 can be seen in Figures 1–3. Tissue biopsy was sent to a tertiary facility for specialized

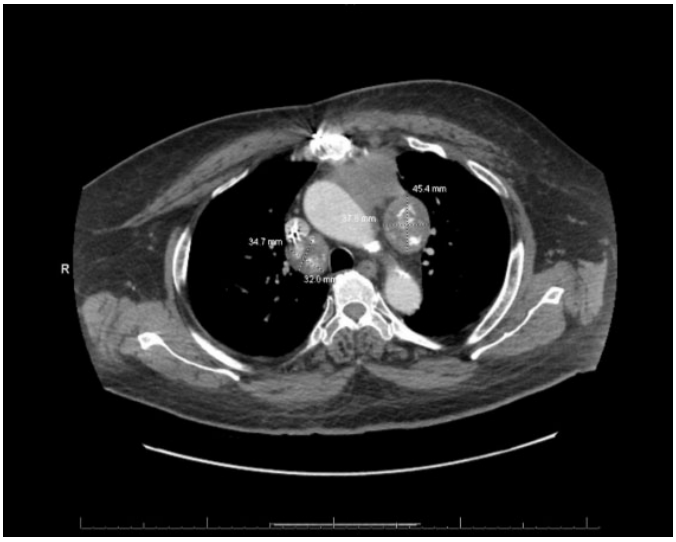

Figure 1: CT chest with IV contrast, 2018.

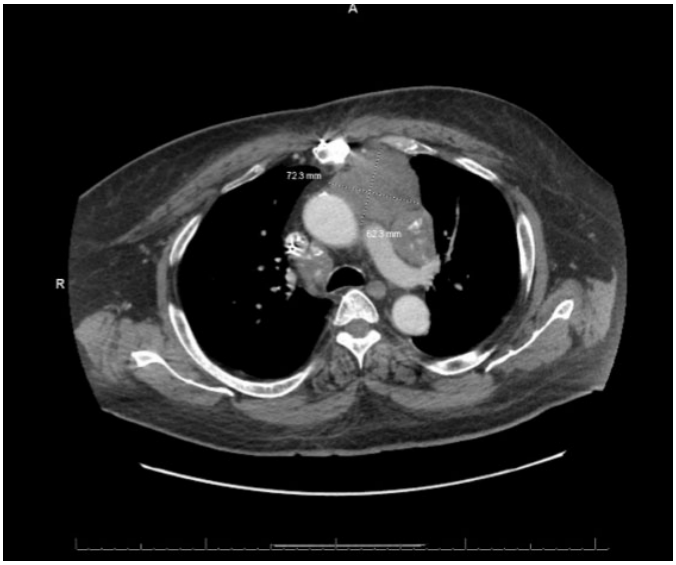

Figure 2: CT chest with IV contrast, 2018.

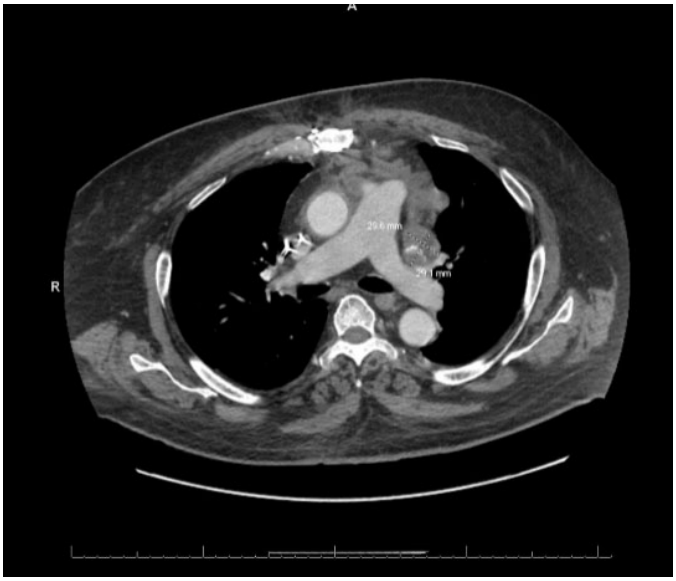

Figure 3: CT chest with IV contrast, 2018.

evaluation. Immunohistochemistry was negative for pankeratin, desmin, myogenin, S100, CD34, and CD99. Additional stains were significant for synaptophysin (+), chromogranin (focal +), and SM311 (+). ALK studies by polymerase chain reaction (exons 23 and 25) and fluorescence in situ hybridization were negative. These findings led to a diagnosis of neuroblastoma.

Due to the location and extent of the neoplasm, he was not a candidate for surgical excision and was treated with 4 cycles of cisplatin and etoposide with adjuvant radiation over the following 18 months. Subsequent imaging revealed L2 vertebral sclerosis suspicious for metastasis as well as multiple calcified mediastinal lymph nodes. Computed tomography-guided biopsy of the L2 vertebrae revealed metastatic disease. He continued chemotherapy with carboplatin and etoposide with radiation at L1–L3 and mediastinum for the following approximately six months. His oncologic course was remarkable for radiation pneumonitis which was treated with prednisone and resolved. Repeat CT imaging at this time showed reduction in anterior mediastinal tumor size (Figure 4) and mediastinal adenopathy. However, follow-up positron emission tomography (PET) revealed new uptake in the C3 vertebrae, consistent with progressive metastasis.

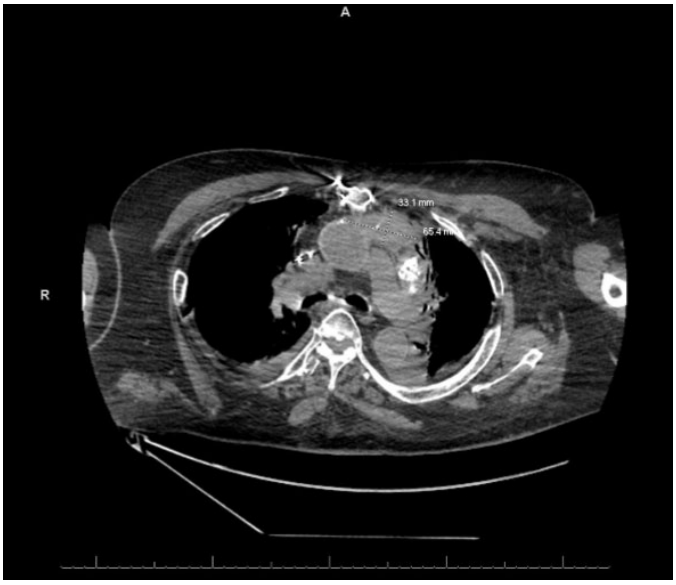

Figure 4: CT chest, 2021—showing reduction in anterior mediastinal mass size compared to prior (Figure 2).

Informed Consent

Protected health information (PHI) removed; no identifying information was present.

Clinical Findings

The patient showed signs of confusion, lethargy, and shortness of breath worsening over several days according to his wife. He arrived via ambulance as a transfer from urgent care on 2 L nasal cannula with stable vital signs.

He was placed on positive pressure ventilation in the ED. He was alert and oriented ×2 and able to answer basic questions. Other physical exam findings were normal.

Diagnostic Assessment and Therapeutic Intervention

Chest X-ray in the ED showed bilateral chronic pleural effusions with no acute changes. He was evaluated for acute respiratory failure and treated with positive pressure ventilation. Head CT without contrast showed chronic atrophy with no acute changes. His workup at urgent care was significant for a serum sodium of 112 mmol/L and he began receiving empiric treatment with 3% normal saline prior to transfer. The hospitalist admitted the patient to the intensive care unit (ICU) for close monitoring. The patient spent five days in the ICU receiving treatment for hyponatremia and respiratory failure including rate-adjusted intravenous (IV) 3% saline with serum chemistries every 3 hours and positive pressure ventilation, respectively before step-down to the medicine floor. He did not require intubation at any point. On hospital day eight, repeat chest CT showed worsening lower lobe pleural effusions. He subsequently underwent bedside thoracentesis which yielded 700 cc of amber fluid and improvement of his respiratory status.

Consultation by nephrology suggested that SIADH was the most likely etiology of this patient's persistent hyponatremia. Definitive diagnosis could not be made in the setting of outpatient diuretic use and inpatient treatment with 3% saline because these pharmacotherapies would skew urine and serum osmolality studies. However, in this patient we could rule out other possible causes of hyponatremia. The presence of a large pleural effusion, stable vital signs, serum sodium of 112 mmol/L, normal renal function (blood urea nitrogen of 13 mg/dL, creatinine of 0.95 mg/dL, and glomerular filtration rate of 74 mL/min), and no signs of infection or liver disease further suggested SIADH as well. All of this is in the context of similar recurrent admissions for hyponatremia in the setting of anterior mediastinal neuroblastoma. Table 1 demonstrates lab values upon admission. The patient was stabilized over the course of 10 days and discharged with normal serum sodium of 137 mmol/L and continuing symptomatic treatment.

Table 1: The patient's laboratory values upon admission, which are most significant for acute respiratory acidosis and severe hyponatremia with hypochloremia

Labs	Value
Na^+	112 mmol/L
Cl^-	79 mmol/L
BUN	13
Cr	0.95
eGFR	74 mL/min
Blood glucose	91 mg/dL
Urine osmolality	370
Urine WBC/HPF	11
Platelets	138 K/uL
WBC	9.4 K/uL
Bilirubin	0.8 mg/dL
ALP	142 U/L
Ammonia	33 mmol/L
PTT	82.8 s
Troponin-I	<0.02 ng/L
Blood pH	7.34
PCO_2	52 mmHg
PO_2	68.9 mmHg
HCO_3	27.6 mmHg
COVID-19 rapid antigen	Negative
Pro-BNP	2641 pg/mL
CRP	30.1 mg/L
Lactate	0.8 mmol/L
Procalcitonin	0.08 ng/mL

Prolonged partial thromboplastin time (PTT) is consistent with outpatient dabigatran use.
Abbreviations: BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; WBC, white blood cell; HPF, high power field; ALP, alkaline phosphatase; PTT, partial thromboplastin time; BNP, brain natriuretic peptide; CRP, c-reactive protein.

DISCUSSION

In general, assessment of volume status is one of the most important first steps in diagnosis and treatment of hyponatremia. The development of hyponatremia is propagated by imbalance between total body water and total body sodium. In a vacuum absent of comorbidities and pharmacologic derangements, SIADH causes a euvolemic hyponatremia. Over-secretion of ADH leads to unbalanced resorption of free water, effectively diluting the serum sodium concentration. The diagnostic workup for hyponatremia can be visualized in Figure 5. There are many different causes of SIADH including drugs, trauma, genetic disorders, and paraneoplastic syndrome. Paraneoplastic SIADH is classically associated with small cell carcinoma of the lung, but has been characterized with many other malignancies. The histogenesis of mediastinal neuroblastomas is unknown but it is postulated that they may arise from mediastinal teratomas, autonomic ganglia in the thymus, residual neuroectodermal cells in the thymus, or thymic epithelial cells that differentiate into neural cells [3, 4].

There are few other accounts of adult anterior mediastinal neuroblastoma with paraneoplastic SIADH. Pelligrino et al. [5] detail the case of an 80-year-old female presenting with severe symptomatic hyponatremia (114

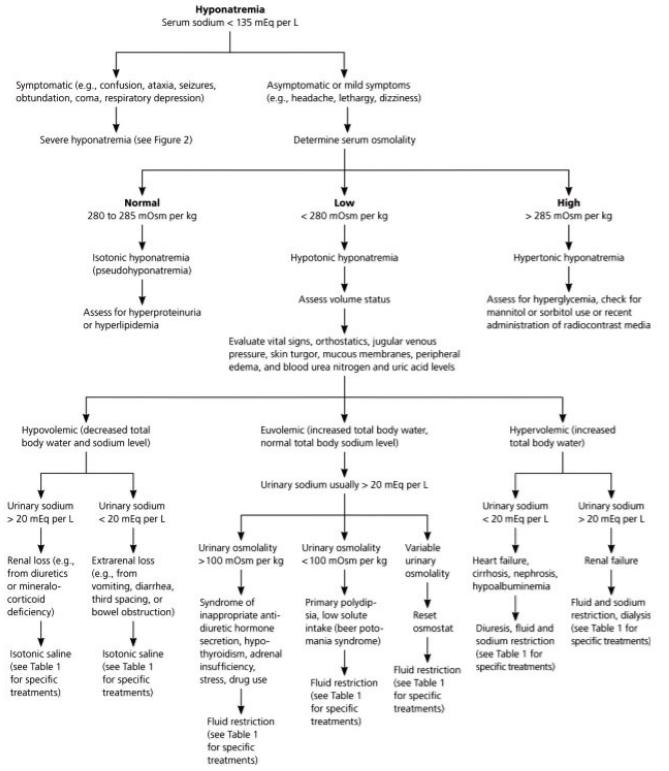

Figure 5: Diagnostic algorithm for hyponatremia from Braun et al. Diagnosis and management of sodium disorders: Hyponatremia and hypernatremia. Am Fam Physician 2015;91(5):299–307 [3].

mEq/L) in the setting of biopsy-confirmed anterior mediastinal neuroblastoma. Similarly, this patient's hyponatremia was refractory to medical intervention, however, surgical resection of the tumor resulted in resolution of symptoms and normalized the patient's serum sodium. Further, Ogawa et al. [6] describe a 60-year-old male with low serum sodium and elevated serum ADH in the presence of a biopsy-confirmed thymic neuroblastoma. Surgical resection of the non-invading mass again resulted in quick resolution of the patient's symptoms and correction of his serum sodium.

Although there is no established standard of care for mediastinal neuroblastomas, most of the literature presents surgical resection as curative whereas symptomatic control and chemoreduction are used when the patient cannot undergo resection.

In our case the patient was not a surgical candidate because he had metastatic disease at time of diagnosis as well as infiltration of the pericardium at the cardiac apex, so instead underwent chemoreduction and supportive care. Interestingly, he had no admissions during his multiple rounds of chemoreduction, likely due to remission of his cancer during treatment. However, as his disease progressed leading to withdrawal of chemotherapy, he had multiple admissions for symptomatic hyponatremia. This can be visualized in Figure 6.

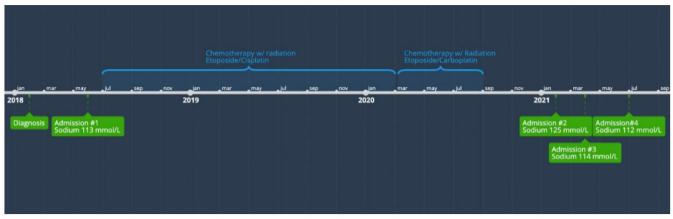

Figure 6: This timeline demonstrates four admissions for symptomatic hyponatremia (green) over a three-year period from 2018 to 2021, with a paucity of admissions during treatment with chemoreduction and adjuvant radiation (blue) likely due to cancer in remission during treatment.

CONCLUSION

Anterior mediastinal neuroblastoma is an exceedingly rare tumor in adults and is associated with SIADH. Our case supports the literature with the unique perspective of a patient who has multiple admissions for refractory hyponatremia over a 3-year period in the setting of non-resectable anterior mediastinal neuroblastoma. Thus, neuroendocrine tumors should remain on the physician's differential diagnosis in elderly patients presenting with SIADH, especially if more common causes can be ruled out.

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Author Contributions

Alexander Black – Design of the work, Acquisition of data, Drafting the work, Revising the work critically for

important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Nishant Gohel – Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Sankarabharan Kanikireddy – Conception of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

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Consent Statement
Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.