THYMIC CARCINOMA AS A CAUSE OF SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE

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Abstract

Thymic neuroendocrine tumors (TNET) are rare neoplasms, typically presenting as anterior mediastinal masses. Often, they present aggressively with locoregional and/or distant metastases. Paraneoplastic syndromes can also be associated with these tumors. A paucity of literature exists on these uncommon malignancies and their treatment options. In rare cases of localized tumors, surgical resection with curative intent may be considered. We present such a case with emphasis on preoperative workup and imaging, minimally invasive technique, and consideration for adjuvant therapies.

A 41year old female with 3-month history of nausea, vomiting, and general weakness with known intractable hyponatremia and reportedly normal imaging at an outside hospital was hospitalized for electrolyte management. She underwent extensive evaluation that ultimately revealed an anterior mediastinal mass with FDG-avidity on Dotatate-PET/CT scan. This, along with a normal brain MRI, confirmed this solitary lesion to be the most likely trigger of her syndrome of inappropriate antidiuretic hormone (SIADH). This paraneoplastic process was leading to profound and refractory hyponatremia and debilitating symptoms. Following intensive preoperative fluid and electrolyte management to achieve eunatremia, she underwent a left thoracoscopic total thymectomy to fully resect the completely encapsulated intrathymic tumor.

Under general anesthesia with double-lumen endotracheal intubation, thoracoscopy with carbon dioxide insufflation was performed in right lateral decubitus position. The thymic lesion was identified and the left lower pole was dissected out. The mass was taken off of the pericardium posteriorly within its own capsule. Both upper poles were dissected to their most cephalad extent prior to division. The dissection was carried along the right lateral border down to the right lower pole with complete excision. No chest tube was used. Postoperatively, she remained eunatremic without further intervention. Final pathology revealed a TNET classified as a thymic small cell carcinoma.

This is the first report of surgical resection of a thymic small cell carcinoma with associated SIADH. These carcinomas make up a small but highly aggressive portion of the uncommon TNETs. They typically present with regional or distant spread and can also be associated with various paraneoplastic syndromes, including SIADH. In the exceptional circumstance of early detection of localized disease, a curative-intent minimally invasive resection is safe and feasible following appropriate preoperative staging and management of paraneoplastic syndromes. It remains unclear whether adjuvant local or systemic therapies are indicated. However, they are likely to be offered due to the poor prognosis of this rare tumor, given that it often presents at later stages.

Case Presentation

HPI:

- 41 F with 3-month history of nausea, vomiting, and general weakness and known hyponatremia with sodium levels as low as 110 mmol/L requiring hospitalization.
- Other associated symptoms: difficulty walking, headaches, palpitations, and cognitive disturbances.
- Treated with fluid restriction and sodium chloride oral supplements for SIADH.

PMHx/PSHx/FHx:

- Previously healthy. Prior breast augmentation (silicone implants).
- Non-contributory family history.

Physical Exam:

- Normal

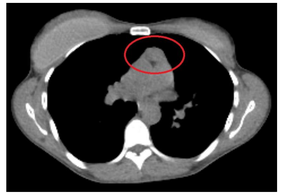
Work-Up

Labs:

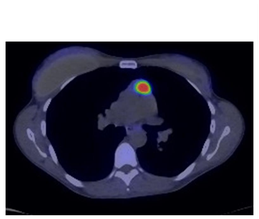
- Na 129 mmol/L, Cl 92 mmol/L.
- Serum osmolality low, urine osmolality normal, and random urine Na inappropriately elevated.
- All other labs including electrolytes, creatinine/GFR, and endocrine panel were normal.

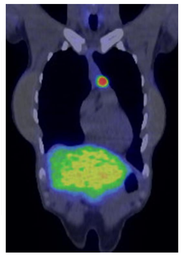
Imaging:

- Brain MRI – normal including pituitary gland and hypothalamus.
- Outside CT chest/abdomen/pelvis – read as normal at outside hospital (see below).



- Dotatate-PET scan performed at our institution – FDG-avid (SUV max 9.7) anterior mediastinal mass measuring 2.4 x 1.7 cm (see below).





Differential Dx:

- Thymoma, thymic NET (carcinoid), thymic cyst, thymolipoma, lymphoma, germ cell tumor, ectopic parathyroid or thyroid tissue, or SIADH with concomitant, occult metastasis and unknown primary → Anterior mediastinal mass is most likely a thymic NET and the cause of SIADH.

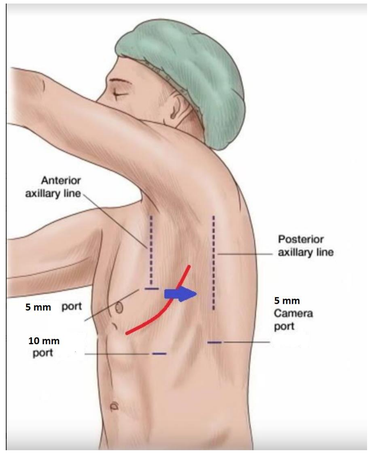
Operative Approach

Approach:

- Thoracoscopic en-block resection of the mass and the thymus gland.
- General anesthesia, a double-lumen endotracheal tube, and right lateral decubitus positioning.

Port placement:

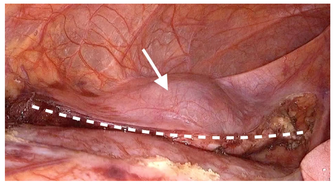
- A 5 mm incision in the 5th intercostal space was made 2 cm anterior to the tip of the scapula. A Veress needle was introduced into the pleural space and a pneumothorax was induced using carbon dioxide gas insufflation. The Veress needle was withdrawn and a 5 mm airtight Thoracoport was then introduced.
- Using a 5mm 30-degree thoracoscope, the left hemithorax was examined and the lungs and pleura appeared normal with no evidence of adhesions or effusions. Another airtight 5 mm Thoracoport was placed in the 3rd intercostal space anterior to the first port. This was placed posterior to the anterior axillary line in order to avoid the patient's left breast implant (see below, blue arrow indicating more posterior placement than usual). A 10 mm Thoracoport was then placed in the 7th intercostal space anteriorly.



Operative Technique

Technique:

- The thymic lesion was easily identified (see below, white arrow) and dissection was initiated on the left lower pole (shown with white dotted line). During the operation, we never grabbed the mass with any instruments and instead deflected away by pushing to create tension.

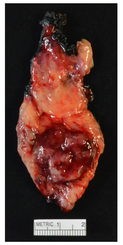


- The mass was taken off of the pericardial surface posteriorly and then anteriorly, within its own capsule. The left phrenic nerve was identified and preserved along its entire course.
- After dissecting the left lateral edge, we turned our attention to the right side of the mediastinum. Following identification of the innominate vein and clipping 2 perforating vessels draining the thymus, we carried our dissection up to the upper poles.
- Both upper poles were dissected to their most cephalad extent prior to dividing. We then completed the dissection along the right lateral border all the way down to the right lower pole, which was completely excised.
- Finally, the retrosternal attachments were divided to fully mobilize the gland and remove it within a surgical bag. No chest tube was placed.
- Frozen pathology: negative surgical margins, 2.7 cm encapsulated thymic carcinoid tumor.

Pathology & Postoperative Course

- Final pathology: 25 g, 2.7 x 1.1 cm fully encapsulated small cell carcinoma confined to the thymus with negative margins.
- Positive for TTF-1, synaptophysin, keratin cam 5.2, and chromogranin (high Ki-67 index).
- The patient was discharged on POD 1 with normal sodium values. Upon follow up, her symptoms had significantly improved.





Discussion

- TNET are the least common primary thymic neoplasm (2-5 %) and <1% of all carcinoids arise in the thymus, leading to incidence of 0.2 per million in the US.
- Median age at diagnosis is 50 and 3x more common in men. 25% of patients have MEN 1. Therefore, genetic testing is crucial.
- 2015 WHO classification for thymic neoplasms is used: low-grade (typical carcinoid), intermediate-grade (atypical carcinoid), and high-grade (large cell neuroendocrine and small cell carcinomas) tumors.
- Small cell carcinomas have >10 mitosis/2 mm^2 and present as anterior mediastinal masses. They can have significant local invasion, and half of patients have involvement of mediastinal lymph nodes while 20-40% have distant metastases at presentation.
- Carcinoid syndrome rarely associated with TNET. Most common paraneoplastic syndrome is Cushing's syndrome (ACTH). There are reports of GH or ANP productions as well. This is the first report of surgical resection of a thymic small cell carcinoma with ectopic ADH production.
- Preoperative imaging was critical to planning a minimally invasive approach for tumor resection. Using CO2 aided in the dissection of the tissues and obviated the need for chest tube placement, allowing for dismissal within 24 hours of operation with minimal pain.

Conclusions

- Thymic small cell carcinomas are very rare anterior mediastinal masses with aggressive locoregional invasion and distant spread.
- They can also present with disabling paraneoplastic syndromes such as SIADH.
- If detected early, and with appropriate preoperative evaluation and imaging, a minimally invasive resection is safe and feasible.
- Using carbon dioxide insufflation and meticulous dissection near critical surrounding mediastinal structures facilitates minimal postoperative pain and morbidity with resolution of debilitating symptoms.

References

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