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A Rare Presentation of Primary Thymic Small Cell Carcinoma Found after Trauma: A Case Report

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Abstract

Thymic small cell carcinoma is an exceedingly rare diagnosis with undefined treatment options and, typically, poor prognosis. A 69-year-old female presented to the Emergency Department with chest pain and was found on Computed Tomography (CT) to have a multilobulated cystic mass in the anterior mediastinum. Magnetic Resonance Imaging (MRI) demonstrated a 7 x 8 x 8 cm mediastinal mass suspicious for thymoma. Biopsies of enlarged lymph nodes in levels 4L and 7 were negative for malignancy.

The patient was taken for surgical resection of the mediastinal mass. After standard sternotomy, the mass was noted to be contiguous with the thymus. The specimen was removed en bloc and surgical pathology revealed high grade neuroendocrine carcinoma, measuring 9.0 cm in greatest dimension, consistent with small cell carcinoma of the thymus. Fibrous adhesions to the lung were noted but all margins and lymph nodes were negative for malignancy. Brain MRI was unremarkable and multidisciplinary tumor board decided to proceed with adjuvant chemotherapy. Patient is currently doing well without symptoms of recurrence one year post-operatively.

Background

Small Cell Carcinoma (SCC) of the thymus is an exceedingly rare diagnosis, occurring in 1 in 5.5 million patients [1]. Thymic SCC is categorized by the World Health Organization as a poorly differentiated, high-grade neuroendocrine carcinoma [2]. Thymic SCC is typically aggressive and often demonstrates local tumor invasion and lymph node involvement upon diagnosis [3]. Due to the low incidence of disease, there is limited data on thymic SCC outcomes and no consensus exists regarding recommended treatment guidelines [4]. This case study describes the diagnosis and management of thymic SCC incidentally found after trauma.

Clinical summary

A 69-year-old female presented to the Emergency Department with chest pain that began after sustaining a fall. She did not have any traumatic injuries upon workup but was incidentally found on Computed Tomography (CT) to have a large, multilobulated cystic mass in the anterior mediastinum. Further workup with Magnetic Resonance Imaging (MRI) was performed, which showed a 7 cm

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x 8 cm x 8 cm mediastinal mass centered at the aortopulmonary window (Figure 1). The mass was heterogenous and multiseptated, demonstrating internal necrosis and delayed enhancement.

A fine needle biopsy was non-diagnostic and an endobronchial ultrasound-guided biopsy of enlarged lymph nodes in levels 4L and 7 were negative for malignancy. Due to persistent chest pain despite lack of traumatic injury, the patient was then taken for surgical resection of the mediastinal mass for therapeutic and diagnostic intent. Standard sternotomy was performed, and the mass was noted to be contiguous with the thymus. Due to dense adhesions, the mass was dissected along with part of the pericardium and a wedge of the left upper lung lobe. The left phrenic nerve was involved with the tumor and sacrificed. The specimen was removed en bloc, measuring 9.0 x 6.0 x 5.0 cm and demonstrating areas of focal hemorrhage and friable necrosis (Figure 2). The patient had an uncomplicated post-operative course and was discharged home on postoperative day 4. Surgical pathology revealed high grade neuroendocrine carcinoma, measuring 9.0 cm in greatest dimension, most consistent with thymic SCC. Focal involvement of the lung with fibrous adhesions was noted but all margins and lymph nodes were negative for malignancy.

Upon diagnosis of thymic SCC, the patient was presented at our multidisciplinary tumor board. A brain MRI was obtained to complete staging, which revealed no metastatic disease. The decision was made to proceed with adjuvant chemotherapy with a regimen including cisplatin and etoposide. Patient completed 3 out of 4 cycles but opted to discontinue further treatment due to adverse effects. She continues to receive routine surveillance that has been unremarkable. Patient is currently doing well without recurrence 2 years post-operatively.

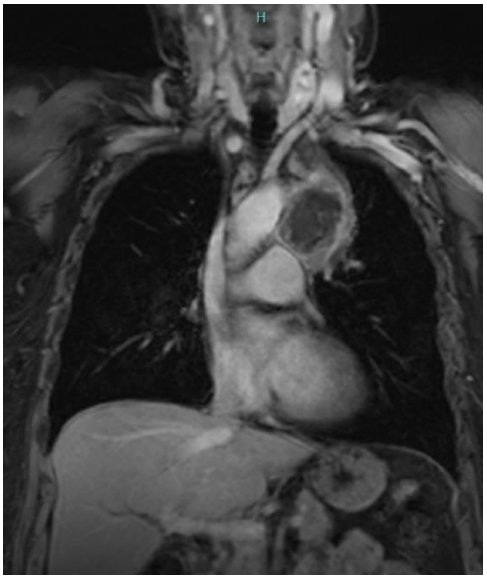

Figure 1: Magnetic resonance image of anterior mediastinal mass.

Discussion

Less than 400 cases of Neuroendocrine Tumors of The Thymus (NETTs) have been reported in the literature, of which only a small fraction represent cases of thymic SCC [5]. NETT outcomes vary based on histologic subtype, with thymic SCC demonstrating a poor prognosis [6]. While the 5-year survival of other NETTs is 30-70%, that of the SCC subtype is 0% with median survival of 13.75 months [7]. When found, NETTs are relatively large tumors

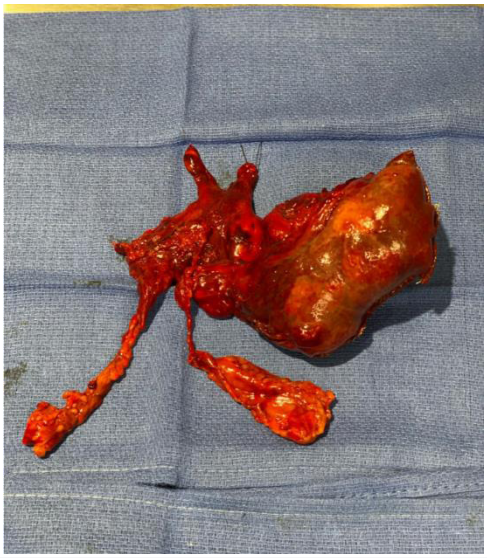

Figure 2: Necrotic, tan-pink mass (9.0 x 6.0 x 5.0 cm) with focal hemorrhage and friable necrosis.

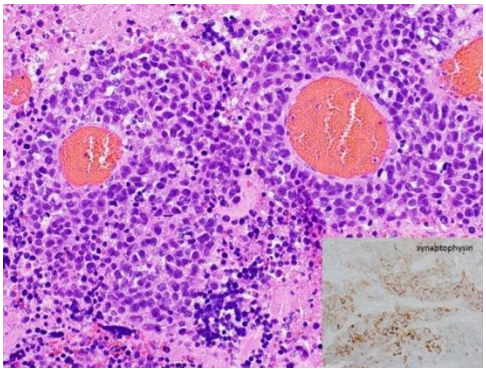

Figure 3: At 200x magnification, cells with eosinophilic cytoplasm in pseudorosettes, cords, and nests and areas of clear cell pattern are seen. Immunohistochemical staining at 200x magnification are positive for pankeratin and synaptophysin, weakly positive for INSM1, and focally positive for CD56.

with a median size of 7.9 cm. Local invasion or compression lead to symptoms like chest pain, dyspnea, or cough in nearly 40% of patients [5,8]. However, a third of patients are asymptomatic and diagnosed incidentally, as was the case in our report [5].

Diagnostic evaluation

Upon discovery of a mediastinal mass, diagnostic workup including imaging and tissue biopsy is recommended. The use of CT or MR imaging techniques are typically used to assess the spread and invasion of disease. Thymic SCC often present radiographically as a large, locally invasive mass in the anterior mediastinum with heterogenous features and areas of necrosis, which was consistent with the characteristics found in our case study [5,9].

Tissue biopsy using core biopsy and parasternal mediastinoscopy have been recommended to obtain histologic diagnosis prior to resection [5]. In our case, fine needle biopsy of the mass and endoscopic ultrasound guided biopsy of suspicious lymph nodes were initially performed. While the lymph node biopsies were negative, the biopsy of the mass was indeterminate. Because of this, further intervention was necessary for diagnosis. While we

would have recommended further minimally invasive interventions for diagnostic purposes, our patient reported persistent chest pain since her fall impacting her quality of life. She did not have radiologic evidence of trauma upon imaging and the pain was not resolving over time, so it was reasonable to believe that the mediastinal mass could be causing this pain. Therefore, the decision to proceed to diagnostic and therapeutic resection was made. In our case, surgical pathology provided diagnosis of thymic SCC with R0 resection and negative lymph nodes. In addition, complete resolution of chest pain was achieved after resection.

Disease management

Complete surgical resection has been associated with improved survival in studies involving patients with thymic SCC and is recommended as the primary treatment for all patients with NETT [5,6,10,11]. In cases of incomplete resection or debulking, survival benefit is reduced or null [6,11]. The addition of lymphadenectomy to resection has been reported with mixed outcomes. While European guidelines recommend including lymphadenectomy to the levels of N1 and N2 for NETTs and thymic carcinomas, there is limited evidence on the survival benefits [6].

While the benefit of surgery has been demonstrated, the role of chemotherapy and radiotherapy is largely unknown. In the neoadjuvant setting, chemotherapy and/or radiation may be helpful in reducing tumor size and increasing rates of R0 resection in NETTs [5]. In the adjuvant setting, studies with patients who achieve complete surgical resection have reported mixed findings. Some studies found chemotherapy to be beneficial while others found it to be a predictor of reduced survival [10,12]. Likewise, radiation after complete surgical resection has resulted in inconsistent findings [11,13]. Literature describing the management of thymic SCCs specifically is limited, as most studies include larger cohorts that include multiple histologic categories. Terada performed a review including 15 cases of thymic SCC. Of these, the most common chemotherapy regimen included a platin-based chemotherapy combined with etoposide [4].

Because patients with thymic malignancy can later be found to have distant metastases, so the addition of adjuvant chemotherapy may be most appropriate in patient groups with high-grade disease, advanced staging, incomplete surgical resection, or recurrence [14]. However, further research including prospective, randomized trials in thymic malignancies as well as studies focused on thymic SCC is needed. As with all cases, it is important to come to a treatment decision after a thorough discussion of risks and benefits. In our case, the decision to pursue adjuvant chemotherapy with carboplatin and etoposide was made.

Surveillance

Approximately 25% of NETTs are associated with MEN-1 syndrome [6]. Bohnenberger and Strobel report that the association between MEN-1 and NETT is limited to typical and atypical carcinoid subtypes [7]. However, the studies describing this association often include a range of NETT histologic subtypes, most often carcinoid in nature [15-17]. Literature describing thymic SCC cases associated with endocrinopathies is limited. There are no guidelines or recommendations regarding the use of genetic testing in thymic SCC. Thorough history and examination, as well as physician discretion, should be utilized.

Regardless of the management strategy selected for thymic SCC, surveillance is recommended due to the high rates of recurrence and distant metastases found in NETTs [5]. Lau and colleagues recommend CT imaging of the head, neck, chest, abdomen, and pelvis at 6-12-month intervals. The addition of nuclear medicine imaging, particularly Gallium-DOTATATE PET/CT, is helpful in cases of uncertainty or bony metastases [6].

Future studies and limitations

The literature describing thymic SCC is limited, and most studies include thymic malignancies of multiple categories within their analyses. Further research investigating outcomes in this patient group is needed, especially due to the poor prognosis associated with this histologic subtype. While prospective, randomized control trials would be ideal, the rarity of this disease would likely make this unfeasible. In the meantime, retrospective cohort studies are beneficial. This report is limited due to its nature as a case report but contributes to the slowly growing pool of thymic SCC patients in the literature.

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