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Case report - Thoracic oncologic

# Neuroendocrine carcinoma of the thymus gland with sternal invasion

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**Abstract**

Large-cell neuroendocrine carcinoma of the thymus is a rare cancer that is more aggressive than other thymic epithelial tumors with poorer prognosis. We report one such case in a 44-year-old male patient with invasion into the upper 2/3rd of the sternum but no endocrinopathy. Complete enbloc resection of the tumor with adherent pericardium, upper 2/3rd of the sternum and mediastinal lymphadenectomy was performed. The chest wall was reconstructed with polypropylene mesh and bilateral pectoralis major muscle advancement flap cover. A search of PubMed database with user query words 'neuroendocrine carcinoma, thymus gland, sternal invasion' revealed no case report in the literature of thymic neuroendocrine carcinoma with invasion of the sternum.


*Keywords:* Neuroendocrine carcinoma; Thymus; Sternal invasion

## 1. Introduction

Thymic neuroendocrine tumors, most of which are atypical carcinoid, have an aggressive biological behavior in contrast with that of generally benign carcinoids that arise elsewhere in the body, in particular, bronchial carcinoid. Rosai and Higa [1] first described this tumor as a distinct clinicopathologic entity separate from thymoma. Large-cell neuroendocrine carcinomas are aggressive tumors composed of predominantly or exclusively neuroendocrine cells which can be demonstrated on immunohistochemistry [2]. Thymic carcinoid tumors represent only 4% of all anterior mediastinal tumors [3]. Symptoms are usually strictly related to the neoplastic mass effects: chest pain, cough, and dyspnea are frequently observed. Complete surgical resection offers the best hope for long-term survival [4–6].

## 2. Case report

A 44-year-old male presented with the complaint of chest pain of four months duration with history of breathlessness on exertion but no complaints of cough, hemoptysis, and loss of consciousness, sweating or palpitation. General physical and systemic examination was unremarkable. Contrast enhanced computed tomography (CECT) scan of the chest and abdomen revealed an $8 \times 7$ cm tumor in the anterior mediastinum with invasion of upper 2/3rd of the sternum (Fig. 1) without any evidence of metastasis. Radionuclide bone scan revealed increased tracer concentration in upper 2/3rd of sternum without any other focus of abnormal radiotracer uptake. A CT-guided fine needle aspirate fine needle aspirate (FNA) from the thymic mass was reported as poorly differentiated carcinoma. Detailed neurological evaluation revealed no evidence of Myasthenia gravis.

The patient underwent enbloc resection of the tumor with pericardium and upper 2/3rd of sternum including terminal 2 cm of costal cartilages of the upper five ribs and medial ends of clavicle on both sides (Fig. 2a). The tumor involved the left phrenic nerve which was also resected. Complete mediastinal lymphadenectomy was performed on both sides. Non-anatomical resection of adherent anterior segment of left upper lobe lung was performed. The pericardial defect was closed with vicryl mesh. The chest wall defect was reconstructed with double layer polypropylene mesh. It was covered with bilateral pectoralis major muscle advancement flap based on thoracoacromial artery (Fig. 2b). Postoperatively, the patient was electively ventilated for 48 h. Following extubation the patient was kept on non-invasive respiratory support for another 48 h. He had an uneventful recovery and was discharged from the hospital on postoperative day 15.

A histological diagnosis of large cell neuroendocrine carcinoma was made based on the morphologic features including necrosis and brisk mitotic activity [$>10$/10 high power field (HPF)] and immunohistochemical positivity for neuroendocrine markers viz. chromogranin and neuron specific enolase (Fig. 2c, d). Lower right paratracheal lymph nodes (two) showed metastatic deposits. Resection margins of the excised tumor specimen were free of tumor.

Following the histopathological diagnosis after surgery, the patient has been started on parenteral octreotide therapy and is also receiving radiotherapy to the mediastinum.

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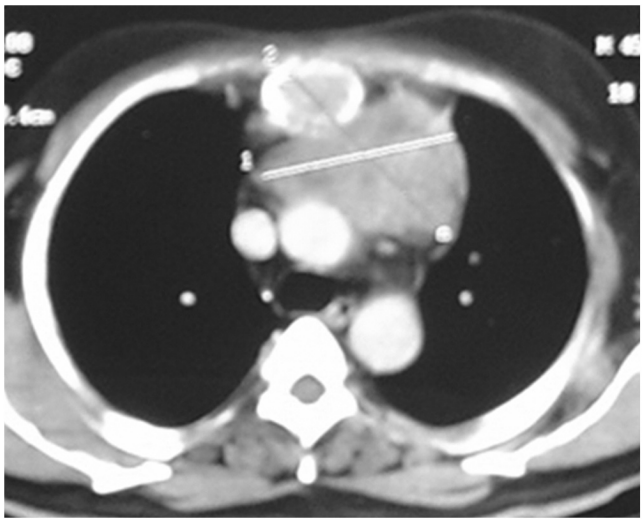

Fig. 1. Contrast enhanced computed tomography (CECT) chest axial section showing a thymic tumor with sternal invasion.

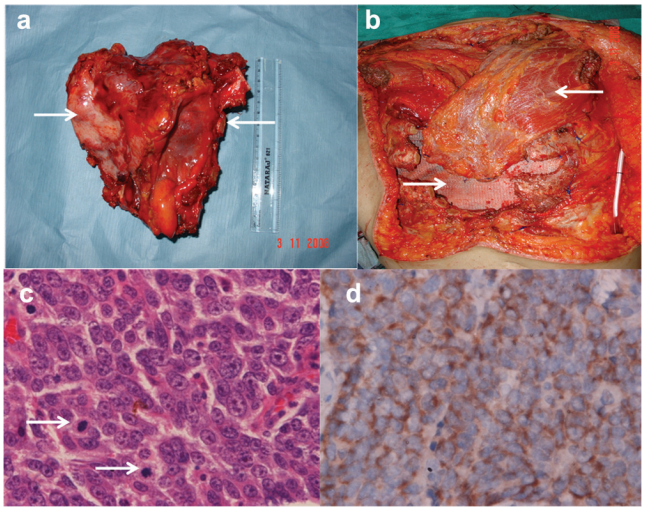


Fig. 2. (a) Excised tumor specimen – right arrow showing pericardium; left arrow pointing to sternum with ends of ribs. (b) Chest wall reconstruction – right arrow (polypropylene mesh); left arrow (pectoralis major muscle). (c, d) Microphotographs (c) showing large tumor cells with frequent mitotic activity (white arrows, hematoxylin and eosin×200). Immunohistochemistry (d) for chromogranin positive in the tumor cells (×200).

## 3. Discussion

The thymus is one of the rarest sites of neuroendocrine tumors (carcinoid) which was first described by Rosai and Higa in 1972 [1]. These tumors are more frequent in men [5]. A clinically apparent endocrinopathy develops in approximately half of the patients, Cushing syndrome being the commonest.

Thymic neuroendocrine carcinomas display an aggressive biological behavior with a tendency to invade adjacent structures (mediastinal fatty tissue, lung, pericardium, and great vessels) and local recurrences as well as distant hematogenous metastases. They often present as locally invasive at the time of diagnosis [7]. Mediastinal lymph node metastases are also frequently observed at presentation [4, 5].

Distant metastases are observed in approximately 20% of patients and the sites include lung, bone, adrenal glands, liver, and spleen, in order of frequency [4].

Radical surgery, when feasible, represents the treatment of choice [4, 6]. Incomplete resections and local recurrences are the factors that influence the outcome [4, 8]. An aggressive approach often includes en-bloc resection of the tumor with the pericardium, lung, great vessels, or all of these [9].

The role of neoadjuvant/adjuvant therapy (chemotherapy or radiotherapy alone or in combination) has not been adequately assessed because of the low number of reported cases. Fukai and associates [5] reported the utility of postoperative radiotherapy to prevent local recurrences of invasive tumor. Similarly, octreotide has demonstrated good antiproliferative activity on neuroendocrine tumors, even if they are metastatic, without important side effects [10].

Our patient had an invasive tumor involving pericardium, mediastinal pleura, and sternum with metastasis to paratracheal lymph nodes. He underwent radical clearance of the tumor and had no postoperative respiratory problem. In view of chromogranin positive tumor, he has been started on long acting octreotide. Serum level of chromogranin A was high before the surgery which became normal at three-month postoperative follow-up visit. He has received adjuvant radiotherapy to the mediastinum to reduce the possibility of local recurrence. We plan to follow-up the patient at three monthly intervals for one year and six-monthly intervals thereafter. These tumors express somatostatin receptors on the cell surface and can be scanned with a radiotracer analogous to somatostatin. We plan to undertake CECT chest along with octreotide scintigraphy and estimation of biochemical marker chromogranin A at six-monthly intervals on the patient to look for loco-regional and distant recurrence of the tumor.

## 4. Conclusion

Primary neuroendocrine thymic carcinomas are rare and aggressive tumors that are often characterized by local invasive behavior as in our patient. The lack of standardized treatment protocol and limited literature experience make it a difficult tumor to treat. Multimodality treatment consisting of radical surgery, adjuvant radiotherapy and somatostatin analogue or chemotherapy is recommended to achieve the best outcome. These experiences should be documented in the literature to learn more about this disease.

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