

An Extremely Rare Case of Primary Anterior Mediastinal Tumor

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Case report

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Abstract

Background: There were very few reports of atypical carcinoid in anterior mediastinum. Atypical carcinoids originating in the mediastinum belong to a neuroendocrine tumor (NET), which is also a very rare clinically aggressive mediastinal tumor.

Case presentation: We herein reported a rare case of NET of mediastinal origin and a review of several cases concerning the clinical and pathological features of this disease, which is often misdiagnosed as atypical carcinoid tumor in mediastinum. The tumor was removed by mid-sternal thoracotomy with superior vena cava formation, left common carotid artery resection and artificial blood vessel replacement, left upper lobe wedge resection, left phrenic nerve resection, left vagus nerve resection and partial pericardectomy.

Conclusions: To the best of our knowledge, this is the sixth atypical carcinoid occurring in mediastinum with proof via histology and IHC. Our findings suggest the difficulty of making a diagnosis before surgery and more cases will need to be reported in order to facilitate the preoperative diagnosis of such a rare tumor.

Introduction

Atypical carcinoids originating in the mediastinum belong to a neuroendocrine tumor (NET), which is also a very rare clinically aggressive mediastinal tumor [1]. NET is divided into typical carcinoid, atypical carcinoid, small cell carcinoma, and large cell neuroendocrine carcinoma according to the different morphology manifested in pathology. Among them, small cell carcinoma and large cell neuroendocrine carcinoma are high-grade tumors, while typical and atypical carcinoids are low-grade tumors [2, 3]. We herein reported a rare case of NET of mediastinal origin and a review of several cases concerning the clinical and pathological features of this disease, which is often misdiagnosed as atypical carcinoid tumor in mediastinum.

Case Presentation

A 45-year-old man was admitted to our hospital for assessment of anterior mediastinum nodule with left chest pain. He had smoked two packs of cigarettes per day for the past 20 years and quit smoking for two months. He denied the other symptoms including the presence of hoarseness, hemoptysis, cough and dyspnea. He had no risk factors for immunodeficiency disease or other infections. Physical examination shown normal breath sound in right of chest field and diminished breath sound on the top of left side of the chest. Laboratory findings were within normal limits. Her Pulmonary function tests and cardiovascular examination revealed normal performance. Contrast-enhanced chest computed tomography (CT) (Figure 1A and 1B) showed partial enhancement in soft tissue, calculating $7.0 \times 5.0 \times 4.0$ cm in size, in the anterior mediastinum, which showed unclear relationship with surrounding blood vessels and tissues.

Then, the mediastinal tumor was removed by mid-sternal thoracotomy with superior vena cava formation, left common carotid artery resection and artificial blood vessel replacement, left upper lobe wedge resection, left phrenic nerve resection, left vagus nerve resection and partial pericardectomy. During the operation, we found that the size of the anterior mediastinum mass was about $7.6 \times 4.8 \times 4.0$ cm. The color of the lesion was yellow-white, whose texture was hard with incomplete envelope and the surface was not smooth. The anterior edge of the lesion was close to the sternum, and the surrounding tissue including the left innominate vein, superior vena cava, left subclavian artery, part of the pericardium and part of the lung tissue were invaded. The lesion also surrounded

the left common carotid artery, left phrenic nerve, left vagus nerve, and recurrent laryngeal nerve. Therefore, we blocked the left common carotid artery during the operation and performed an artificial blood vessel replacement (Figure 1C, arrow). After complete resection of the lesion, tissue of the mass was taken out from the tumor for quick frozen pathology.

Microscopically it showed clusters of medium-sized cells, sometimes with cuboidal morphology, eosinophilic cytoplasm with nuclear pleomorphism and small nucleoli, arranged in trabeculae, nests and lobules and immersed in a hyaline stroma with areas of necrosis. The tumor surrounded medium-sized vessels with perineural and vascular invasion. An infiltration of the adjacent lung parenchyma was observed. No thymic tissue was found. Immunohistochemically, CgA, CD56, Syn, CK19, PCK and GLUT-1 staining was strong positive. But thymus-associated epithelial cell indicators P63 were negative. SSTR2, TdT and CD5 were also negative, and Ki67 index was about 20%-30% in lymphocytes and plasma cells (Figure 2).

After the surgery, contrast-enhanced and 3D reconstruction of thoracic blood vessels CT scan showed successful reconstruction of left common carotid artery (Figure 1D and 1E, Red arrow). The patient was discharged 7 days after the operation with no complication. He had been followed up for one month without evidence of recurrence.

Discussion

Primary neuroendocrine tumor (NET) is mainly composed of neuroendocrine cells, and many organ systems can produce such cancer [2]. NET is divided into three categories based on mitosis count, Ki-67 labeling index, and presence or absence of necrosis, including G1, G2, and G3, corresponding to low-level, intermediate-level, and high-level, respectively [4]. Among them, primary atypical mediastinal neuroendocrine tumors are only reported in very few documents [2, 3, 5-7]. We have summarized them in the Table. At the same time, atypical carcinoids usually have obvious aggressive clinical results, and about 20-30% of patients present with local recurrence or distant metastasis [8]. This aggressive behavior is closely related to its histological grading, and the histological grading itself is directly proportional to the degree of differentiation [9].

In several previous case reports, the primary NET of the anterior mediastinum is highly aggressive and malignant [2, 3, 5-7]. There are significant differences in clinical manifestations of low-grade and intermediate-grade neuroendocrine tumors with high-grade neuroendocrine carcinoma. The first two often occur in young patients (average age 50 years) without obvious gender orientation or smoking history, while high-grade NET mainly occurs in elderly male patients (average age 65 years) and heavy smokers. However, in our case, the patient is only 45 years old and he is a heavy smoker. Common clinical manifestations include chest pain or chest tightness, difficulty breathing, coughing, sweating, superior vena cava obstruction, hoarseness, fainting, or difficulty swallowing. The occurrence of these symptoms may be due to invasion of important tissue structures in the adjacent thoracic cavity or related to the tumor's production of hormones or cytokines. However, the most terrible clinical manifestations during the perioperative period are tracheal compression, sitting breathing or wheezing, which indicates a significant increase in the risk of airway complications. In addition, syncope symptoms or pericardial effusion can increase the risk of cardiovascular complications.

Radiological diagnosis is usually difficult in the process of clinical diagnosis and treatment with non-specific imaging manifestation in NET. Contrast-enhanced CT scan is the preferred imaging method for this disease [3]. It can accurately show the location, size, density and shape of the tumor. This technology can also clearly show the relationship between the tumor and the surrounding environment, such as the relationship between the tumor and

the pericardium, large blood vessels, and chest wall [10]. The NET that originated in the mediastinum appears as irregular soft tissue masses on enhanced CT, with uneven enhancement, and sometimes partial calcification or infringement of surrounding normal structures [6, 7]. A few case reports show that the MR signal is low on the T1-weighted image and high on the T2-weighted image [2, 5].

Atypical and typical carcinoids have similar immunohistochemistry factors. However, high mitotic counts, nucleus polymorphisms, hyperpigmentation, disordered cell arrangement and focal necrosis are more common in atypical carcinoids [5-7]. In our case, the immunohistochemistry results revealed CgA, CD56, Syn, CK19, PCK and GLUT-1 staining was strong positive. But thymus-associated epithelial cell indicators P63 were negative. SSTR2, TdT and CD5 were also negative, and Ki67 index was about 20%-30% in lymphocytes and plasma cells.

The differential diagnosis of NET includes adenocarcinoma, small cell carcinoma (SCC) and thymic neuroendocrine SCC. The exclusion of adenocarcinoma is mainly due to the presence of dense neurosecretory granules in the lesion and no bronchial tissue in the tumor [3]. Considering SSC, the cytoplasm of tumor cells in our case is larger than usually seen in SCC. In addition, the presence of nucleoli and a Ki67 proliferation index of 10% to 20% can also rule out the diagnosis of SCC [2, 5]. In addition, in our case, thymus markers such as P63 and CD5 were negative in immunohistochemistry.

Complete surgical resection is strongly recommended for localized primary NET, according to the newest version of the National Comprehensive Cancer Network (NCCN) guidelines [11]. Surgical resection includes complete removal of the tumor and removal of the surrounding fat tissue, as well as selective removal of lymph nodes. For tumors that are not completely resected, postoperative adjuvant chemotherapy or radiotherapy is recommended. However, no large-scale randomized controlled clinical trials have confirmed the effectiveness of this method so far. For unresectable cases with distant metastases, complete surgical resection of the primary and metastatic foci is still the first choice [12]. Once the patient is unable to undergo surgery, systemic treatment is recommended. Currently, the most commonly used drug is temozolomide [7]. In our case, we did the surgery through mid-sternal thoracotomy with superior vena cava formation, left common carotid artery resection and artificial blood vessel replacement, left upper lobe wedge resection, left phrenic nerve resection, left vagus nerve resection and partial pericardectomy.

In conclusion, NETs are very rare epithelial neoplasms. They usually present as a large mass with an infiltrative nature located in the mediastinum. Early and accurate diagnosis are very important, and surgery remains the mainstay of treatment [12]. Our findings suggest the difficulty of making a diagnosis before surgery and more cases will need to be reported in order to facilitate the preoperative diagnosis of such a rare tumor.

Declarations

Ethics approval and consent to participate not applicable.

Availability of data and materials

All data for this study are publicly available and are ready for the public from database of hospital.

Competing interests

The authors have no conflicts of interest to declare.

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Consent for publication

All the authors consent to publish the paper.

Authors' contributions

CS was involved in drafting the manuscript. LM designed and revised the manuscript. All authors have read and approved the final manuscript.

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Tables

Table 1 Clinical features of the primary anterior mediastinal mass

No.	Age (years)	Sex	Smoking history	Symptoms	Tumor size (cm)	Treatment	Follow up	Author
1	38	male	none	nonspecific fatigue, nausea, subjective weight gain	9.0×10.3×6.1	Resection of the anterior mediastinal mass and thymectomy en bloc with pericardium	Alive	Landry ²
2	66	male	yes	dyspnea and fatigue	8.0×5.0×3.3	Resection of the anterior mediastinal mass	Alive	Kosmas ³
3	66	male	none	acid reflux, dysphagia, chest pain, shortness of breath	16.1×9.2×12.3	Resection of the mass and en bloc with pericardium, left brachiocephalic vein, left phrenic nerve	Alive	Panjeton ⁶
4	56	male	none	intermittent chest tightness, cough and developed hemoptysis	16.5×8.0×13.0	Surgical excision after combined chemotherapy	Alive	Xuan ⁵
5	50	male	none	asthenia, dyspnea, substernal sense of weight	5.4×5.6×8.0	Surgical excision through a median sternotomy with a double pulmonary wedge resection, a partial resection of the vena cava and reconstruction	Alive	Ventura ⁷
6	45	male	yes	chest pain	7.6×4.8×4.0	Resection of the mass with superior vena cava formation, left common carotid artery resection and artificial blood vessel replacement, left upper lobe wedge resection, left phrenic nerve resection, left vagus nerve resection,	Alive	Ours

Figures

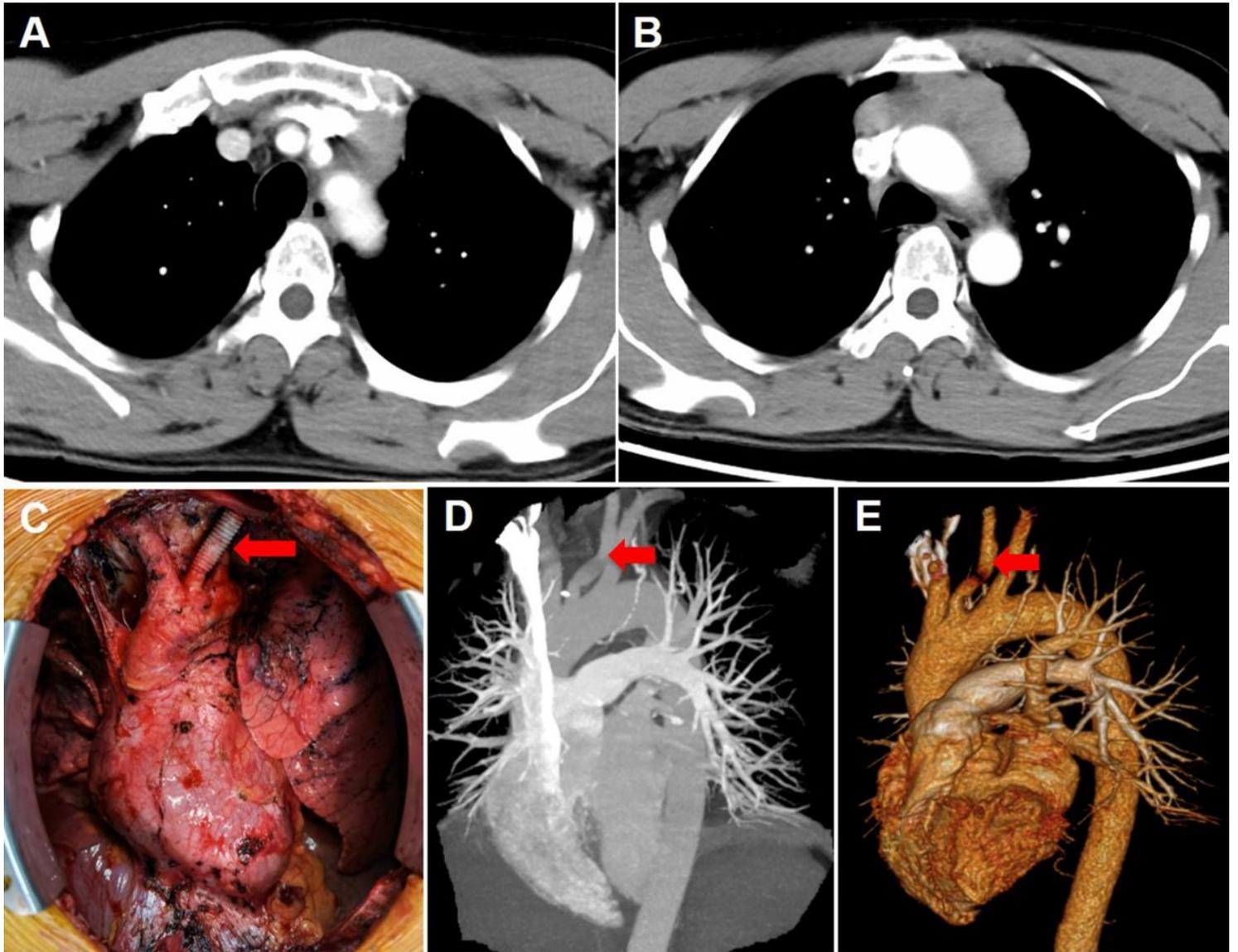


Figure 1

Chest contrast-enhanced CT and intraoperative pictures of the case. A and B: Contrast-enhanced CT scan showing partial enhancement in soft tissue, calculating $7.0 \times 5.0 \times 4.0$ cm in size, in the anterior mediastinum, which showed unclear relationship with surrounding blood vessels and tissues. C: We blocked the left common carotid artery during the operation and performed an artificial blood vessel replacement (Red Arrow). D and E: After the surgery, contrast-enhanced and 3D reconstruction of thoracic blood vessels CT scan showed successful reconstruction of left common carotid artery (Red Arrow).

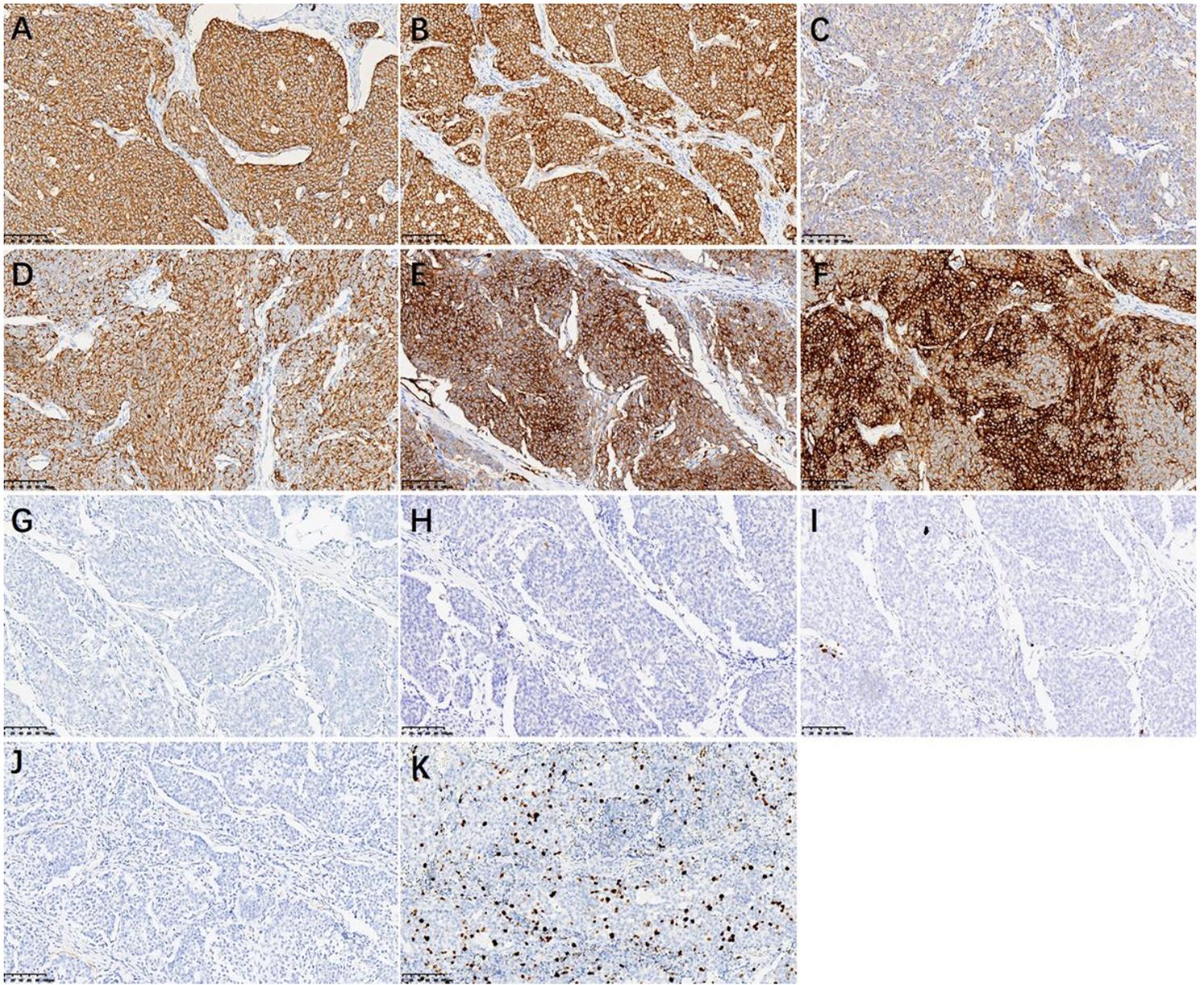


Figure 2

Immunohistochemistry Results. CgA, CD56, Syn, CK19, PCK and GLUT-1 staining was strong positive. But thymus-associated epithelial cell indicators P63 were negative. SSTR2, TdT and CD5 were also negative, and Ki67 index was about 20%-30% in lymphocytes and plasma cells. (A: CgA, B: Syn, C: CK19, D: PCK, E: GLUT-1, F: CD56, G: P63, H: TdT, I: CD5, J: SSTR2, K: Ki67)

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