

Atypical carcinoid: A rare finding of a man with mediastinal mass: A case report

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Abstract. The present case report describes a case of mediastinal atypical carcinoid and a favorable outcome linked with the treatment. Mediastinal atypical carcinoid is a rare and aggressive type of neuroendocrine tumor. A 56-year-old man was admitted at the Respiratory Department due to intermittent tightness of the chest for 1 month. An initial diagnosis of a mass in the left anterior mediastinum was conducted using CT scan and immunohistochemistry. Laboratory data revealed the following values: Neuron Specific Enolase of 62.13 ng/ml (reference range, 0-40 ng/ml); CYFRA21 of 3.01 ng/ml (reference range, 0-3.3 ng/ml); CEA of 4.22 (0-6.5) ng/ml; SCC of 0.5 (0-1.5) ng/ml; CA125 of 67.24 (0-35) U/ml; AFP of 23 (0-25) U/ml; CRP of 96.7 (0-10) mg/l; PCT <0.05 (0-0.05) ng/ml; and ESR of 48 (0-20) mm/h. Tissue pathology revealed tumor cells with small cell pattern, and cell proliferation activity was 10%. Combined chemotherapy with bevacizumab (0.4 g, qd, once every 21 days) and capecitabine (0.15 g, Bid, Po) and timozolamine (0.34 mg, qd, po) was administered for 6 cycles. After the patient was given chemotherapy, the symptoms and CT exhibited improvement. On March 11, 2018, the lesion progressed into the lymph and pleura. The patient was commenced on radiotherapy and new chemotherapeutic regimen etoposide (0.5 g)-carboplatin (0.4 g)-bevacate (0.4 g). Another CT scan was performed after a month which revealed a substantial decrease in tumor size. Hence, a CT scan was performed for this patient who further revealed a decrease in tumor size. Currently patients are treated with bevacizumab maintenance therapy. Further studies of conservative treatment of chemotherapy and radiotherapy may provide a treatment to improve atypical carcinoid.

Introduction

Mediastinal atypical carcinoid is a type of neuroendocrine tumor which is rare and aggressive mediastinal tumor (1). Neuroendocrine carcinoma is often divided into typical carcinoid, atypical carcinoid, small cell carcinoma and large cell neuroendocrine carcinoma based on morphology. Small cell carcinoma and large cell neuroendocrine carcinoma are high-grade tumors. Typical and atypical carcinoid tumors are low-medium grade tumors (2). Clinically, patients may be asymptomatic or show local symptoms because of the compression or invasion of mediastinal structures, or systemic symptoms secondary to the tumor ability to produce hormones or cytokines (3). Neuroendocrine tumors (NETs) are epithelial neoplasms with major neuroendocrine differentiation that begin in most organs of the body. Primary NET of the mediastinum are very occasional (2), they have been the source of investigation and debatable in the literature because of their origin.

Thymic carcinoids characterize by unusual neoplasms. Their yearly over all age-adjusted occurrence has been described to be estimated 1 of 10,000,000 (4), and roughly 200 cases have been stated in the literature (5). Thymic carcinoids occur mainly in men with a ratio of 3:1 to that of women. It has a middling age of 43 years (range 39–60 years)(6). Neuroendocrine carcinomas of the thymus and are reasonably differentiated with a high rate of metastasis. These tumors reveal a 5-year survival rate of 60% and their reappearance is common.(7,8) Furthermore, the brutality of the illness is frequently abandoned since the medical appearance is somewhat benign. Hence, thymic carcinoids are usually revealed at a far advanced stage, which may also account for the poor prognosis (9)

Thymic carcinoids often act destructively. Thorough surgical removal of the thymus is the first treatment of high-quality for thymic carcinoids as chemotherapy and radiotherapy are not active for lengthening survival (9,10). When the tumor is destructive to the patient, surgery is still the best way to eradicate the tumor for causing death. Different options have been raised on the functions of chemotherapy and radiotherapy in the postoperative management of thymic carcinoids. However, adjuvant treatment may also assist in the disease control, it is not active to eliminate tumors and to inhibit the growth of tumor or metastases (11). On the other

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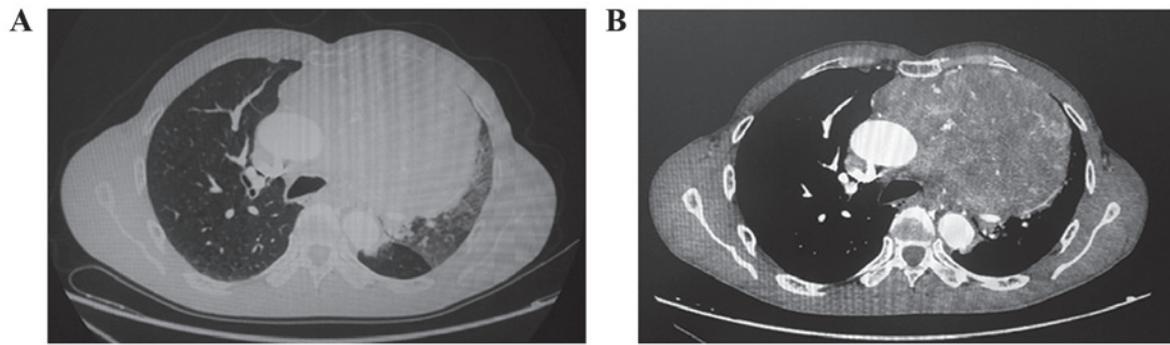


Figure 1. CT scan showing a mass of soft tissue density of 16.5x13.0 cm in the left anterior mediastinum with a clear boundary and uneven density. The enhancement scan demonstrated uneven and distinct enhancement. There was no obvious fracture destruction in the adjacent bone. The adjacent trachea and bronchial cavity were compressed and narrowed, and the heart moved to the right. (A) Lung window. (B) Mediastinal window.

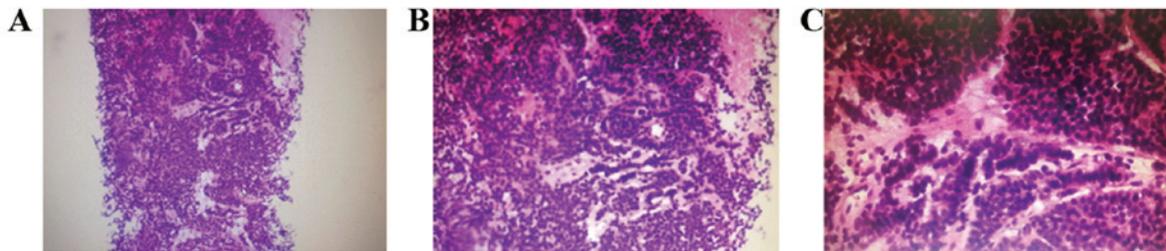


Figure 2. Hematoxylin and eosin staining. (A) Original magnification, x10. (B) Original magnification, x20. (C) Original magnification, x40.

hand, adjuvant radiotherapy has been described in avoidance of local-regional reappearance (12). Utilization of the following therapy only or in combination chemotherapies with 5-fluorouracil, streptozocin, carmustine, VP-16, and cisplatin have been administered earlier without any significant influence on the reappearance rate or overall survival (13). Herein we reported a very special case of primary cutaneous NET (atypical carcinoid) expressing CA125 and CRP with immunohistochemical markers (CD 56+, CD 117+, Syn+, CgA+, and CK+).

Case report

A 56-year-old male was presented with intermittent chest tightness for 1 month. His chest tightness was aggravated with movement. He began to cough and developed hemoptysis after 11 days. The hemoptysis was a bright red and small amount. He did not have a history of chemicals, fumes, or dust exposure and no history of tobacco or alcohol abuse. Chest enhanced CT demonstrated a 16.5x13.0 cm soft tissue mass in the left anterior mediastinum (Fig. 1). Laboratory data revealed the following values: Neuron Specific Enolase of 62.13 ng/ml (reference range, 0-40 ng/ml), CYFRA21 of 3.01 ng/ml (reference range, 0-3.3 ng/ml), CEA of 4.22 (0-6.5) ng/ml, SCC 0.5 (0-1.5) ng/ml, CA125 67.24 (0-35) U/ml; AFP 23 (0-25) U/ml, CRP 96.7 mg/l (0-10); PCT <0.05 ng/ml (0-0.05); ESR 48 mm/h (0-20). Tissue pathology revealed tumor cells with small cell pattern, cell proliferation activity was 10% (Fig. 2). Neuroendocrine carcinoma is characterized by invasive growth, lymphatic and blood metastasis. Therefore, it has been incorporated into low-grade malignancies by WHO. The cytoplasm of atypical carcinoid contains neuroendocrine granules, which

has a secretory function and can lead to carcinoid syndromes such as paroxysmal skin flushing, diarrhea, asthma, tachycardia, and ectopic adrenocorticotrophic syndrome. But these symptoms are not presented rare, and there is no appeal, in this case, however, thyroid, parathyroid and sex hormones assay were done and it was normal in this patient. The results of immunohistochemistry in this patient's tissue biopsy show: CD117(+), CD1a(-), CD5(-), CD56(+), CD99(-), CgA(+), CK(AE1/AE3)(+), CK19(+), Ki67(10%+), LCA(-), SYN(+), TdT(-) TTF-1(-). Synaptophysin (Syn), chromaffin (CgA) and CD56 are the immunohistochemical markers for the diagnosis of neuroendocrine tumors (Figs. 3 and 4), recent research shows that Ki-67 is a potentially meaningful marker for sub-categorization of lung neuroendocrine tumors, the cut-off value of Ki67 for typical/atypical carcinoids was 7.5% with sensitivity and specificity of 91.4 and 100% (area under curve is 0.9685) (14). CK19 assisted diagnosis of thymic epithelial origin, TTF-1 assisted diagnosis of lung and thyroid tissue origin. Therefore, the mediastinal mass is considered as a neuroendocrine tumor originates from the thymus. Considering that a tumor had been transferred to the pleural and multiple lymph nodes. We decided to have surgical excision after combined chemotherapy with bevacizumab + capecitabine + timozolamine. After the patient was given chemotherapy, the symptom and CT showed improvement but the patient and his family rejected surgery. On March 11, 2018 the lesion progressed into the lymph and pleura. Patient was commenced on radiotherapy and new chemotherapeutic regimen (etoposide-carboplatin-bevacate). Another CT scan was performed after a month which revealed a substantial decrease in tumor size (Fig. 5). Subsequently CT scan was performed for this patient which further revealed a decrease

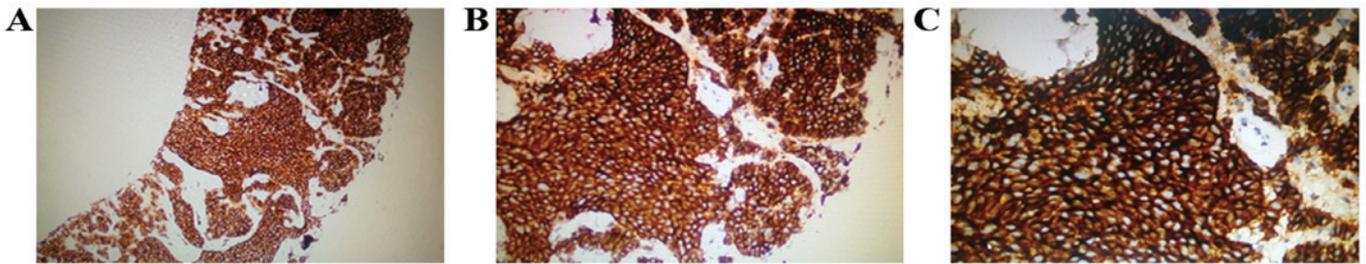


Figure 3. CD56 staining. (A) Original magnification, x10. (B) Original magnification, x20. (C) Original magnification, x40.

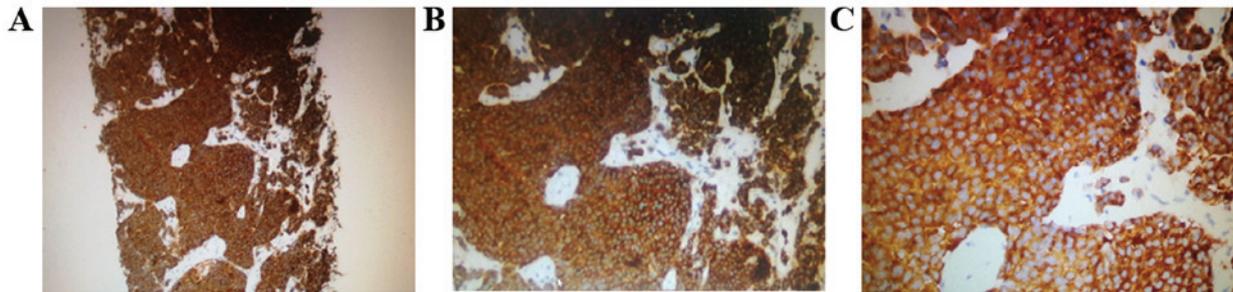


Figure 4. Synaptophysin staining. (A) Original magnification, x10. (B) Original magnification, x20. (C) Original magnification, x40.

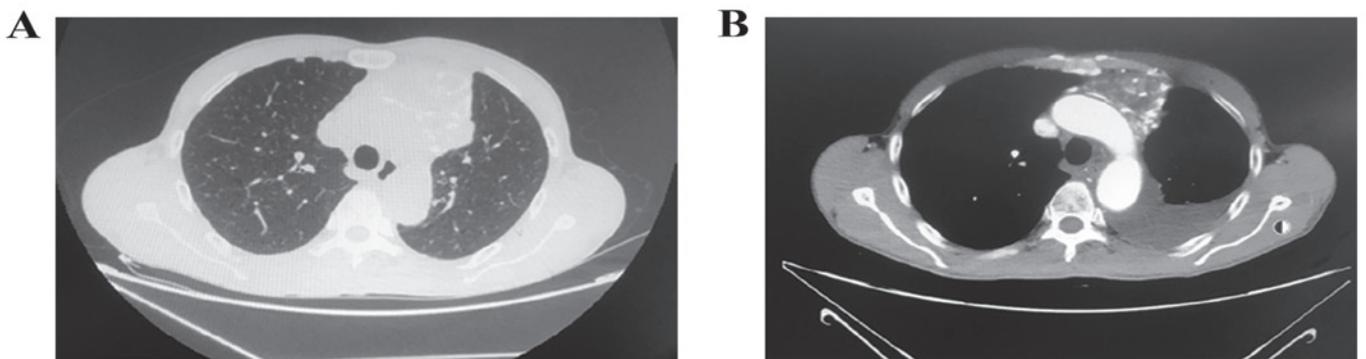


Figure 5. Alterations in CT scan after mediastinal radiotherapy and chemotherapy. Inflammation of the lungs, a few old lesions; limited thickening and adhesion of the bilateral pleura; a small amount of effusion in the pericardium; pleural effusion on the left side and local lung; insufficient tissue expansion; T8 vertebral body nodules, L1 vertebral body flattened, upper edge rough. (A) Lung window. (B) Mediastinal window.

in tumor size. Currently, patients have been treated with bevacizumab maintenance therapy.

Discussion

Atypical carcinoid may occur in many organs and tissues. They are more usually found in the gastro-entero-hepatic or respiratory system (15,16). NETs of the mediastinum are very uncommon and usually, thymic NETs are the most common they are totally found in the anterosuperior mediastinum and account for 2 to 4% of all mediastinal tumors (17). Mediastinal NETs have been the foundation of considerable care and disagreement among experts and investigators because of their origin, that is still debatable. Their terminology and grouping have evolved over the years. Likened with bronchopulmonary carcinoid, primary NETs of the mediastinum are described by a poor prognosis due to their high tendency for local reappearance and previous distant metastases (13). The function

of chemotherapy is disputed; in this case chemotherapy was used for the patient and it caused a reduction of tumor size and a decrease of proliferation rate. In the previous cases, of mediastinal NETs successfully treated by a combination of chemotherapy and Y-DOTATOC (18) or by radiotherapy alone (19) have been described. Hence, we utilized both chemotherapy and radiotherapy. Various investigators debated that a co-expression of CD117 (c-kit) and CD5 could be indicative of a neoplasm of thymic origin (20). In this case report, only CD117 was positive, thus not signifying a thymic origin. CD117 is frequently positive in small cell lung carcinoma and large cell NET and it is frequently negative in typical and atypical carcinoid. The positivity detected for c-kit could have vital therapeutic implication, such as the administration of etoposide (0.5 g)-carboplatin (0.4 g)-bevacate (0.4 g). The prognosis of atypical carcinoid is worse than that of typical carcinoid. Hence, it requires a multidisciplinary team approach for optimal treatment. This patient presented with

pleural effusion. CT was progressive and the primary tumor shrank. But the patient feels that the general situation is okay and cannot be operated. It was first discovered in the late stage, with lymph node metastasis and pleural metastasis. We believe that further study of conservative treatment of chemotherapy and radiotherapy is a treatment to improve atypical carcinoid.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article or are available from the corresponding author on reasonable request.

Authors' contributions

XJZ conceived the project and designed the experiments. WXX, JLL and YJS performed the experiments. WXX analyzed the data. WXX and XJZ wrote the paper. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Henan Provincial People's Hospital (Zhengzhou, China). Written informed consent was obtained from all patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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