

Treatment of Thymic Neuroendocrine Carcinoma with Lung Metastasis: A Case Report

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Abstract

Thymic neuroendocrine carcinoma (NEC) is a rare type of tumor arising in thymus. Here we report a 60-year-old male presented with acid reflux, chest tightness and shortness of breath in April 2009, and the computed tomography (CT) scan revealed a tumor in mediastinum around the aortic arch. The patient was diagnosed NEC following partial surgical resection due to severe adhesions. Combined chemotherapy and radiotherapy was performed after surgery, and the tumor disappeared after chemoradiotherapy. The patient's condition is stable seven years after surgery and the combined chemoradiotherapy. The present case study describes the pathological and clinical features, and the treatment of thymic NEC.

Keywords: Thymic neuroendocrine carcinoma; Lung; Metastasis; Chemotherapy; Radiotherapy

Introduction

Thymic NEC accounts for 2-4% of all the anterior mediastinal tumors [1]. It was first described in 1972, and the number of cases reported is limited [2-4]. This type of tumors were found in thymus and showed more aggressive behavior than their counterparts in other locations. Its overall survival rates were poor, with 10 years survival previously reported as 10% to 35% [5,6]. However, a recent study from a single tertiary referral center reported the overall 3, 5 and 10-year survival as 89%, 79% and 41%, respectively. The prognostic factors include tumor size, histological grade, paraneoplastic syndrome, symptoms, Masaoka staging and condition of surgical resection [3]. Here we report a case of NEC with combined surgery and chemoradiotherapy, which should be of interest to pathologists and clinicians.

Case Report

A 60-year-old male was referred for an investigation of acid reflux, chest tightness and shortness of breath. The patient had a gastroscopy examination and a CT scan. The CT revealed a tumor in mediastinum around the aortic arch (Figure 1A). A needle biopsy was performed under the endoscopy. The diagnosis was not confirmed as the amount tumor tissue obtained by needle biopsy was not enough. In order to confirm the diagnosis, the patient was recommended for an exploratory thoracotomy. Intraoperative exploration was performed and severe adhesions were observed around the tumor. The tumor was irregular with a maximum diameter of approximately 7 cm, locating in the left center of the middle superior mediastinum. Rapid pathological examination by frozen section revealed that the tumor was malignant. Due to severe adhesions and the large size of the tumor, partial resection was performed in surgery. Subsequent pathological diagnosis confirmed the tumor as NEC. Immunohistochemical examination was performed using antibodies for cytokeratin (CK), cell proliferation associated antigen Ki67, Chromogranin A (CgA), Synaptophysin (Syn), neuron-specific enolase (NSE), CD199, S-100 proteins (often styled without the hyphen, S100), neurofilament (NF), glial fibrillary acidic protein (GFAP) and Vimentin. It showed positive results in CK, Ki67, CgA, Syn, and NSE. The results for H&E staining and the immunohistochemical examination were shown in Figures 2A-2C. Based on the American Joint Committee On Cancer (AJCC) Staging System for neuroendocrine tumors, the patient was categorized as stage A(T4N0M0). The patient received two cycles chemotherapy (Cyclophosphamide +Pirarubicin+Cisplatin) both before and after radiotherapy with thoracic fields (Dt55.98Gy/27f). The tumor disappeared two month after irradiation, and the most recent CT scan from July, 2016 revealed that his condition is stable without evidence of recurrence (Figure 1B).

Discussion

Gaur and colleagues performed the largest study of thymic neuroendocrine tumors including 160 patients, with the male-

to-female ratio of 3:1, and the mean age at 57 years [7]. Generally, patients first presented with symptoms of local tumor growth, such as cough, chest tightness, chest pain and/or other symptoms.

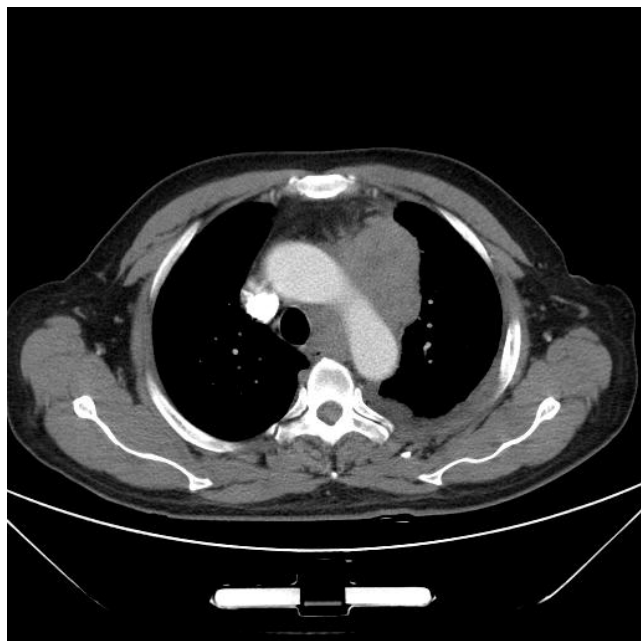


Figure 1A: The CT images showing the presence of the NEC tumor before surgery and the situation at 7 years after surgery and combined chemo- and radiotherapy. CT image demonstrates a soft tissue tumor in mediastinum around the aortic arch (July, 2009).

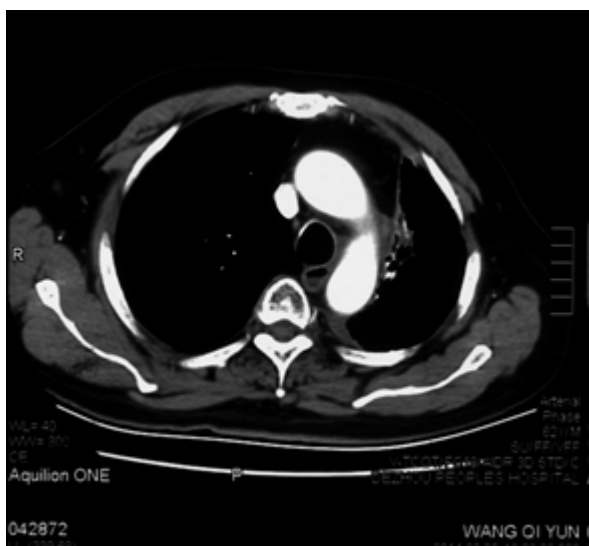


Figure 1B: The CT images showing the presence of the NEC tumor before surgery and the situation at 7 years after surgery and combined chemo- and radiotherapy. CT image reveals no evidence of recurrence (July, 2016).

In this report, the 60 years old patient had an acid reflux, chest tightness and shortness of breath. Thymic NECs are

divided into three categories, including well-differentiated, moderately-differentiated and poorly differentiated (or small cell carcinoma), depending on the degree of tumor differentiation [8].

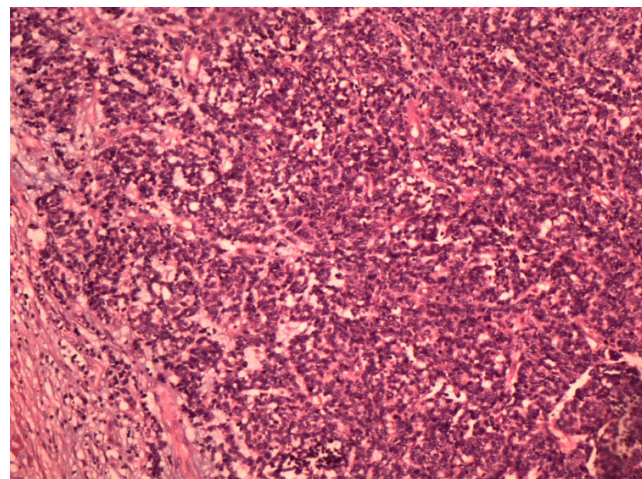


Figure 2A: Microscopic features and immunohistochemical observations of the NEC tumor. Hematoxylin and eosin (H&E) staining ($\times 100$) show the typical tumor cells arranged like cords.

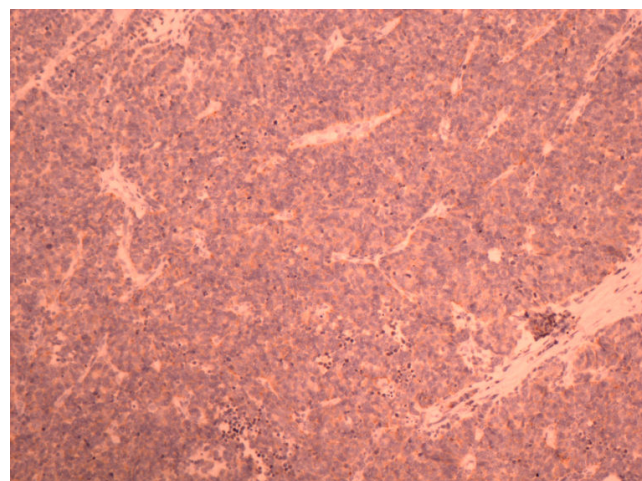


Figure 2B: Microscopic features and immunohistochemical observations of the NEC tumor. Syn positive staining by immunohistochemistry ($\times 100$).

The case in this report was a moderately-differentiated neuroendocrine carcinoma. Previous studies showed that all cases exhibited positive staining for CAM5.2 low-molecular-weight cytokeratin, and some cases showed positive staining for leu-7, 8, chromogranin, synaptophysin, broad-spectrum keratin cocktail and p53 [9,10]. Our case showed positive staining for CgA and Syn. Syn was regarded as one of the most specific markers of neuroendocrine differentiation, exhibiting a much higher sensitivity than CgA and NSE [11]. Specific markers that may be used to establish neuroendocrine differentiation include CgA, Syn, and CD56, although CD56 has been recently proved to

be less specific. The lung origin of a tumor can be supported by positive thyroid transcription factor 1 (TTF-1), while the intestinal or pancreatic origin can be supported by positive caudal-related homeobox transcription factor 2 (CDX2), however, there was no specific marker available for thymic origin so far [5]. Thymic neuroendocrine tumors have been associated with adrenocorticotrophic hormone (ACTH) production and are a cause of Cushing's syndrome [6]. The patient in this report did not present Cushing's syndrome.

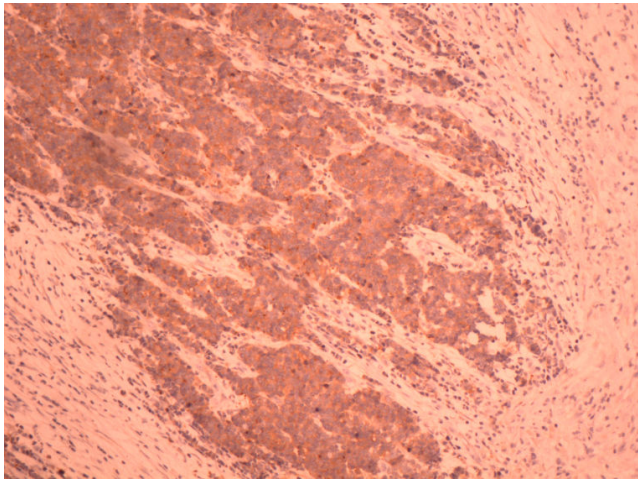


Figure 2C: Microscopic features and immunohistochemical observations of the NEC tumor. Neuroendocrine marker CgA positive staining by immunohistochemistry ($\times 100$).

The more recent report of overall 5-year survival rate of 79% and the overall 10-year survival rate of 41% showed an improvement of survival compared with previous studies [3]. In our report, the tumor was treated with partial resection due to severe adhesions and large size, and the tumor disappeared following the treatment with combined chemotherapy and radiotherapy. This patient has been in good condition and no evidence of local recurrence and distant metastasis has been found, indicating that the tumor is still under control after chemotherapy and radiotherapy. In contrast, many patients experience local recurrence and distant metastasis following surgical excision of thymic NECs [12], and regional lymph nodes are often affected and distant metastases are common. Therefore, early diagnosis and early surgical intervention are the most important survival factors for thymic NECs; however, it is still lack of effective prognostic markers on guiding decision-making between aggressive and conservative therapy. Current treatment is largely dependent on experience of specialists, and the treatment of these rare tumors should be performed by highly specialized units.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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