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CASE REPORT

Primary Neuroendocrine Carcinoma of the Mediastinum

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A mediastinal mass was found in a 37 year old male who presented with fever, weight loss and fatigue. The chest CT revealed a 9x6x4 cm well circumscribed mass located paratracheally in the upper mid-mediastinum. The mass was removed by right thoracotomy. Macroscopically the tumor weighed 195 g and measured 9x6x4 cm. Microscopically the tumor consisted of small blue cells in solid and trabeculer patern. Immunohistochemical studies performed for differential diagnosis of small blue cell tumors. The tumor was diagnosed as primary neuroendocrine carcinoma of the mediastinum. This case is presented for its rare recurrence in that particular location. (Pathology Oncology Research Vol 8, No 3, 200–201)

Keywords: Neuroendocrine carcinoma, mediastinum, carcinoid, chromogranin

Introduction

A 37 year old male presented to the Chest Surgery clinic with the complaints high fever, fatique and weight loss for 4 months duration. His fever peaked consistently to 39.5°C around 3 pm and was resistant to antipyretics. A chest CT was obtained which revealed a paratracheal mass located in and infiltrating the upper-mid mediastinum (*Figure 1*). All serologic and microbiological tests were negative for infectious agents.Tumor markers were not elevated. A bronchoscopy was performed which was reported as negative for malignancy. A mediastinoscopy was performed during which an incisional biopsy was obtained. The diagnosis rendered was "undifferentiated malignant epithelial tumor". Primary location for the tumor was investigated by systemic scans and bone marrow biopsies which were all negative for malignancy. The mass was considered a primary mediastinal tumor and totally excised following a right thoracotomy. The mass was well circumscribed, with no invasion to the surrounding structures. No lymphadenopathy was detected.

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Pathological findings

A 9x6x4 cm well circumsribed encapsulated tumor mass with a lobulated surface was obtained. The cut surface was solid, tan colored and rubbery. Microscopic examination showed a small blue cell tumor in solid and trabecular pattern. The cytoplasm was scant while nuclear chromatin had granular appearance. Nucleoli were indistinct *(Figure 2).* In some areas pseudo-rosette formation could be observed. The tumor was focally necrotic and the mitotic rate was high (15-20/10 HPF). The tumor cells were mucicarmine and PAS negative. Immunohistochemically the tumor cells were positive for EMA, chromogranin, synaptophysin, and focally for S100 while they were negative for LCA, CD3, CD30, CD79a, ALK, vimentin, and mic-2 (CD99). With these findings a diagnosis of primary neuroendocrine carcinoma of the mediastinum was rendered. The patient had no other lesions or lymphadenopathy in any other location and the bone marrow examination was negative for metastatic tumor. The tumor was completely excised surgically and no chemotherapy was given. The patient is free of disease and symptoms during 22 months follow up period.

Discussion

Neuroendocrine carcinomas can be seen in many organs and tissues. Most commonly reported tumors include neuroendocrine carcinomas of the lung, thymus, parathyroid,

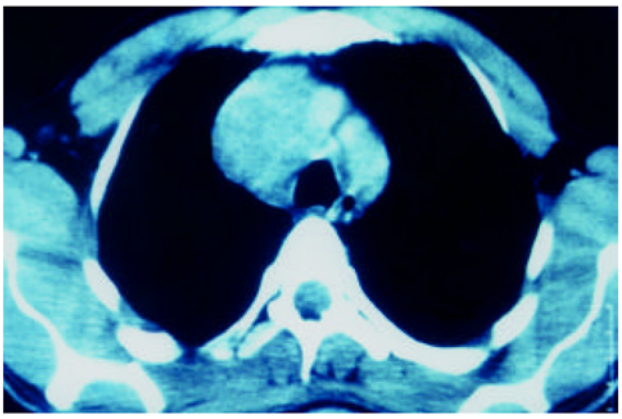

Figure 1. *Chest CT demonstrating a well circumscribed paratracheal mass measuring 9x6x4 cm. Pulmonary parenchyma is within normal limits.*

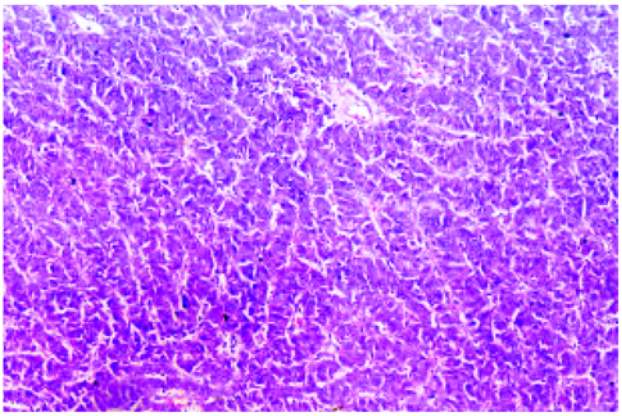

Figure 2. *High power view of the tumor showing pseudorosette formation and granular chromatin pattern of the nuclei. HE x400*

ovary, gasrointestinal system and biliary system.[1,2] In addition, neuroendocrine carcinomas of the retroperitoneum, inferior vena cava, mesentery, and presacral region have been reported.[3-5] There is also a report of a single case of posterior mediastinal neuroendocrine carcinoma.[6]

The case presented here is a neuroendocrine carcinoma localized to the upper-mid mediastinum. In the differential diagnosis, a group of small round cell tumors commonly localized to the mediastinum such as basaloid squamous carcinoma (primary or metastatic), PNET/Ewing sarcoma, neuroblastoma, lymphoma, and rhabdomyosarcoma were considered. [1,2,5,6] In our case, the positivity for epithelial markers excluded rhabdomyosarcoma, while lack of neural differentiation excluded neuroblastoma. Positivity of neural markers was against a diagnosis of basaloid squamous carcinoma. The negativity for lymphoid markers and ALK excluded a lymphoid lesion. The differential diagnosis between a PNET/Ewing sarcoma and a neuroendocrine carcinoma is based on the expression of mic-2 (CD99) and the presence of t(11;22). In our case the tumor cells were negative for mic-2, did not contain PAS positive granules. These features excluded the diagnosis of Ewing Sarcoma.[5,7] Based on pathological and radiological findings the tumor was considered as a primary neuroendocrine carcinoma of the mediastinum.

The neuroendocrine carcinomas are usually located in parenchymatous organs.[1-5,8] Rare cases of neuroendocrine carcinomas located in the mesentery, retroperitoneum, inferior vena cava, presacral region and posterior mediastinum have been reported.[3-6]

The origin of the primary neuroendocrine carcinomas of the mediastinum is not clear. There are two main hypotheses regarding the origin of these tumors. One hypothesis suggests that the tumors arise from ectopic tissues misplaced due to migratory anomalies during embryogenesis. The other hypothesis suggests that the tumors arise from teratomatous components.[3,6] In our case we could not demonstrate any relation of the tumor with a parenchymatous organ including the thymus. Most of the non-pulmonary neuroendocrine carcinomas arising in the mediastinum are of thymic origin. In our case, no evidence for involvement of thymus or no thymic tissue remnant was identified within the lesion. We found a single case of posterior mediastinal neuroendocrine carcinoma so far.[6] We believe that our case represents a very rare occurence of primary mediastinal neuroendocrine carcinoma that is not based on thymus or lung. The patient is free of disease during 22 months follow up period.

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