Thymic Seminoma with Regressive Changes Obscured by Granulomatous Reaction

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ABSTRACT

Primary thymic seminoma is an exceedingly rare tumour. There are few case reports about mediastinal thymic seminoma accompanied by secondary changes. We report a case of a 29-year male admitted to our hospital because of chest pain and dyspnea for 8 months. Computed tomography of the thorax revealed hypodense, solid masses showing calcification and cystic degeneration in the anterior mediastinum. Histopathological examination of the resected specimen revealed a diagnosis of thymic seminoma with regressive and reactive changes. The present case was unique in its presentation as a primary seminoma showing combination of cystic degeneration, follicular hyperplasia, fibrosis, calcification and granulomatous reaction in one case. High level of suspicion is necessary to identify seminomas in a thymic lesion accompanied by secondary changes. Excluding the possibility of metastasis from testicular seminoma is very important before making this diagnosis.

Key Words: *Thymus, Seminoma, Granuloma, Calcification, Cyst.*

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INTRODUCTION

The most common tumours found in the anterior mediastinum originate from thymic, lymphoid or germ cells.[1] Germ cell tumours (GCTs) of the mediastinum are uncommon in adults and account for only 1-4% of all mediastinal tumours, and 10 to 20% of anterior mediastinal tumours. The most common type of primary extragonadal GCT of the mediastinum is mature teratoma. Among malignant GCTs, seminomas are the most common ones, accounting for 25-40% of all mediastinal GCTs.[2,3]

Primary thymic seminoma is a very rare tumour. Only a few cases with secondary changes have been reported in the medical literature.[1,2,4] We herein report an interesting case of thymic seminoma obscured by a granulomatous reaction and florid follicular hyperplasia, leading to difficulties in the diagnosis. The combination of regressive and reactive changes such as cysts, calcification, fibrosis, granulomatous reaction, and follicular hyperplasia was so prominent that the seminoma component was indistinct.

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CASE REPORT

A 29-year male was admitted to the hospital because of chest pain and dyspnea for 8 months. Routine haematological and biochemical parameters were within normal limits. Computed tomography of the thorax revealed hypodense, solid masses showing calcification and cystic degeneration in the anterior mediastinum (Figure 1). A thymo-thymectomy was performed by video-assisted thoracoscopic surgery (VATS) with a preliminary diagnosis of thymoma and teratoma due to the cystic components. On macroscopic examination, a 11.5×10×2.5 cm mass was encountered. There were two firm, well-circumscribed, semi-solid, calcified masses measuring 4.5×5×2.5 cm and 3.5×3.5×2 cm, on the cut section. On histopathological examination, low magnification of the resected specimen revealed lobulated masses in a background of fibrosis, calcification, focal ossification, cholesterol clefts, cystic degeneration, lymphoid cells showing reactive follicular hyperplasia intermixed with granulomatous reaction (Figure 2). The small clusters of cells with irregular-shaped nuclei and clear cytoplasm were dispersed between Hassall's corpuscles and non--caseating granulomas, which became prominent on higher magnification (Figure 2). The periphery of the lesion showed normal thymic tissue and there was a unilocular thymic cyst nearby the lesion. The thymic cyst had a few layers of bland squamoid cells and a thin wall containing thymic tissue. Immunohistochemically, the neoplastic cells were positive for SALL4, OCT3/4, and CD117 (Figure 2). Immunohistochemical staining for pancytokeratin, CK19, CD5, CD45, CD20, CD30, CD15 and MUM-1 was negative. The lymphoid T cells were posi-

tive for TdT, CD5 and CD99. Ziehl-Nielsen staining was negative. Upon the morphological and immunohistochemical findings, a diagnosis of seminoma with regressive and reactive changes was made. The possibility of metastasis from a testicular seminoma and a coexisting tuberculosis infection was excluded by a clinical workup. Clinical and histopathological findings supported the diagnosis of primary thymic seminoma. The patient was treated with chemotherapy comprising cisplatin, bleomycin, and etoposide, tri-weekly for 6 cycles.

The patient's postoperative CT findings revealed no evidence of disease recurrence or metastasis after a follow-up of 1 year.

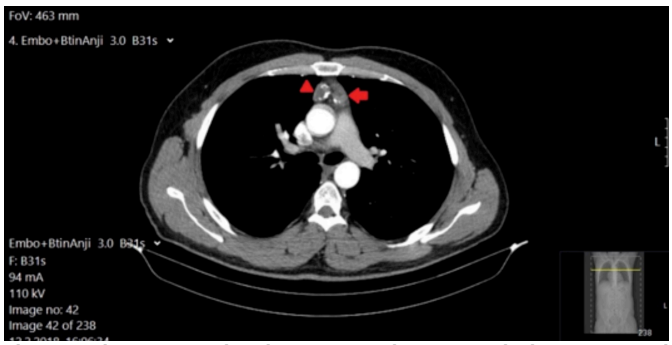


Figure 1: The preoperative chest CT reveals two mass lesions separated by fatty tissue in the anterior mediastinum. The one shown with the arrowhead shows gross calcification, while the other lesion (arrow) has cystic components in it.

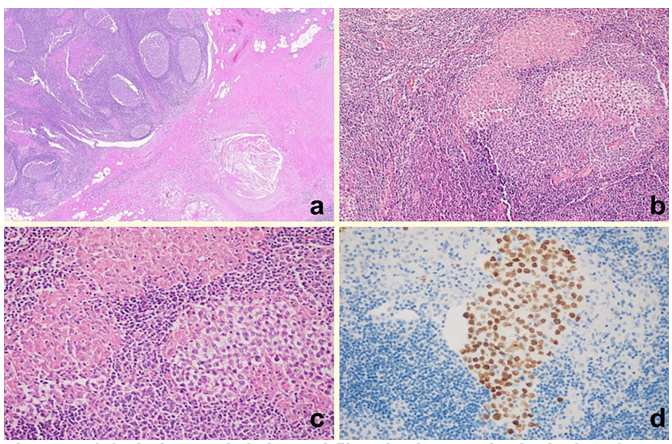


Figure 2: (a) Cholesterol clefts and fibrotic changes in the lesion. (H&E, ×10) (b) Granulomas in the reactive follicular hyperplasia areas. (H&E, ×100) (c) Seminoma cells near by the granuloma, (H&E, ×200) (d) Immunohistochemical SALL-4 positivity in the neoplastic cells (×200).

DISCUSSION

Primary mediastinal seminoma was first described by Woolner *et al*. in 1955.[5] Its histogenesis remains controversial to this day, but a primary origin in extragonadal germ cells is considered most probable. It is believed that mediastinal seminomas arise from extragonadal germ cells in the thymic gland due to chromosomal abnormalities.[6] Specific genetic alterations such as chromosome 12p abnormalities are found both in testicular and mediastinal seminomas.[7] However, Przygodzki *et al*. showed that primary mediastinal seminomas present different genetic findings from testicular ones, namely a unique pattern of a *KIT* exon 17 mutations.[8]

Seminomas of the mediastinum almost always arise from the thymus. Morphological and immunohistochemical findings are similar to those seen in the testicular counterpart. The differential diagnoses of thymic seminoma include thymoma, large cell lymphoma and Hodgkin's lymphoma, especially in tumours with a predominant granulomatous reaction component.

We herein describe a primary thymic seminoma with florid follicular hyperplasia, granulomatous reaction, and regressive changes. There are few case reports of thymic seminoma with secondary changes that might complicate the diagnosis. The secondary changes can be classified as regressive changes such as fibrosis, ossification, calcification, cystic degeneration, and reactive changes like florid follicular hyperplasia and epithelioid granulomas.[1,2,4,9] This case demonstrated all of the secondary changes mentioned above, and the difficulty in the diagnosis stemmed from the predominance of the granulomatous reaction and the low number of scattered neoplastic cells within these granulomas. It was impossible to identify the neoplastic component on low-power examination because of the focal distribution of small number of tumour cells, which were masked by the inflammatory reaction. The differential diagnosis of this case included Hodgkin's lymphoma because of the small amount of neoplastic cells. The neoplastic cells with the granulomatous reaction were suspected of being the lacunar cells seen in Hodgkin's lymphoma. In order to exclude a diagnosis of lymphoma, immunohistochemical markers such as CD30, CD15, MUM-1, Fascin, and EMA were used. The neoplastic cells were also negative for cytokeratins.

Granulomatous reactions within stromal tumours and metastatic tumours in the lymph nodes have been reported in various neoplasms. Granulomatous reaction is not an uncommon finding in testicular seminomas. Although the mechanisms responsible for the granulomatous reaction are still unclear, the presence of granulomas may be an immunological response to tumour antigens[10,11]. Granulomatous inflammation can be present in several conditions such as tuberculosis and fungal infections, chemical exposures and tumours. The synchronous occurrence of a tumour and tuberculosis infection is unusual. However, before considering the granulomatous reaction as an immunological response, the other causes of granulomatous inflammation such as tuberculosis should be excluded clinically.

Primary thymic seminoma should be differentiated from Hodgkin's lymphoma, thymoma, thymic carcinoma, thymic hyperplasia, and anaplastic large cell lymphoma by using a wide immunohistochemistry panel, particularly if the neoplastic cells are obscured by regressive changes and granulomatous reaction.

In conclusion, a high level of suspicion is necessary to identify seminomas in a thymic lesion accompanied by secondary changes.

DISCLOSURE:

The manuscript was presented as a poster presentation in the

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PATIENT'S CONSENT:
Written informed consent was obtained from the patient.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
ANA, ES, MRC: Contributed to the conception and design of the case report,
ANA, SA, HU: Collected the data and wrote the initial manuscript.
ANA, MRC: Prepared the figures and performed the last evaluation.
ES, HU, NA: Critically revised the manuscript.
All authors have read and approved the final version of the manuscript.

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