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Case Report

Thymomas: Case Report of an Aggressive Metastatic Thymic Carcinoma in a Young Female Patient

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Abstract: A young 22-year-old female patient with a known Thymoma, under yearly surveillance, presented with upper respiratory tract infection symptoms. She returned 3 weeks later with an unresolved cough. A chest radiograph demonstrated a retrocardiac homogenous opacity with another opacity obliterating the left cardiac margin. Further, two well-defined homogenous pleural-based opacities in the left upper and lower lung zones were noted. Further evaluation was done with a CT chest and PET scan. CT Thorax confirmed interval invasive features of previously seen left anterior mediastinal mass with direct involvement of pleura, pericardium, and multiple pulmonary nodules denoting invasive malignant thymoma. PET scan reported intensely hypermetabolic left pleural masses likely representing the patient's thymoma. She underwent a guided tissue biopsy which concluded as Thymoma probably Type B2. She received chemotherapy, radiotherapy, and surgical resection of the lesion with full resolution of the lesion.

Keywords: Thymoma, Invasive thymoma, Pleural involvement, Chest CT, Chemotherapy.

INTRODUCTION

Thymic tumours are rare neoplasms of the anterior mediastinum. Thymomas and Thymic carcinomas are the most common neoplasms of the Thymus in adults.

Thymomas incidence is about 20 percent of all mediastinal neoplasms. Thymoma presents between 40 and 60 years of age with equal incidence affecting both genders [1]. There are no known risk factors associated with it but a strong association with myasthenia gravis and other paraneoplastic syndromes has been reported.

Thymic Carcinoma, however, is more aggressive than thymoma. They tend to demonstrate local spread to the mediastinal structures in the majority of the patients [2]. Like Thymomas, the majority of the patients present with cough, chest pain, phrenic nerve palsy, or superior vena cava syndrome. Extra-thoracic metastasis is seen in less than 7 percent of patients at clinical onset. The liver and bone are the most common sites with metastases also reported in other locations including the brain, kidney, extra-thoracic lymph nodes, adrenals, and thyroid [3].

CASE DESCRIPTION

A young 22-year-old female patient with known thymoma [Fig 1, Fig 2] presented in a primary health care setting with 2-day history of fever, sore

throat, cough, and headache during the COVID-19 pandemic.

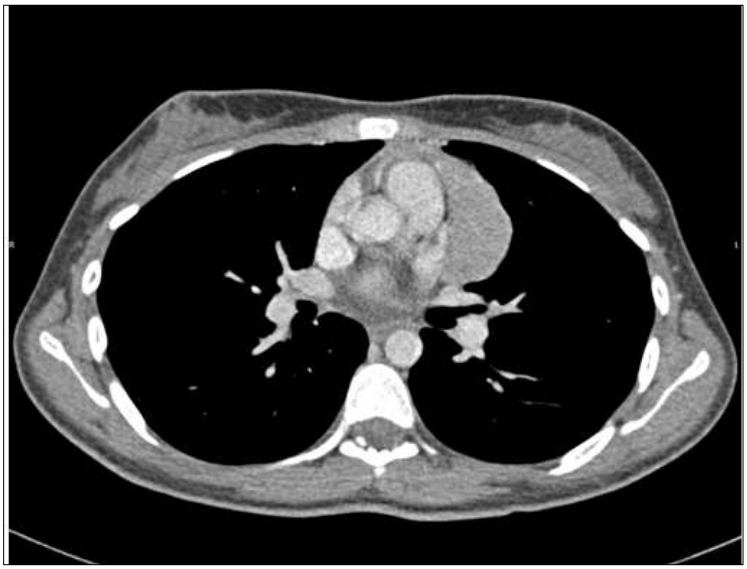

Figure 1: Axial CECT of the chest demonstrating moderately enhancing soft tissue density lesion in the anterior mediastinum 2018

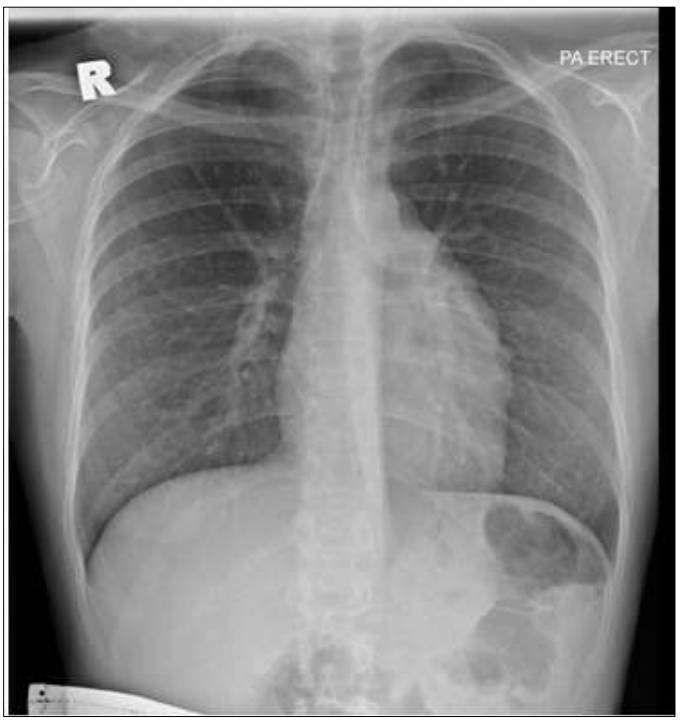

Figure 2: Initial Chest radiograph from 2021 showing nodularity along the left cardio mediastinal border

Her COVID-19 Rapid Antigen Test was negative, and she was offered symptomatic treatment for URTI. However, she presented again after 3 weeks with an unresolved cough. A chest radiograph was performed to rule out COVID-19 pneumonia. The chest X-ray report [Fig 3] described a retrocardiac homogenous opacity with another opacity obliterating the left upper cardiac silhouette. Two well-defined homogenous sizeable pleural-based opacities were also seen in the left upper and lower lung zones. The right lung field and both CP (costophrenic) angles were clear. There was no evidence of mediastinal shift or pneumothorax. The report was suggestive of multicentric pathology/metastatic lesions. Further evaluation by CT scan/MRI was highly recommended for optimal care.

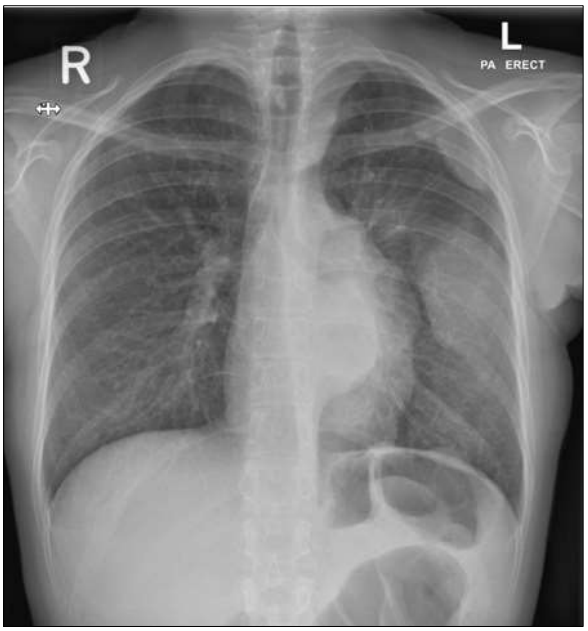

Figure 3: Chest radiograph demonstrating mediastinal and left upper and mid-zone mass (2022)

She was urgently referred to a tertiary care hospital where she underwent an urgent CT Thorax [Fig 4]. The report suggested an interval increase in the size of a large invasive anterior mediastinal mass measuring approximately 9.8 x 6.8 x 6.6 cm when compared with the previous CT scan of 2018 [Fig 1]. The matrix of the mass demonstrated predominantly soft tissue density with areas of internal calcification and low-density areas of necrosis. There was an interval invasion of mediastinal structures and surfaces. The lesion was seen in contact with the left upper cardiac border with no clear demarcation from the pericardial surfaces. The major mediastinal vascular structures were encased, however, there was no significant displacement, compression, or thrombosis of the vascular structures or bronchial tree. There was lobulated nodular thickening of the pleural surfaces along the left upper hemithorax, pericardium, and diaphragmatic surface with obliteration of the left CP angle due to soft tissue density pleural mass. Multiple variable size randomly scattered soft tissue ground glass nodules were noted in both lungs with peri bronchial distribution. The largest nodule in the left lung measured 9mm in the left upper lobe superior lingular segment. The largest nodule in the right lung measured 7mm in the apical segment of the right upper lobe. There were multiple subcentimeter small lymph nodes in the lower cervical, mediastinum, and perihilar regions. There was no evidence of pleural or pericardial effusion. No skeletal metastases were demonstrated.

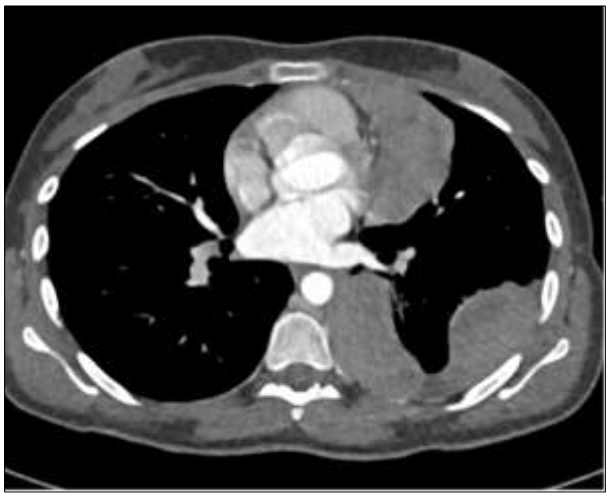

Figure 4: CECT axial images demonstrate disease progression with soft tissue density extending along the left posterior and lateral chest wall (2022)

PET CT [Fig 5] demonstrated increased activity in the corresponding soft tissue lesion in the left epicardiac and chest wall region. The patient was reviewed by surgeons and underwent a CT-guided biopsy. The histopathology showed D3, CD5, and TdT: positive in lymphocytes.

HISTOPATHOLLGY: CKAE1/AE3, PAX8, P63: Positive in neoplastic epithelial cells. Ki67: 80% Thymoma (probably type B).

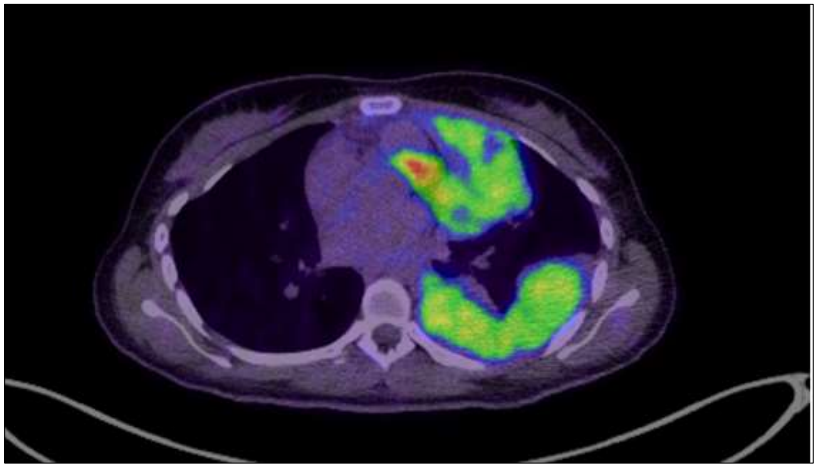

Figure 5: PET CT demonstrates increased activity in the corresponding soft tissue lesion in the left epicardiac and chest wall region (2022)

The case was discussed in the MDT (multidisciplinary team) meeting and was offered chemotherapy. She received 5 cycles of CAP (Cisplatin + Adriamycin + Cyclophosphamide) protocol chemotherapy. Surgery was planned and she recovered well after thymectomy. The radiotherapy was completed in June 2023.

Follow-up after surgery and post-chemotherapy demonstrated resolution of the primary and pleural-based lesions [Fig 6].

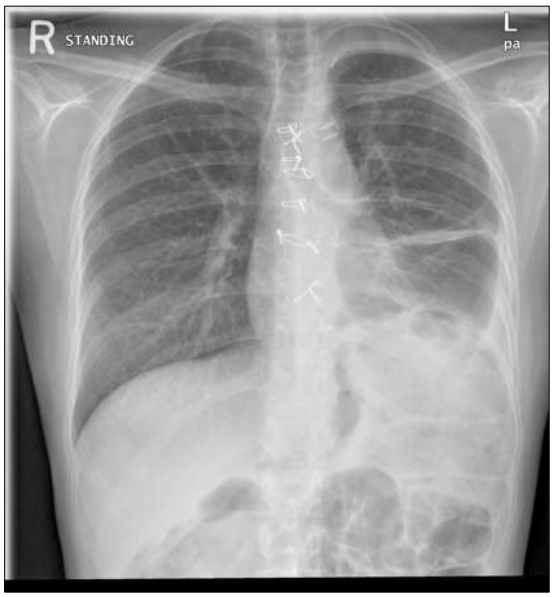

Figure 6: Post-chemotherapy and after-surgery chest radiograph demonstrating resolution of the primary and pleural-based lesions (2023)

However, after thymectomy and radiotherapy, she developed Pure Red Cell Aplasia that required a blood transfusion. Other side effects, like numbness in her hands and paraesthesia in her arms, were temporary and resolved once she finished her chemotherapy. During her illness, she also developed binocular diplopia and ptosis with a squint. However, this resolved after she started chemotherapy. She was seen by a neurologist who attributed these symptoms to myasthenia gravis. She

showed a good response to immune suppressive therapy of prednisolone + Rituximab. The patient also developed steroid-related diabetes mellitus which was controlled with insulin. Follow-up PET CT scan showed a reduction in size and tracer uptake in the pericardiac and pleural-based lesions [Fig 7].

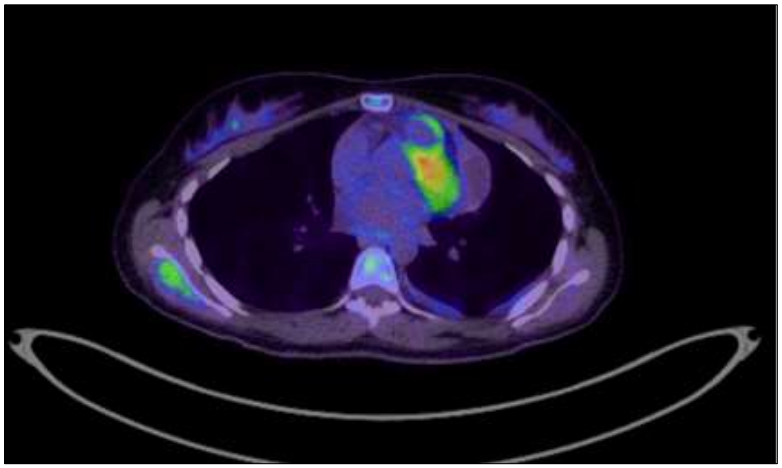

Figure 7: Reduction in size and tracer uptake in the pericardiac and pleural based lesions (2023)

The patient was regularly followed up by the oncology team and her latest PET CT scan showed complete resolution of the pericardiac and pleural-based soft tissue lesions post-chemo and radio in 2024 [Fig 8].

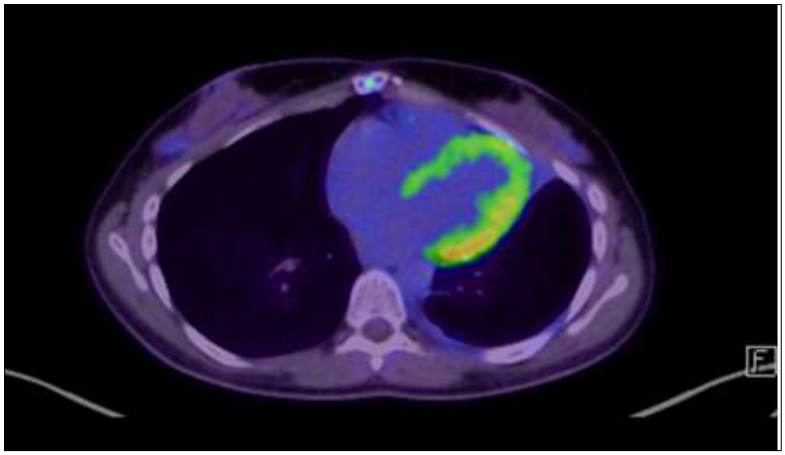

Figure 8: Complete resolution of the pericardiac and pleural-based soft tissue lesions post chemo and radio (2024)

DISCUSSION

Thymomas can occur at any age, from as young as 8 months [4], to 90 years [5], with a mean age of about 53 years. However, paraneoplastic syndromes, and in particular myasthenia gravis (MG) associated tumours tend to occur at younger ages.

Thymomas and invasive thymic carcinoma have low incidence and recurrence rates. Due to these reasons, the treatment strategies are not completely standardized, and no consensus has yet been established among the spectrum of treatment options. This young patient was diagnosed with Thymoma at the age of 18 and was on yearly surveillance. She had a normal chest radiograph a year before her presentation. She was offered a repeat chest radiograph to rule out a chest infection.

Such tumours present with a variable and unpredictable evolution, ranging from an indolent non-invasive attitude to a highly infiltrative and metastasizing one. Patients with invasive tendencies tend to show a prolonged clinical course with multiple operations performed for diagnosis, primary resection, and treatment of recurrences. Surgery is usually offered alongside cycles of chemo/radiotherapy administered in an attempt to improve outcomes. This group of patients is generally younger and more fit than those with other thoracic malignancies (lung, oesophagus, pleura). Such patients are offered aggressive medical and surgical

treatments. However, long-term prognosis often does not correspond to cure and disease-free survival.

Myasthenia gravis is one of the commonest paraneoplastic syndromes associated with Thymic tumours [6]. Other frequently associated conditions with Thymomas are pure red cell aplasia and hypo-gamma-globulinaemia, occurring in 2-5% of patients [7]. Association between these conditions and thymomas is universally accepted but the mechanism of onset is still unclear, particularly to hypo-gamma-globulinaemia.

Clinically, thymic carcinomas are discovered at an advanced stage and often present in aggressive behavior. The survival rate is significantly lower than thymomas, with a 5-year survival of 30% to 60% in most series. Population-based studies indicate an average 16% resection rate in patients with thymic carcinoma [8], with a 5-year survival rate of only 17% in nonresectable, advanced stages [9].

Thymoma's most recent classification is the 2021 WHO Classification of Tumors of the Thymus and Mediastinum. Thymomas are classified as type A thymoma (including an atypical variant), AB thymoma, type B thymoma (separated into B1, B2, and B3 thymomas), micronodular thymoma with lymphoid stroma, and metaplastic thymoma by histologic features and, rarely, immunohistochemistry, such as immature T cell content.

Table 1: WHO Classification of Thymic Epithelial Tumors, Including Thymomas, Thymic Carcinomas, and Neuroendocrine Tumors

ICD-O Morphology and Behavior Codes	
Epithelial tumors	
Thymomas	
8580/3	Thymoma, NOS
8581/3	Thymoma, type A[a]
8582/3	Thymoma, type AB
8583/3	Thymoma, type B1
8584/3	Thymoma, type B2
8585/3	Thymoma, type B3
8580/1	Micronodular thymoma with lymphoid stroma
8580/3	Metaplastic thymoma
9010/0	Lipofibroadenoma
Squamous carcinomas	
8070/3	Squamous cell carcinoma, NOS
8123/3	Basaloid carcinoma
8082/3	Lymphoepithelial carcinoma[b]
Adenocarcinomas	
8140/3	Adenocarcinoma, NOS
8260/3	Low-grade papillary adenocarcinoma[c]
8200/3	Thymic carcinoma with adenoid cystic carcinoma-like features
8144/3	Adenocarcinoma, enteric type[d]
Adenosquamous carcinomas	
8560/3	Adenosquamous carcinoma
NUT carcinomas	
8023/3	NUT carcinoma
Salivary gland-like carcinomas	
8430/3	Mucoepidermoid carcinoma
8310/3	Clear cell carcinoma[e]
8033/3	Sarcomatoid carcinoma
8980/3	Carcinosarcoma[f]
Undifferentiated carcinomas	
8020/3	Carcinoma, undifferentiated, NOS
Thymic carcinomas	
8586/3	Thymic carcinoma, NOS[g]

Reprinted from WHO Classification of Tumours Editorial Board. Thoracic Tumours. Lyon, France: International Agency for Research on Cancer; 2021 (WHO Classification of Tumours Series, 5th ed.; vol. 5, page 7, Copyright; 2021).

A. Including atypical variants

B. Previously labeled lymphoepithelioma-like carcinoma.
C. Previously labeled papillary adenocarcinoma.
D. Newly delineated mucinous or nonmucinous adenocarcinoma with expression of at least one intestinal marker, CK20, CDX2, or MUC2.
E. Including hyalinizing clear cell carcinoma.
F. Subtype of sarcomatoid carcinoma.
G. Including hepatoid carcinoma, rhabdoid carcinoma, undifferentiated large cell carcinoma associated with Castleman disease-like reaction, and sebaceous carcinoma.

SUMMARY AND CONCLUSION

Although thymoma and thymic carcinomas are commonly seen in the middle age group but can occur in any age group. Thymic carcinomas are reported in very young age with poor prognosis [10]. This is a classic case of thymoma that started as a benign asymptomatic lesion and developed into an aggressive carcinoma with rapid spread. This could present a challenge to both clinician and patient about the right approach to evaluate such cases. There are no clear guidelines as to how aggressively these lesions need to be investigated from the beginning. Clearly, this young girl was diagnosed at the age of 18 and was put on yearly surveillance. She had chest radiographs before her presentation with URTI symptoms as part of the yearly surveillance. Management of an individual case will certainly depend on the symptoms and extent of the disease at the time of presentation. However, knowing that such cases can change to an aggressive course, the clinician needs to be wary of the early intervention and more aggressive diagnostic and therapeutic approach. This also raises the question of more detailed guidelines for monitoring Thymomas as currently there are no clear guidelines for early intervention.

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