Case report

Multifocal Primary Intrapulmonary Thymoma: A rare subtype of ectopic thymoma

Albert Iruthiaraj Lourdesamy Anthony a,*, Taranjit Kaur Satnam Singh b

a Respiratory Unit, Hospital Taiping, Taiping, 34000, Malaysia
b Department of Radiology, Hospital Taiping, 34000, Malaysia

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ABSTRACT

Primary Intrapulmonary Thymoma (PIT) is an infrequent ectopic lung tumor that poses a diagnostic dilemma and has a poorly understood origin. We report a previously healthy 61-year-old lady who presented with cough and weight loss for a month. Diagnostic imaging showed a large left upper lobe mass and two multifocal pleural based nodules in the left lower lobe. She underwent Computed Tomography (CT) guided biopsy of the lung mass and histopathological findings was consistent with a combined Type B1 and B2 thymoma. She was planned for 6 cycles of neoadjuvant chemotherapy with the intent of achieving tumor downstaging and resectability. Due to the lack of established evidence for management of unresectable disease, we wish to highlight the importance of multidisciplinary consensus before pursuing multimodality treatment.

1. Introduction

PIT is a thymic epithelial cell neoplasm that occurs in the lung without a mediastinal lesion. It was first reported in 1951 and is a rare disease that accounts for approximately 20% of ectopic thymomas. Only 37 cases have been reported worldwide until 2007 [1–3]. Diagnosis is heavily reliant on histopathological confirmation as imaging features can be nonspecific. The pathogenesis is also poorly understood because of the paucity of publications on the subject which were predominantly single institution studies [±].

We present the case of a patient who was initially suspected to have primary lung cancer but was later diagnosed with PIT following a histopathological examination.

2. Case report

A 61-year-old nonsmoking, healthy lady presented to us with a 1-month history of nonproductive cough and 5kg weight loss. There was no history of previous hospitalizations. She did not require supplementary oxygen. Physical examination findings were unremarkable other than the discovery of diminished breath sounds over the left lung. Her CRP was less than 10 mg/L and white blood cell count was normal at 4.1 × 10⁹/L, whereas her fasting blood glucose levels were within the normal limits. The patient’s chest radiograph revealed opacification of the left hemithorax with tracheal deviation to the right (Fig. 1A). Contrasted chest CT imaging demonstrated a large heterogeneously enhancing mass measuring 10.2 × 9.0 × 14.8 cm that involved the left upper lobe without sparing of the lingular segments. There were two other lobulated pleural-based lesions seen at the posterior basal segment of the left lower lobe, and the largest measured 2.8 × 2.6 cm (Fig. 1B).

Flexible bronchoscopy revealed an extrinsic compression of the left main bronchus, 2 cm from the main carina. A CT-guided tru-cut biopsy of the left upper lobe lung mass was performed and 5 fragments of greyish-white tissue was obtained.

Histological analysis revealed that the tumor to be consisted of two cell populations: a neoplastic epithelial cell component and a highly proliferative immature lymphocytic population. The epithelial cells were round to oval in shape lacking nuclear atypia, whereas the lymphocytes were predominantly of T-cell lineage. Immunohistochemical analysis further showed that the epithelial tumor cells were diffusely immunoreactive to the cytokeratin cell network, specifically to cytokeratin AE1/AE3, cytokeratin 5 and 6, cytokeratin 7, and cytokeratin 19. The tumor cells also had a positive expression for p40, but had

Abbreviations: PIT, Primary Intrapulmonary Thymoma; CRP, C-reactive protein; CT, Computed Tomography; TdT, Terminal deoxynucleotidyl Transferase; WHO, World Health Organization; PET-CT, Positron Emission Tomography – Computed Tomography.

* Corresponding author.

E-mail address: albert5409@yahoo.com (A.I. Lourdesamy Anthony).

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negative staining for CD5 and CD117. The lymphocytes, however, stained positively for CD3 and TdT, and negatively for CD20 (Fig. 2).

In accordance to the WHO classification, this histopathological findings were consistent with a lymphocytic-rich thymoma (combined type B1-75% and B2-25%). From an oncology multidisciplinary discussion which included input from thoracic surgeons, a consensus was achieved that the disease was potentially resectable following neoadjuvant chemotherapy. The patient was planned for 6 cycles of cisplatin-cyclophosphamide-doxorubicin regimen before reevaluation to assess the feasibility of the surgical resection. However, the patient succumbed to neutropenic sepsis at the end of the third cycle of chemotherapy.

3. Discussion

To the best of our knowledge, unresectable PITs have been under reported since its first report back in 1951 [1–3]. The origin of PIT brings us back to the early phases of embryogenesis. Several hypotheses exist, but the accepted theory proposes that PIT originates from stem cells. This theory is also described in relation to the origin of several other ectopic diseases such as meningiomas and melanomas. The second most popular hypothesis suggests that PIT is a residue of thymic tissue displaced during embryogenesis, but the theory fails to explain how this is possible when the lungs develop much earlier than the thymus [5].

From literature review of previous publications, we discovered that PITs have a marginal female predisposition and occurrence in adults with a mean age of 55 years, the youngest and oldest patients reported at 19 and 79 years respectively. Lung involvement commonly affects the right side and the upper lobe. In most cases, PIT was discovered as an incidental finding in asymptomatic individuals and symptoms were only seen when the mass became large enough to compress adjacent structures. Tumor sizes averaged about 35mm in diameter ranging from 15mm to 128 mm [2,4,6–10]. Type B thymomas was reported to be slightly commoner than Type A thymomas, which has a less aggressive disease behaviour [2,7]. Although our patient shared most of the common epidemiological and clinical characteristics for PITs, the fact that the pulmonary lesions were multifocal made this case unique. Only a few cases described previously had multifocal lung lesions, and they encountered significant challenges to achieve resectability [7].

Under the WHO histological classification of lung tumors, PIT is classified as a malignant lung tumor with an ectopic origin. The Masaoka staging system is not suitable to stage PITs because of the absence of mediastinal tumor [11]. Therefore, PITs should be clinically staged under the TNM lung cancer staging system. Our patient had T4 disease caused by the enormous size of the tumor in the left upper lobe and ipsilateral multifocal lesions in the left lower lobe. Because there was no

nodal involvement and distant metastases, she was classified as having Stage IIIA disease. A PET-CT scan at this point may have detected nodal involvement and distant metastasis that could have been potentially missed from CT scan and upstaged clinical staging. However, it was not pursued as the disease was unresectable from multidisciplinary consensus. Instead, it was tentatively scheduled to be performed after the completion of neo adjuvant chemotherapy as a part of reevaluation to determine the feasibility of complete surgical resection.

PITs are frequently diagnosed postoperatively followed by the resection of the primary tumor. Although histological evaluation of the entire tumor is ideally required to make a confident diagnosis, as we suspected primary lung cancer clinically and as the lesion was not amenable to resection right in the first instance, we pursued a preoperative tissue diagnosis. The biopsy samples were not reflective of the entire tumor and lacks information on the microinvasion of tumor cells into the adjacent tissues [12].

PITs share similar histological features with mediastinal thymomas and there are a few differential diagnoses from which it need to be distinguished[12]. The lack of cellular atypia and low mitotic activity in the epitheloid component as seen in our patient does not favour the diagnosis of metastatic carcinoma or poorly differentiated carcinoma of the lungs. Additionally, immunohistochemistry staining was instrumental to assist the exclusion of thoracic lymphomas. The highly proliferative lymphoid component stained positively for T-cell phenotype which is a characteristic of thymic tissue rather than for the B-cell phenotype which is seen in lymphomas [2,6].

Surgical resection of PITs is the cornerstone of management and patients who achieved complete resection survived longer compared with those who were managed conservatively. For unresectable disease, the prognosis is poor despite the histological subtype. ([2, 6, 10] The role of adjuvant radiotherapy and neo adjuvant chemotherapy in unresectable disease is not established as it lacks evidence from randomised phase III clinical trials. Therefore, the management of such cases, including ours, required a multidisciplinary approach [13,14]. We prescribed neo-adjuvant chemotherapy with the intent to downstage disease and achieve resectability that alters prognosis. If complete resection was not feasible, adjuvant radiotherapy would have been considered for disease control.

In conclusion, PIT is an unusual disease that is difficult to diagnose. Diagnosis requires the pursuit of histological evaluation. There are uncertainties in the management of an unresectable disease. Management is best when individualised with a multidisciplinary approach. The lack of evidence for management in unresectable disease warrants collaboration in research to elevate the quality of management.

Fig. 1. Chest Radiograph and Computed Tomography Images. (A) Chest radiograph showed opacification of the left hemithorax with tracheal deviation to the right. (B) Computed tomography of the thorax showed a large mass in the left upper lobe and two pleural based nodules in the left lower lobe.
4. Declarations of interest

None.

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