Received: 14 October 2022 | Revised: 5 January 2023 | Accepted: 7 January 2023

DOI: 10.1002/ccr3.6897

CASE REPORT

Clinical Case Reports Open Access WILEY

Primary intrapulmonary thymoma a case report

Sheikh Muhammad Wasim Jamal[1,2] | **Mousa Hussein**[3] | **Mutaz Albakri**[3] | **Ibrahim Rasheed**[2,3] | **Mansoor Hameed**[2,3] | **Irfan Ul Haq**[2,3] | **Merlin Thomas**[2,3] | **Issam Al Bozom**[2,3] | **Hisham Abdul Sattar**[2,3]

[1]Hazm Mebaireek Hospital, Hamad Medical Corporation, Doha, Qatar

[2]Weill Cornell Medicine-Qatar, Cornell University, Ar-Rayyan, Qatar

[3]Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar

Correspondence
Sheikh Muhammad Wasim Jamal, Hazm Mebaireek Hospital, Hamad Medical Corporation, Doha, Qatar.
Email: docwasimjamal@gmail.com; sjamal2@hamad.qa

Funding information
Qatar Foundation

Abstract

Primary intrapulmonary thymoma (PIT), defined as the presence of thymoma tissue in the lung without an accompanying mediastinal component, is uncommon and so offers a diagnostic quandary. We describe the case of PIT in an 81-year-old man.

KEYWORDS

oncology, primary intrapulmonary thymoma, respiratory medicine, thymoma

1 | INTRODUCTION

Thymomas are tumors originating from thymic epithelial cells with an occurrence rate of 0.15 per 100,000.[1] They are typically accompanied with an anterior mediastinal mass. Primary intrapulmonary thymoma (PIT), defined as the presence of thymoma tissue in the lung without an accompanying mediastinal component, is uncommon and so offers a diagnostic quandary. We describe the case of an 81-year-old man who presented with hemoptysis. His history and CT imaging suggested metastatic lung cancer at first, but an image-guided biopsy of his lung lesion proved to be PIT.

2 | CASE DESCRIPTION

An 81-year-old gentleman, ex-heavy smoker presented with a 10-day history of hemoptysis. There was no history of chest pain, shortness of breath, fever, or weight loss. His past medical history included type II diabetes mellitus, coronary artery disease, and atrial fibrillation. His regular medications included metformin, atorvastatin, carvedilol, and dabigatran. A physical examination was unremarkable, and his blood workup revealed a normal CBC, coagulation profile, and biochemistry panel. His chest radiograph indicated a retrocardiac opacity on the left side. A subsequent CT chest with contrast showed a heterogeneous mass lesion in the right upper lobe (Figure 1). In addition, there were multiple bilateral solid nodules (Figure 2). Flexible fiberoptic bronchoscopy showed narrowing of the right upper lobe anterior segment bronchus. RUL bronchus also had an abnormal-looking mucosa and necrosis. Endobronchial biopsies taken from the site revealed chronic inflammation and necrosis without evidence of malignancy. His BAL cytological examination was also negative for malignancy and granulomas. His positron emission tomography (PET) scan showed high 18F-fluorodeoxyglucose (FDG) uptake in the right upper lobe lesion and multiple pulmonary

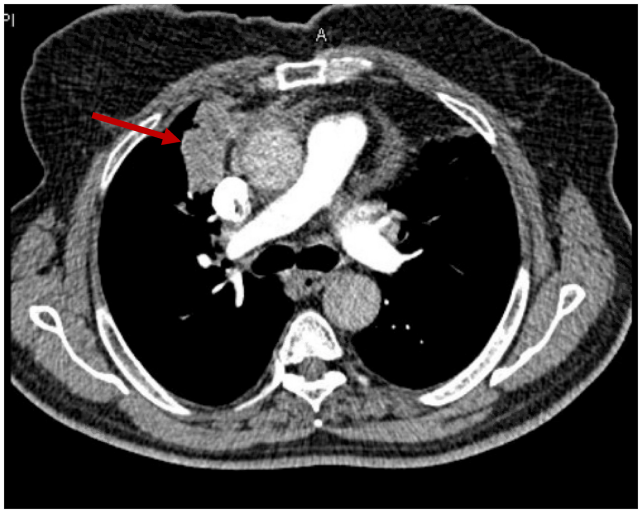

FIGURE 1 CT Chest indicating right upper lobe lesion (arrow).

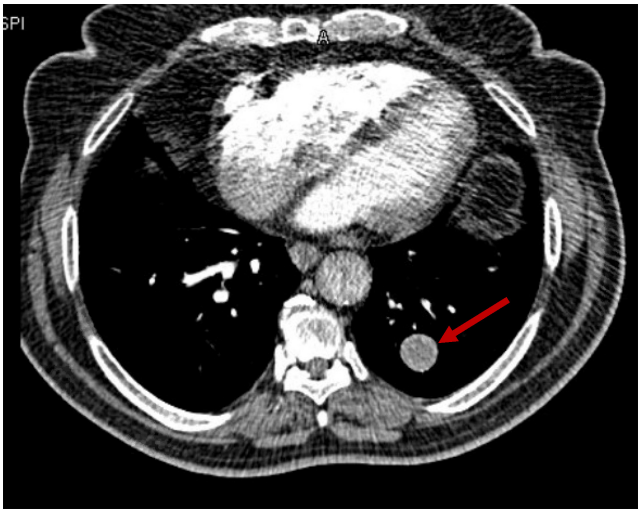

FIGURE 2 CT Chest indicating left lower lobe pulmonary nodule (arrow).

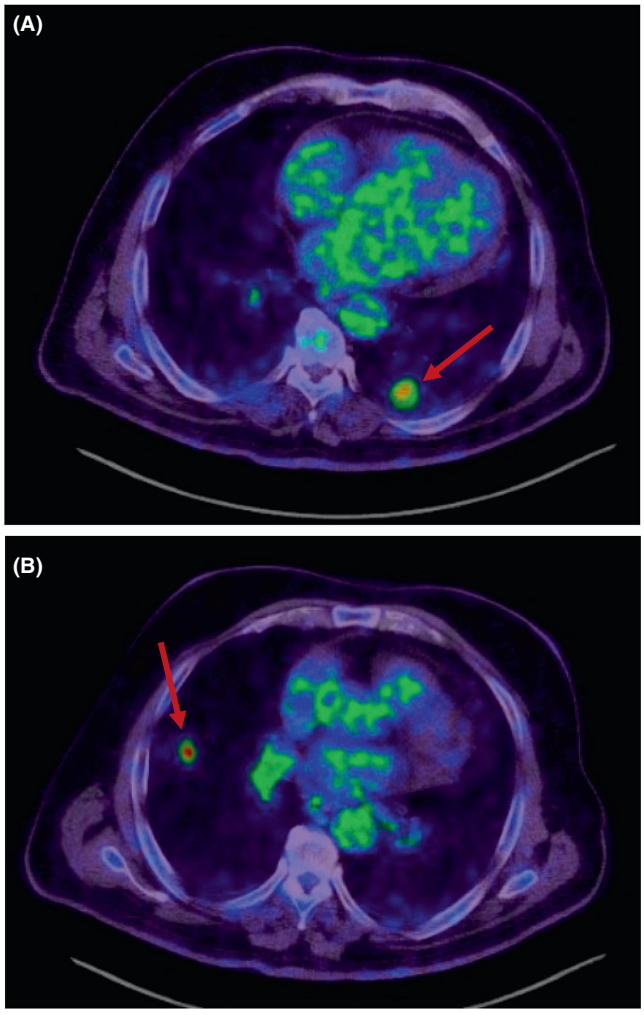

FIGURE 3 (A) FDG-PET showed abnormal accumulation in multiple nodules including left lower lobe nodule (arrow). CT-guided biopsy was performed from this nodule. (B) FDG-PET showing abnormal accumulation in the right lung pulmonary nodule (arrow).

nodules (Figure 3A,B). High FDG uptake was also noted in the left hilar lymph nodes. Computerized tomography (CT)-guided biopsy of the left lung nodule was subsequently performed. Microscopic examination revealed lung alveolar tissue replaced by a well-circumscribed unencapsulated tumor compatible with thymoma type AB. The thymoma is characterized by lymphocyte-rich and lymphocyte-poor areas (Figure 4A). The lymphocyte-rich areas (Figure 4A–green arrow) are characterized by dense sheets of immature T-lymphocytes that are admixed with rare epithelial cells (type B thymoma); these lymphocytes are staining positive with CD3, CD5, and TdT (Figure 4B). In the lymphocyte-rich areas, there are numerous perivascular spaces composed of central venules surrounded by a clear space containing proteinaceous fluid and a variable number of lymphoid cells (Figure 4B, red arrows). Lymphocyte-poor areas are devoid of lymphocytes and characterized by proliferation of spindle epithelial cells with ovoid nuclei having staghorn vasculature in the background (type A thymoma; Figure 4A, black arrow). These epithelial cells are positive with CK AE1/AE3, p63, CK 7, and PAX 8 (Figure 4C). Unfortunately, he did not meet the criteria for resection and chose to go for the best supportive care.

3 | DISCUSSION

Primary intrapulmonary thymomas are epithelial neoplasms occurring in the lung without any mediastinal involvement. They display characteristic histological features of thymomas. They are not only rare but also likely

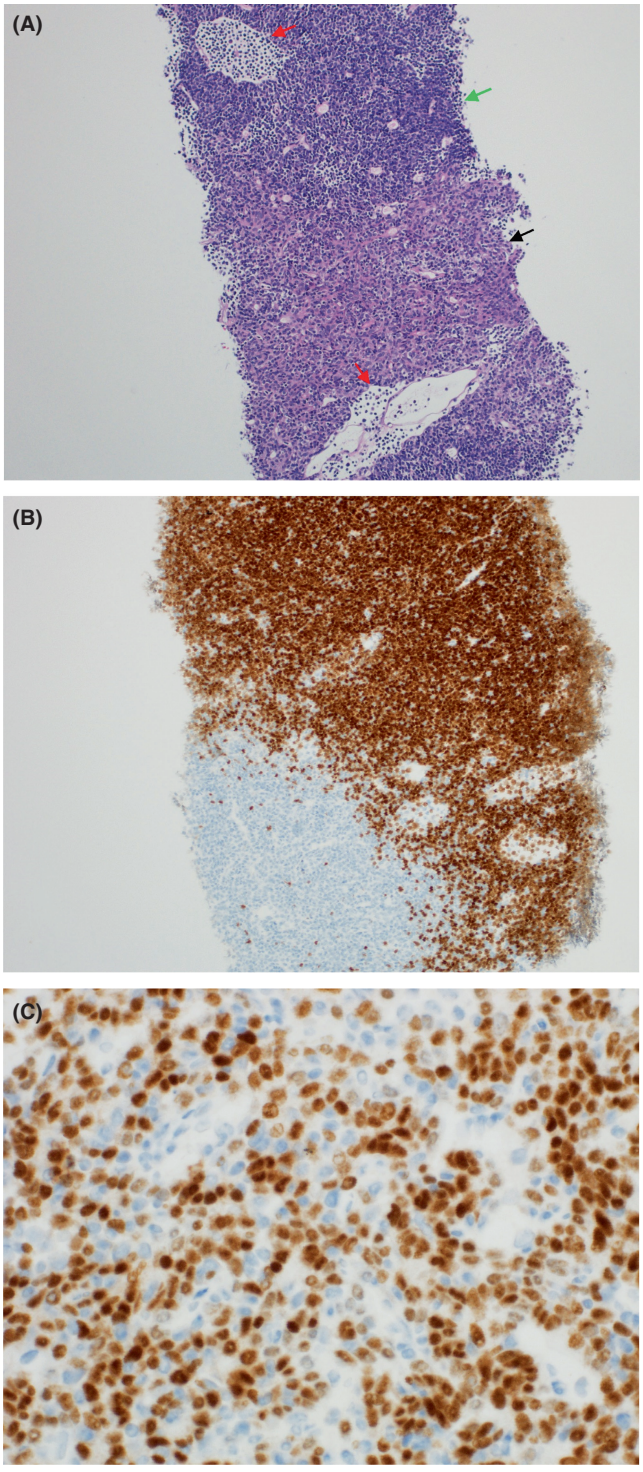

FIGURE 4 (A) Light microscopic examination reveals thymoma type AB consisting of lymphocyte-poor area (black arrow) and lymphocyte-rich area (green arrow), notice the prominent perivascular spaces (red arrows) (H&E×100). (B) Immunohistochemical staining with TdT highlights the dense population of immature T-lymphocytes (immunoperoxidase ×100). (C) Immunohistochemical staining with PAX 8 highlights the epithelial cell population in type A component of the thymoma (immunoperoxidase ×400).

under-reported. Less than 50 cases have been reported since Mc Burny reported the first case in 1951.[2] Unlike other cases, ours is unique because of its histological findings and bilateral pulmonary involvement which to our knowledge has not been reported before. Although the biopsy was taken from one lesion, CT and PET findings were consistent with multifocal bilateral involvement. Zhang et al. have previously reported a case of PIT with multiple bilateral intrapulmonary nodules which were all excised; however, their pathological findings of primary intrapulmonary spindle cell thymoma differ from the histological profile of our patient.[4] Furthermore, Myer et al.[3] have described two cases with multifocal but unilateral PIT in his systematic review. In his review, he indicates a broad range of distribution in terms of the patient's age at the time of diagnosis, with a maximum age of 77 years. Our patient's age at the time of diagnosis was 81 years and hence reflects the extreme end of the spectrum in this regard. With our case report, we hope to contribute to the pool of data collected concerning patient characteristics, clinical features, and imaging aspects of PIT along with the unusual presentation and bilateral involvement.

There remains uncertainty regarding the pathogenesis of PITs. One theory suggests that the PITs may occur due to the migration of mediastinal thymoma into the lungs. However, the fact that the pulmonary system develops much earlier than the thymic primordia, makes this theory doubtful. Another opinion is that the stem cells, which are pluripotent cells and capable of differentiating along a range of lines, give rise to thymomas. In addition, Fukayama et al.[6] hypothesized that a monodermal teratoma may develop into an intrapulmonary thymoma.

Primary intrapulmonary thymomas are slow-growing tumors and are usually discovered as an incidental finding in asymptomatic individuals. Symptoms begin to appear when the mass becomes large enough to compress nearby structures. Hemoptysis and chest pain have been described as common presenting symptoms. Like mediastinal thymomas, they can be related to paraneoplastic syndromes like myasthenia gravis or goods syndrome.[5] Our patient presented with a short history of hemoptysis without any other symptoms. He did well even several months after the diagnosis, reflecting an indolent course of the disease (He died unfortunately, 13 months after his diagnosis with COVID pneumonia).

Due to its rarity and nonspecificity of symptoms and radiological findings, it is a challenge to diagnose PITs. Computed tomography imaging usually shows a nonspecific well-circumscribed, heterogeneous mass. Similarly, in our patient, there was a heterogeneous mass lesion in the right lung and multiple bilateral solid pulmonary nodules. The differential radiologic diagnosis of PIT is wide

and includes lipomas, hamartomas, low-grade malignant tumors, metastatic lung cancers, and angiolipomas. When a lung tumor's pathology shows uncommon features, the possibility of PIT should be considered. It is important to perform an immunohistochemical examination to determine the exact diagnosis. Mediastinal thymomas and PITs both have similar histological features. Bronchoscopy may have a role in the diagnosis of endobronchial lesions, which can be seen in metastatic thymomas. Our patient on bronchoscopy had bronchial narrowing reflecting extrinsic bronchial compression by the tumor, but no obvious endobronchial lesions and the endobronchial biopsy results were inconclusive.

Thymomas have been reported to show an increased FDG uptake on PET, much like lung cancers. The accumulation of FDG in thymic epithelial tumors has been reported to be correlated with WHO histological types.[7,8] However, PET findings remain nonspecific and standardized uptake value (SUV) max as a measure of activity still shows a lot of overlap between low- and high-grade thymic tumors, with some benign lesions like thymic hyperplasia showing moderate-to-high uptake while some aggressive thymic cancers showing only moderate uptake.[7,9] Our case has shown variation in the FDG uptake among the lesions with the highest being in the left lower lobe nodule from which the biopsy was taken.

The typical histologic appearance ranges from lymphocyte-predominant to epithelioid-predominant or a heterogeneous mixed pattern. The lymphocytic component is highlighted by CD3, CD5, TdT, and Ki-67, while the epithelial component is highlighted by CK7, Vimentin, CK AE1/AE3, p63, and Pax-8. These epithelial markers are usually similar to those seen in metastatic lung cancer or poorly differentiating carcinomas; however, the presence of low mitotic activity and minimal atypia makes aggressive carcinomas unlikely. In our patient, there was a heterogeneous mixed pattern with strong positivity for CD3 and Pax-8 in addition to low mitotic activity.

According to the WHO histological classifications, the primary intrapulmonary thymoma is classified as a malignant tumor of the lung and hence is staged using a lung cancer staging system. Our patient had stage IVA disease based on the bilateral lung involvement and an increased metabolic activity in the mediastinal lymph nodes.

Although there are limited data with regard to the best management of PIT, there has been a consensus that complete resection of the tumor, when possible, is the best treatment option and results in the highest survival rate. As reported in the systematic review of Myers et al., patients treated surgically had a better chance of survival than patients treated conservatively. Radiation therapy can be considered as an adjuvant treatment in cases of incomplete resection.[10] Our patient had an advanced-stage PIT with bilateral lung and mediastinal nodal involvement. This made him unsuitable for surgical and/or radiation treatment. The decision was to start him on palliative chemotherapy; however, the patient himself chose to opt for the best supportive care.

In conclusion, PITs are rare; however, it can be argued that this is because of possible under-reporting. They present a diagnostic challenge due to their rarity and nonspecific symptoms, and radiological findings. As a result, comprehensive histopathological and immunohistochemistry analysis remains the gold standard test to confirm the diagnosis.

AUTHOR CONTRIBUTIONS

Sheikh Muhammad Wasim Jamal: Conceptualization; methodology; supervision; writing – original draft; writing – review and editing. **Mousa Hussein:** Conceptualization; project administration; writing – original draft; writing – review and editing. **Mutaz Albakri:** Conceptualization; writing – original draft; writing – review and editing. **Ibrahim Rasheed:** Conceptualization; methodology; writing – original draft; writing – review and editing. **Mansoor Hameed:** Conceptualization; methodology; project administration; supervision; writing – original draft; writing – review and editing. **Irfan Ul Haq:** Conceptualization; writing – original draft; writing – review and editing. **Merlin Thomas:** Conceptualization; writing – original draft; writing – review and editing. **issam AL-Bozom:** Conceptualization; investigation; writing – original draft; writing – review and editing. **Hisham Abdul Sattar:** Conceptualization; supervision; writing – review and editing.

ACKNOWLEDGMENT

The publication of this article is funded by Qatar National Library.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

CONSENT

I confirm that written patient consent has been signed and collected in accordance with the journal's patient consent policy.

ORCID

Sheikh Muhammad Wasim Jamal https://orcid.org/0000-0003-1796-1636

REFERENCES

1. Engels EA, Pfeiffer RM. Malignant thymoma in the United States: demographic patterns in incidence and associations with subsequent malignancies. *Int J Cancer*. 2003;105:546-551. doi:10.1002/ijc.11099
2. McBurney RP, Clagett OT, McDonald JR. Primary intrapulmonary neoplasm (thymoma?) associated with myasthesia gravis: report of case. *Mayo Clin Proc*. 1951;26:345-353.
3. Myers PO, Kritikos N, Bongiovanni M, et al. Primary intrapulmonary thymoma: a systematic review. *Eur J Surg Oncol*. 2007;33(10):1137-1141. doi:10.1016/j.ejso.2007.02.033
4. Zhang C, Xu W, Jin C, Li J, Hu J. Bilateral multiple intrapulmonary nodules: a puzzled and rare disease. *J Thorac Dis*. 2015 Jul;7(7):E182-E185. doi:10.3978/j.issn.2072-1439.2015.06.06
5. Ryman NG, Burrow L, Bowen C, Carrington C, Dawson A, Harrison NK. Good's syndrome with primary intrapulmonary thymoma. *J R Soc Med*. 2005;98(3):119-120.
6. Fukayama M, Maeda Y, Funata N, et al. Pulmonary and pleural thymoma. Diagnostic application of lymphocyte markers to the thymoma of unusual site. *Am J Clin Pathol*. 1988;89(5):617-621.
7. Endo M, Nakagawa K, Ohde Y, et al. Utility of 18FDG-PET for differentiating the grade of malignancy in thymic epithelial tumors. *Lung Cancer*. 2008;61:350-355.
8. Kaira K, Endo M, Abe M, et al. Biologic correlation of 2-[^{18}F]-fluoro-2-deoxy-D-glucose uptake on positron emission tomography in thymic epithelial tumors. *J Clin Oncol*. 2010;28:3746-3753.
9. Sung YM, Lee KS, Kim BT, Choi JY, Shim YM, Yi CA. 18F-FDG PET/CT of thymic epithelial tumors: usefulness for distinguishing and staging tumor subgroups. *J Nucl Med*. 2006;47:1628-1634.
10. Veynovich B, Masetti P, Kaplan PD, Jasnosz KM, Yousem SA, Landreneau RJ. Primary pulmonary thymoma. *Ann Thorac Surg*. 1997;64:1471-1473. doi:10.1016/S0003-4975(97)00935-1

How to cite this article: Wasim Jamal SM, Hussein M, Albakri M, et al. Primary intrapulmonary thymoma a case report. *Clin Case Rep*. 2023;11:e6897. doi:10.1002/ccr3.6897