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Lung mass with bilateral mediastinal hypermetabolic lymphadenopathy in a chronic smoker indicative of lung cancer?

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ABSTRACT

We present the case of an asymptomatic woman, a chronic heavy smoker, who presented with an incidental lung mass and mediastinal lymphadenopathy. Bronchoscopy with transbronchial biopsy and endobronchial ultrasound-guided transbronchial needle aspiration did not show malignancy. A positron emission tomography/computed tomography scan showed increased uptake with a standardized uptake value of 26.4 in the mediastinal lymph node and an additional hypermetabolic right supraclavicular lymph node. Surgical biopsy of the supraclavicular node revealed non-necrotizing granuloma. Discussion of the clinical dilemma is provided.

1. Introduction

Positron emission tomography (PET) or PET with computed tomography (PET/CT) is often employed in the evaluation of lung nodules and masses. The positive predictive value of a positive PET scan for malignancy exceeds 80% [1]. However, positive or false positive PET scan findings have been reported in many other conditions, from benign tumors to inflammatory or infectious processes [2–4].

Some of the most common etiologies for false positive PET scan results include pneumonia, tuberculosis, post-radiation pneumonitis, and sarcoidosis.

2. Case presentation

A 41-year-old Hispanic woman, daily smoker of 20 packs/year, with positive purified protein derivative and medical history remarkable for hypertension, mild persistent well-controlled asthma, and obesity was found to have abnormal findings on chest imaging while undergoing a pre-employment evaluation. Chest roentgenography (CXR) showed a novel left lower-lobe mass that was not present on a normal CXR performed 1 year previously.

The patient was asymptomatic, with no constitutional or respiratory symptoms. She had not traveled nor come in contact with ill individuals. Her family history was unremarkable. Physical examination was completely normal.

Laboratory testing including a basic metabolic panel, liver function test, calcium, and blood cell counts returned normal results. The angiotensin converting enzyme was low (<7 u/L).

Our main differential diagnosis included malignancy based on her smoking history and radiological presentation, followed by infectious and noninfectious conditions. Chest CT revealed a 3.6 cm left lower-lobe mass abutting the pleura, two additional nodes (10 mm and 6 mm, respectively) along the left major fissure, and mediastinal lymphadenopathy involving stations 4R, 4L, 7, 10R, and 10L (Fig. 1a and b).

She underwent fiberoptic bronchoscopy with transbronchial biopsy (TBBX) and endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA). The TBBX revealed chronic inflammation and mature lymphocytes; no malignant cells were seen on EBUS-TBNA. Stainings for tuberculosis and fungi were negative and all bronchoscopy cultures were negative.

PET/CT showed a hypermetabolic left lower-lobe mass and mediastinal/hilar lymphadenopathy with standardized update values (SUVs) of 18.9 and 26.4, respectively (Fig. 2) as well as a hyper-metabolically active right supraclavicular lymph node with an SUV of 15.9 (Fig. 3).

Surgical excisional biopsy of the supraclavicular lymph node revealed non necrotizing granulomas (Fig. 4), while no malignancy was observed.

Additional investigations including pulmonary function testing showed normal spirometry, lung volume, and diffusion capacity. No abnormalities were found on electrocardiography or echocardiography. The ophthalmological examination was normal.

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Abbreviations

CXR	Chest roentgenography
EBUS	Endobronchial ultrasound
PET/CT	Positron emission tomography/computed tomography
SUV	Standardized uptake value
TBBX	Transbronchial biopsy
TBNA	Transbronchial needle aspirations

At this point, there was a diagnostic and management challenge. The differential diagnosis was mainly narrowed to malignancy versus sarcoidosis. In view of the patient being asymptomatic with non-caseating granuloma on lymph-node biopsy, we favored sarcoidosis; however, her radiological manifestation was atypical and there was no systemic evidence of sarcoidosis. The options of thoracic surgical biopsy of the lung mass and mediastinal lymph nodes versus a wait-and-watch approach versus a trial of prednisone were discussed with the patient. She opted for a prednisone trial with close follow up.

She received 40 mg of prednisone; the follow-up PET/CT 6 weeks later showed almost complete resolution of the lung mass and decrease in the mediastinal lymph nodes with SUVs of 3.5 and 2.9, respectively (Fig. 5a and b).

Prednisone was tapered and discontinued within 12 weeks. Another chest CT 6 month after completion of steroid treatment showed no recurrence of the lung mass or lymphadenopathy. The patient remains under close follow up.

3. Discussion

Sarcoidosis is a multi-systemic chronic granulomatous disease characterized by the presence of non-caseating granulomas affecting the lungs in over 90% of the patients [5].The prevalence of sarcoidosis in the United States is 40–60 per 100,000 individuals, with an age-adjusted annual incidence among African Americans three times higher than that among Caucasians. Clinical symptoms can be absent in up to 50% of cases, and when symptomatic, patients can present with cough, dyspnea, bronchial hyper reactivity, fatigue, night sweats, weight loss, and erythema nodosum or symptoms related to the site involved [6,7]. The radiological manifestation of sarcoidosis varies. The most common findings on chest CT are small parenchymal nodules along the broncho-arterial bundles, interlobular septa, major fissures, and in the

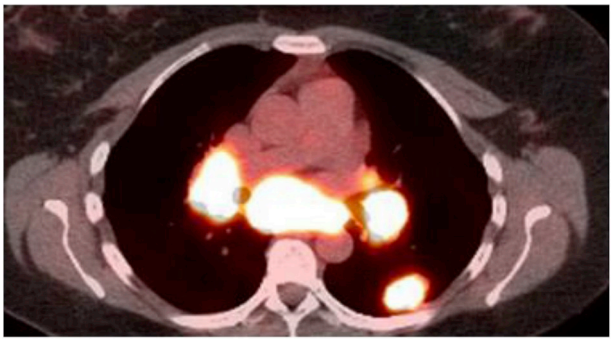

Fig. 2. Positron emission tomography/computed tomography showing a hypermetabolic left lower-lobe mass with lymph nodes.

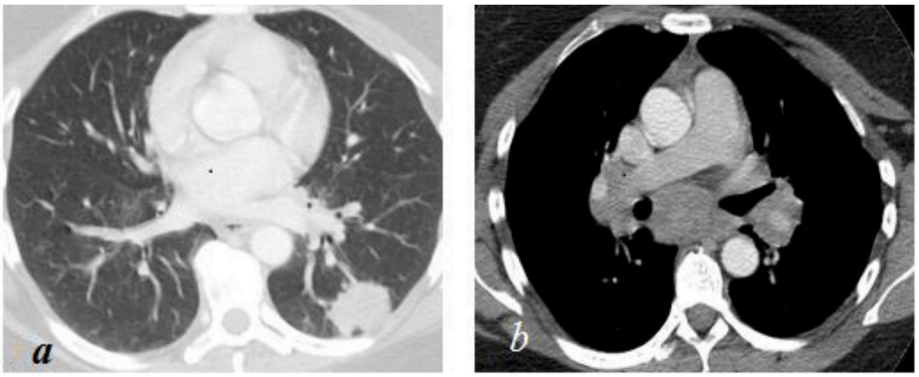

Fig.1. 1a, 1b: Chest CT showing a left lower-lobe mass and enlarged mediastinal lymph nodes.

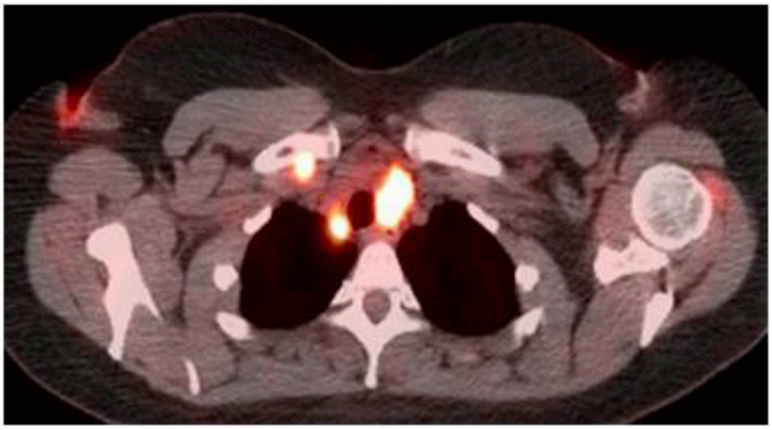

Fig. 3. Positron emission tomography/computed tomography showing a hypermetabolic right supraclavicular lymph node.

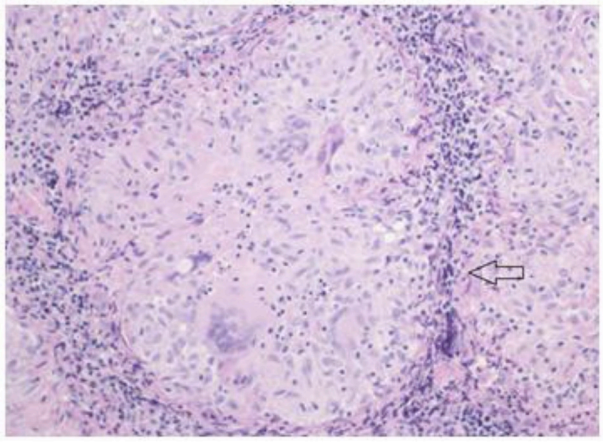

Fig. 4. Non-caseating granuloma shown with hematoxylin and eosin staining (400x).

subpleural regions [8]. Pulmonary nodules and masses are seen in 15%–25% of patients with parenchymal opacities. Bilateral hilar lymph-node enlargement is the most common mediastinal finding. On high-resolution CT, the most typical findings of pulmonary involvement are micronodules with a perilymphatic distribution, fibrotic changes, and bilateral perihilar opacities. Atypical manifestations, such as mass-like or alveolar opacities, honeycomb-like cysts, miliary opacities, mosaic attenuation, tracheobronchial involvement, and pleural disease, and complications such as aspergillomas may also be seen [9].

Nodular sarcoidosis is rare with an incidence of 1.6%–4% in patients with pulmonary sarcoidosis. There are limited data on this form of sarcoidosis, and its presentation can mimic primary or metastatic pulmonary neoplasms [10,11]. On CT, the nodules usually appear as ill-defined irregular opacities measuring 1–4 cm in diameter representing coalescent interstitial granulomas. These lesions are typically multiple and bilateral [9]. Nodular sarcoidosis is an uncommon form of sarcoidosis and is prevalent in 2.4%–4% of cases [12]. The first case of nodular sarcoidosis was reported by McCord and Hyman in 1952 with multiple bilateral nodules mimicking metastatic disease [13]. Most of the patients with nodular sarcoidosis are African–American women between 20 and 40 years of age [14]. Nodular sarcoidosis has a favorable prognosis, and resolution can be attained with use of systemic corticosteroids.

PET/CT is a sensitive technique for detecting inflammatory activity in sarcoidosis but is not indicated in the standard workup. The use of PET to assess the extent of the disease can uncover a suitable location for biopsy to obtain histological evidence for the diagnosis or to explain the (mainly extra-thoracic) symptoms [15]. Maturu et al. evaluated the role of F-18 fluorodeoxyglucose PET/CT scanning in assessing the treatment response and predicting relapses in patients with symptomatic sarcoidosis; in their series, the SUV-max was 18.6, and there was significant decline in the median SUV-max of the mediastinal lymph nodes, peripheral lymph nodes, and the lung parenchyma in the follow up PET scan after treatment [16]. In another large series of 137 patients with sarcoidosis, PET/CT showed an SUV ranging from 2 to 15.8 [17]. There is no reported cutoff for the SUV value to distinguish benign from malignant lesions.

In addition, there is the concern of malignancy in the presence of sarcoidosis. Three possibilities have been reported in the literature. First, patients with hematologic malignancies, including sarcoidosis-lymphoma syndrome; the patients develop lymphoma at least 1–2 years after the diagnosis of sarcoidosis. This also includes patients with sarcoidosis who develop other hematologic malignancies or patients with cancer and hematologic malignancies who subsequently develop sarcoidosis. Second, patients diagnosed with sarcoidosis who develop solid tumors and patients with tumors in whom sarcoidosis appears later. Commonly reported malignancies include melanoma and non-melanoma and cervical, liver, lung, testicle, and uterine cancers. Third, malignancy-related sarcoidosis occurs when sarcoidosis presents as a paraneoplastic syndrome for the associated cancer; usually, the cancer is concurrent with or appears within 1 year of the diagnosis of sarcoidosis or vice versa. Sarcoid-like reactions can be found closer to the area of the malignancy or in the regional lymph nodes involved [18].

Two other differentials which would be responsive to corticosteroid therapy were tuberculosis and lymphoma. Use of corticosteroids as adjunctive treatment in patients with tuberculous pleurisy, meningitis and pericarditis has reported some benefits [19]. However, the role of corticosteroids in pulmonary tuberculosis is controversial; Yang et al. reported a mortality benefit in patients with pulmonary tuberculosis and acute respiratory failure [20]. Patients with lymphoma usually respond to high dose of steroids which is usually used in a cyclical fashion along with other chemotherapeutic agents, rarely they can have a temporary response to a single dose of steroids [21]. Our patient had all cultures negative for tuberculosis and no evidence of tuberculous pleurisy, meningitis or pericarditis. In addition, close and adequate follow up failed to show any recurrence of the pulmonary mass, which argues against malignancy or infection process.

In summary, our patient had an extremely rare presentation of a common disease. She had an atypical radiological presentation and very high SUV in the mass and lymph nodes on PET/CT; all these findings are commonly observed in cases of malignancy.

Patients with lung masses and positive PET scan findings can initially be evaluated by various specialists including pulmonologists, thoracic surgeons, oncologists, and interventional radiologists. It is important to recognize rare presentations of benign diseases and to consider sarcoidosis as part of the differential diagnosis. In cases of clinical dilemmas such as the present one, shared decision with the patient is mandated to plan further management. Occasionally, the empiric administration of trial steroids could be a diagnostic and therapeutic choice considering that this is not the standard of care due to the associated side effects of steroids and potential diagnostic delay of malignancy if present. Such patients require close follow up to monitor for the development of malignancy.

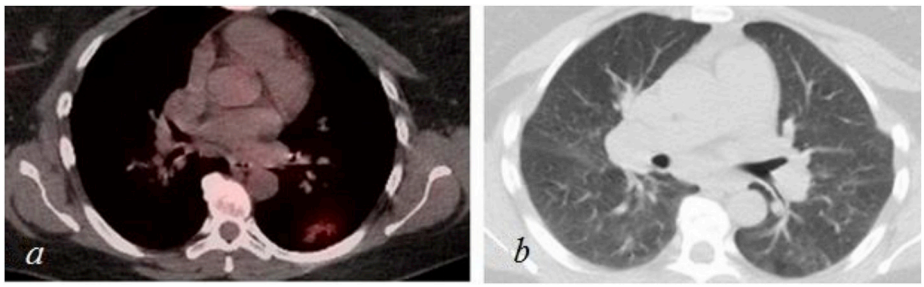

Fig. 5. 5a,5b: Post treatment positron emission tomography/computed tomography and chest computed tomography showing resolution of the left lower-lobe mass.

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Author contributions

S Venkatram and A Ali searched the literature and wrote manuscript. G Diaz-Fuentes conceived and edited the manuscript. M Niazi reviewed the pathology slides. S Venkatram supervised patient treatment. All authors have made significant contributions to the manuscript and have reviewed it before submission. All authors have confirmed that the manuscript is not under consideration for review at any other journal.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100982.

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