A case of chronic cough due to sarcoidosis

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Abstract

Sarcoidosis is a multisystemic, chronic granulomatous disease of unknown aetiology that often affects the lungs. Diagnosis and treatment of sarcoidosis can be strenuous. Patients may be asymptomatic or experience cough, dyspnoea, fatigue, unintentional weight loss or night sweats. Computed tomography is valuable in the diagnosis of sarcoidosis. The typical histopathological lesion of sarcoidosis is granuloma without caseous necrosis in the involved organs. As tuberculosis is endemic in our region, clinicians should not forget this great mimicker. The cornerstone of treatment of sarcoidosis is corticosteroids but newer agents such as steroid-sparing agents and biological agents are available. We report a case of pulmonary sarcoidosis presenting with chronic cough.

Keywords

Cough, non-caseating granuloma, sarcoidosis

Case report

A 30-year-old non-smoker, Indian, female patient reported chronic dry cough and weight loss of 15 kg for one month’s duration. Physical examinations were unremarkable with no erythema nodosum, uveitis, cranial nerve palsy or parotid enlargement. Chest radiograph showed bilateral upper lobe consolidation. Early morning sputum for acid fast bacilli and gene X-pert were negative. Her baseline lung function test showed forced expiratory volume in 1 s (FEV₁) 2.51 L (89%), forced vital capacity (FVC) 2.85 L (92%), FEV₁/FVC 88% and diffusing capacity of lung for carbon monoxide (DLCO) 57%. Lung volume was normal with slightly reduced DLCO. Thoracic contrast enhanced computed tomography showed multiple nodular consolidations at her upper lobes, medial segment of the right middle lobe and superior segment of the right lower lobe (Figures 1 and 2). There were multiple nodular consolidations at her upper lobes, medial segment of the right middle lobe and superior segment of the right lower lobe (Figures 1 and 2). There were multiple enlarged mediastinal nodes. Bronchoscopy with lavage was negative for common respiratory infections, fungal and Mycobacterium tuberculosis. An endoscopic bronchoscopy ultrasound-guided biopsy was performed via rigid bronchoscopy under general anaesthesia, with successful biopsy of her mediastinal lymph nodes (Figure 1(a)). She had undergone a transbronchial lung biopsy (TBLB), bronchial mucosal biopsy and bronchoalveolar lavage (BAL). Her BAL from RB2 cytology showed a lymphocyte predominant fluid of 78%, alveolar macrophages 1.5%, neutrophils 1.8% and eosinophils 0.2%. The transbronchial lymph node biopsy of her RB2 showed non-necrotising granulomatous inflammation, confirming the diagnosis of pulmonary sarcoidosis (Figure 3(a)–(f)). There were scattered granulomas seen in her TBLB. She was diagnosed with stage II pulmonary sarcoidosis (bilateral hilar lymph nodes and parenchymal infiltrates). Laboratory testing revealed normal full blood count, chemistry panel, HIV, calcium and vitamin D values. Sputum examination was normal with no evidence of uveitis. High resolution computed tomography showed no evidence of pulmonary fibrosis. She was started on oral prednisolone 20 mg daily as she was symptomatic. Her echocardiographic results were normal, with no evidence of pulmonary hypertension. Slit lamp examinations were normal. Her symptoms improved and she remained well during her follow-up.

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Figure 1. (a) Patient's endoscopic bronchoscopy ultrasound showed the conglomerate appearance of the lymph node. (b) Axial view of contrast enhanced computed tomography (CT) thorax showing mediastinal lymphadenopathy. Bilateral calcified hilar lymphadenopathy (white arrow) and subcarinal. (c) Coronal view of contrast enhanced CT thorax showing matted and enlarged nodes at right paratracheal region (white arrow).

Figure 2. (a) Axial images of lung window showing multiple pulmonary nodules (white arrow) with ‘tree in buds’ changes in both upper lobes (White arrows). (b) Focal consolidation in the superior segment of right upper lobe. (c) Consolidation with air bronchogram in the middle lobe (white arrow) and (d) focal consolidation in the superior segment of right upper lobe (white arrow). (c) Multiple pulmonary nodules noted in both lungs (upper, middle and lower lobes). The larger nodules are surrounded by smaller nodules with associated interlobular septal thickening giving rise to ‘tree in buds’ appearance. Confluence of consolidation with air bronchogram noted in the middle lobe. Multiple enlarged mediastinal nodes, seen in right paratracheal, pretrachea, anteroposterior (AP) window, precarina, subcarinal and both hilar region. Calcified nodes noted in both hilar regions. No cavitating or bronchiectatic changes seen. Overall findings are suggestive of stage II pulmonary sarcoidosis (mediastinal lymphadenopathy with lung infiltrate).
Sarcoidosis is an uncommon chronic systemic inflammatory and infiltrative disorder characterised by non-caseating granulomas. A broad differential list should be considered due to a highly variable clinical presentation and disease course prior to the diagnosis of sarcoidosis. There are numerous differential diagnoses which include mycobacterium infections, viral, fungal, protozoan, autoimmune diseases and hematological malignancy. A diagnosis of sarcoidosis is based on compatible clinical and radiological findings, histological evidence of non-caseating granulomas and the exclusion of any alternative causes of granulomatous disease. As our patient had a negative mycobacterium and fungal work-up, she underwent a mediastinal lymph nodes biopsy via endoscopic bronchoscopy ultrasound-guided biopsy.

Sarcoidosis is common among adults less than 40 years old and peaks between 20 and 29 years with a modest female predominance. A classic case of sarcoidosis includes a presentation of Lofgren syndrome with erythema nodosum, hilar adenopathy, ankle oligoarthritis and iritis. Other presentations include lupus pernio, acral papulo nodules and plaques, Heerfordt's syndrome with a triad of uveitis, cranial nerve palsy and parotid enlargement. It is a diagnostic challenge and clinicians should correlate the clinical presentation along with the histological findings of granulomatous inflammation after excluding other mimickers. A lymph node excisional biopsy would provide additional information. The British Thoracic Society of Interstitial Lung Disease guideline advocates the utility of endobronchial biopsies as adjunct biopsy in cases with suspected pulmonary sarcoidosis. Serum angiotensin-converting enzyme (ACE) is imperfect as it may be elevated in normal subjects including those with tuberculosis.

In patients with suspected sarcoidosis and mediastinal and/or hilar lymphadenopathy which requires tissue sampling, an endobronchial ultrasound (EBUS)-guided lymph node sampling is preferred over mediastinoscopy. TBLB through a fiberoptic bronchoscope could provide a diagnostic yield up to 80–90% if more than four adequate biopsies are performed in line with the European Respiratory Society recommendation. The yield may be as high as 70–80% in stage 1 disease. Even in cases with grossly normal bronchial mucosa, a biopsy of the bronchial mucosal could demonstrate the evidence of granuloma in approximately 50% of cases. However, the yield of endobronchial biopsies can exceed 90% if there is evidence of mucosal nodularity seen endoscopically. A lymphocytic study can be done with BAL and bronchoscopy biopsy together as a CD4/CD8 ratio of greater than 3.5 to 4 offers a sensitivity of 52–59% and a specificity of 94–96% in the diagnosis of sarcoidosis.

The management of sarcoidosis is multi-disciplinary and will depend on the systems affected. A watch and wait strategy is appropriate in asymptomatic pulmonary sarcoidosis. Up to 60–70% of spontaneous remissions are reported internationally. Spontaneous remission is often seen in Lofgren syndrome. Treatment is indicated in symptomatic individuals or when there is lung function worsening. In pulmonary sarcoidosis, the initial prednisolone dose is 20–40 mg daily and a higher dose may be required for cardiac or neurological sarcoidosis. Glucocorticoids remain the first line therapy of choice for the treatment of many sarcoidosis manifestations. The indications for systemic steroids include persistent hypercalcemia, persistent renal dysfunction, hepatic dysfunction, fatigue, weight loss, myopathy and
disfiguring skin lesions. Patients who fail first line corticosteroids should add in another drug such as methotrexate, mycophenolate, leflunamide or azathioprine. In the third line, biological agents such as pro-inflammatory cytokine tumour necrosis factor (TNF) blockers such as infliximab can be considered. A repeat thoracic imaging is required to ensure treatment resolution. There is a risk of inadequately treated pulmonary sarcoidosis leading to irreversible pulmonary fibrosis. Osteoporosis is often a complication due to long-term steroid therapy and hypercalciuria and endogenous hypercalcemia. Hence, close monitoring of vitamin D and a calcium supplement for osteoporosis prevention should be taken.

Conclusion
This case illustrated multiple learning points to clinicians in the diagnosis of sarcoidosis as many aspects remain challenging. A good history and interpretation of all clinical information is imperative before making clinical decisions. Clinicians should remain open minded and vigilant as both tuberculosis and sarcoidosis are great mimickers.

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Authors’ contributions
Qin Jian Low conceived and designed the manuscript. Mohd Nadzri Bin Misni drafted the manuscript. Khai Lip Ng and Noorul Afidza Muhammad reviewed the manuscript. Seng Wee Cheo critically revised the manuscript.

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