Original Article

Necrotizing sarcoid granulomatosis misdiagnosed as pulmonary tuberculosis and malignancy: a case report

Xinyu Ren1*, Hui Zhang1*, Songyang Yuan2, Rui’e Feng1

1Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 1 Shuaifu Yuan, Beijing 100730, PR China; 2Department of Pathology, Mount Sinai Beth Israel Medical Center, Icahn School of Medicine at Mount Sinai First Avenue at 16th Street, New York, NY 1003. *Equal contributors.

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Abstract: Necrotizing Sarcoid Granulomatosis (NSG) is a rare form of pulmonary vasculitis and granulomatosis, characterized by a combination of sarcoid-like granulomata, a prominent vasculitis and a variable degree of necrosis. However, clinical and radiological findings are nonspecific. NSG can be confused with pulmonary infectious disease and malignancy. We present a case of 31-old female with the symptoms of hyposmia and cough. She was diagnosed with tuberculosis and was given anti-TB therapy. Half a year later, her chest CT scan showed a 5 cm mass in left lower lobe basal segment. A left lower lobectomy was then performed due to suspicion of malignancy. The lobectomy specimen was diagnosed as tuberculosis. The patient was given another 19 months anti-TB therapy until the pathological review of the slides at our institute that confirmed the diagnosis of NSG. She was treated with prednisolone, which led to improvement of her symptoms.

Keywords: Necrotizing sarcoid granulomatosis, hyposmia, granuloma, vasculitis, necrosis, bronchoscopy

Background

Necrotizing Sarcoid Granulomatosis (NSG) is a rare form of pulmonary vasculitis and granulomatosis originally described by Liebow in 1973 [1]. Histologically, NSG is characterized by a combination of sarcoid-like granulomata, a prominent vasculitis and a variable degree of necrosis. Radiological findings are nonspecific. NSG cases usually present with multiple pulmonary nodules without enlarged hilar lymph nodes [2]. Solitary nodule or a mass is not considered as a common presentation. NSG primarily affects lungs and extrapulmonary involvement is rare [3-6]. Although the etiology and pathogenesis of NSG are unknown, most of NSG had a benign prognosis.

We report a case of NSG with sinus and pulmonary involvements, which was misdiagnosed as pulmonary tuberculosis for two years. Left lower lobectomy was also performed due to suspicion for malignancy.

Case presentation

A 31-year-old female presented at a local hospital for cough with a small amount of white sputum and hyposmia in December 2010. She had an intermittent fever without chills and the maximum temperature was 38°C. She had no history of night sweat, weight loss, chest pain, palpitation, arthralgia or skin rash. There was no history of systemic disease or allergy. She was treated for influenza, but her symptoms were not improved. A month later, she was admitted to a local tuberculosis hospital. A chest CT scan showed no significant abnormalities. However, Bronchoscopic findings were consistent with tuberculosis. Anti-tuberculosis (Anti-TB) therapy was started, comprising isoniazid, pyrazinamide, and rifampicin. Her cough improved, but her hyposmia was getting worse. Three month later, she had a stabbing pain in the lower left chest when breathing. A contrast enhanced multidetector CT scan of the chest showed a 5 cm, well-demarcated, heterogeneous mass in the left lower lobe posterior
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basal segments (Figure 1A). An enlarged left hilar shadow and left pleural effusion were also observed. Despite of negative findings on bronchoscopy, a malignant neoplasm was suspected clinically and left lower lobectomy was performed in May 2011. Macroscopic examination of left lobe revealed consolidation with a 5 cm well-demarcated nodule with medium texture in posterior basal segments. Microscopic examination of the resected lesion showed necrotizing granulomatous inflammation with multinucleate giant cells. Special stains for fungi and acid fast bacilli (AFB) as well as acid fast bacilli culture were negative. Final pathology report gave a differential diagnosis between tuberculosis and sarcoidosis, and the patient revealed a patchy shadow in the right upper lobe. Another two new similar round nodules appeared in August, 2011. The lesions of lung kept progressing with bilateral pleural effusion in November, 2011. Steroid therapy was administered and resulted in symptomatic and clinical improvement. A chest CT scan showed improvement of pulmonary lesions and absorbance of bilateral pleural effusion. However, she developed new nodules and patch infiltration of bilateral lungs (Figure 1B), once steroid was tapered down.

The patient was referred to our hospital in December, 2012. Her routine blood test and urine analysis were normal. Erythrocyte sedimentation rate (ESR) was also within normal limits. Antinuclear factor (ANF), anti-O, RF, serum P-ANCA, C-ANCA, and rheumatoid factor (RF) were negative. Pulmonary function test showed significantly decreased pulmonary ventilation function with normal pulmonary gas exchange function. Flexible bronchoscope was performed with normal bronchoscopic airway findings. Enhanced CT scan of sinus showed soft tissue opacification of bilateral ethmoid and right maxillary sinuses and round shaped low density opacification of right sphenoid sinus (Figure 1C). Review of histology of left lobectomy specimen showed confluent well-defined granulomata with giant cells, lymphocytes and plasma cells, forming mass-like lesion. Some were related to bronchovascular bundles. Extensive necrosis was evident within granulomata and the adjacent lung parenchyma (Figure 1D). The vasculitis was characterized by infiltration of lymphocytes and macrophages with areas granulomatous inflammation (Figure 1E and 1F). Acute necrotizing vasculitis was not identified. Repeat of special stains for fungi and acid fast bacilli and acid
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fast bacilli culture for tuberculosis was negative. The final diagnosis was rendered as necrotizing sarcoid granulomatosis. Her anti-TB therapy was discontinued. She was administered with prednisone (30 mg, qd). Her symptoms improved dramatically. Her sense of smell was retrieved after corticosteroid therapy. The shade of lung disappeared on chest CT scan in June, 2013. She is currently on follow-up, with no obvious symptoms.

Discussion

Necrotizing Sarcoid Granulomatosis (NSG) was firstly described by Liebow in 1973, in five different forms of pulmonary angiitis and granulomatosis: Wegener’s granulomatosis, limited Wegener’s disease, lymphomatoid granulomatosis, bronchocentric granulomatosis and NSG [1, 7]. NSG is a rare systemic disease with chief features: sarcoid-like granulomata with a prominent granulomatous vasculitis and varying degrees of necrosis; radiographic features with pulmonary nodules without enlarged hilar lymph nodes; most have a benign prognosis.

In the present case, we present a 31-year-old female with initial symptoms of hyposmia and cough. She was given anti-TB therapy based on bronchoscopic findings. Half a year later, a chest CT scan revealed a 5 cm mass in the basal segments of left lower lobe. A malignant neoplasm was suspected and left lower lobectomy was performed. The histology of lobectomy specimen showed typical features of NSG. However, the pathologist of local hospital over looked the presence of vasculitis. The patient was given another 19 months anti-TB therapy. For two years, her disease was progressive due to misdiagnosis. Until the patient was referred to our institution, a correct diagnosis of NSG was rendered.

NSG is usually diagnosed on the basis of pathological features, including sarcoid-like granulomas, granulomatous vasculitis and variable degree of necrosis. Regarding the finding of granulomatous inflammation with necrosis in the Chinese patients, tuberculosis represented the most likely diagnosis in the differential. In this case, surgical specimen was negative for fungi and acid fast bacilli (typical and atypical mycobacteria) on histologic stains and cultures.

Liebow suggested that NSG could be a variant of angiocentric granulomatosis. It still remains controversial whether NSG is a variant of sarcoidosis or a distinct entity. NSG differs from typical sarcoidosis by the presence of significant noncaseating necrosis and confluent granulomatous inflammation consisting of epithelioid histiocytes, lymphocytes, and plasma cells, usually with an associated granulomatous vasculitis [8-10]. The necrosis surrounding the blood vessels is ischemic necrosis resulting from granulomatous vasculitis. This is a unique pathological feature of NSG. Necrosis and granulomatous vasculitis in NSG act together to make the disease progress. Besides those pathological differences between NSG and sarcoidosis, NSG does have distinct clinical features from sarcoidosis such as negative serum angiotensin converting enzyme (SACE) and Kveim test. There are no asteroid bodies and Schaumann bodies, which are often found in sarcoidosis patients [11].

The other form of pulmonary angiitis and granulomatosis disorders should also be excluded. Wegener’s granulomatosis (WG) is clinically and histopathologically different from NSG. WG mainly affects the upper respiratory and lower respiratory tract and the kidneys. Increased serum C-ANCA level is associated with WG. Histologically, WG is characterized by parenchymal necrosis, necrotizing vasculitis, and granulomatous inflammation accompanied by inflammatory infiltration including neutrophils. The neutrophilic microabscesses in collagen are unique feature of WG. Geographic necrosis of WG is basophilic and may be surrounded by palisading histiocytes, bronchocentric granulomatosis and Churg-Strauss syndrome. Patients with bronchocentric granulomatosis and Churg-Strauss syndrome usually have asthma with increased eosinophils in peripheral blood. Histologic feature of bronchocentric granulomatosis is granulomatous inflammation that surrounds and replaces bronchial wall and mucosa with destruction of the airway lumen. In addition, vasculitis is not a feature of this entity. Patients with Churg-Strauss syndrome always have systematic vasculitis with increased serum P-ANCA level. Lung biopsy from those patients may show eosinophilic pneumonia, extravascular “allergic granulomas”, and vasculitis.
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The vast majority cases of NSG affect the lungs. Extrapulmonary involvements rarely occur and have been reported in skin, subcutaneous tissue, kidney, lacrimal gland, gastrointestinal tract, orbit, liver and spinal column, and central nervous system [12-14]. To our knowledge, NSG with sinus involvement has not been reported previously. The patient presented with hyposmia and CT scan of sinuses show typical features of NSG involvement.

Radiologic findings of NSG are not specific. NSC usually manifests as multiple nodules in bilateral lungs, ranging from 2 to 4 cm [2, 3]. Nodules may be well-demarcated or have ill-defined borders. Solitary nodule or a mass is not a common presentation. Lung hilar and mediastinal lymph nodes are not typical in NSG patients. In our case, initial chest CT scan was negative. A 5 cm solitary pulmonary mass with enlarged hilar shadow was identified on subsequent CT scan, which was mimicking malignant neoplasm. A left lower lobectomy was performed based on radiological and clinical findings.

The clinical course of NSG is usually benign with good responsiveness to steroid treatment or even without treatment. In our case, low-dose oral corticosteroid therapy was effective. Her sense of smell was retrieved after corticosteroid therapy. The shade of lung disappeared on chest CT scan in June, 2013. The patient was free of the disease until now.

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Disclosure of conflict of interest
None.

Address correspondence to: Rui’e Feng, Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 1 Shuaifu Yuan, Beijing 100730, PR China. Tel: +86 010-69159373; E-mail: fengruie1@163.com

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