Necrotising sarcoid granulomatosis. A rare granulomatous disease

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Abstract. Introduction: Necrotizing sarcoid granulomatosis (NSG) is a very rare disease of unknown etiology characterized by sarcoid-like granulomas, vasculitis and necrosis in pulmonary and extrapulmonary localizations. Case report: We describe a case of a 34-year-old Caucasian male with fever, pleural pain, and nodular pulmonary opacities on chest radiograph. Histological examination of the lung tissue confirmed NSG. Diagnostically, infectious causes, vasculitis, and malignancy were excluded. A tendency to partial regression was observed, without the need for corticosteroid treatment. Conclusion: NSG is a rare disease which must be distinguished from other systemic diseases including vasculitides. The key to diagnosis, emphasized in our paper, is the histopathological finding. The course of NSG is similar to sarcoidosis. Corticosteroids are considered the treatment of choice, but the disease exhibits a tendency towards spontaneous regression. (Sarcoidosis Vasculit. Diffuse Lung Dis 2018; 35: 395-398)

Key words: differential diagnosis, histopathological diagnosis, necrotising sarcoid granulomatosis

Introduction

Necrotizing sarcoid granulomatosis (NSG) is a rare systemic disease characterized by sarcoid-like granulomas, central necrosis and vasculitis (1-3). It was first described by American pathologist, Averill Abraham Liebow in 1973 (1).

Case report

A 34-year-old Caucasian male, an ex-smoker, presented with fever and breathing-related pleural pain. The patient had a long-term antihypertensive medication. His family history was negative. Physical examination revealed pleural friction rub on the right side of the chest; the rest of the physical examination was unremarkable. The posteroanterior chest radiograph showed nodular opacities mostly in the right lung. Multiple subpleural nodular opacities, the largest 13mm in diameter, were seen on the chest CT (Figures 1, 2, 3). Pulmonary function testing revealed no ventilation or diffusion defect. Arterial blood gas analysis was also normal. Laboratory tests at admission showed (reference values between brackets): C-reactive protein (CRP) 45mg/L (0-5), serum calcium 2.57 mmol/l (2.25-2.55), IgE 1.281 g/l (reference value <90 g/l), angiotensin-converting enzyme (ACE) 8 U/L (20-70) – the low ACE probably being influenced by the ACE inhibitor medication for high blood pressure. Total IgG, IgA, IgM concentrations were normal. The IgG4 subtype concentration was increased to 2.46 g/L (0.08-1.40 g/L). Serum protein electrophoresis complete with
paraprotein and clonal IgE was normal. Complete blood count including white blood cell differential was normal, without eosinophilia. The liver function tests were normal.

Treatment with antibiotics (amoxicillin) was started – without any effect on the pulmonary lesions. As the finding persisted and metastatic disease has to be excluded, video-assisted thoracoscopic surgery (VATS) with pulmonary biopsy was indicated.

Histopathological examination then confirmed necrotizing sarcoid granulomatosis. Pulmonary parenchyma with peribronchovascular epitheloid granulomas including a few multinucleated giant cells, with a sparse perifocal lymphocytic inflammatory infiltrate. Minute, spotty areas of necrosis are present in the centre of some granulomas. Granulomas are well-circumscribed, well-formed, of the sarcoid type. In some places, granulomas merge into nodules with large central necrosis with chromatin dust. Granulomas are visible both in the lung parenchyma and, abundantly, in the vessel wall (with focal destruction). No cavitation is present. While granulomatous vasculitis is predominant, focally the inflammation is lymphocytic in character. The pleura exhibits identical lesions. Special staining on mycobacteria and fungi are negative (Figure 4). Searching for NSC’s extrapulmonary manifestions, hypodense deposits were discovered in the liver and renal cortex. A tiny (6mm) deposit was also found in a non-enlarged spleen. Further investigations were focussed on the exclusion of infectious causes or systemic diseases including vasculitides. The immunological screening including ANCA (antineutrophil cytoplasmatic antibodies) was negative. For the detection of elevated serum IgG4, immunohistological examination of the lung tissue was performed but no increase in the number of IgG4-positive plasma cells was found, and the histopathological finding did not meet the criteria of IgG4-related disease. Infectious exami-
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Serology of Chlamydophila pneumoniae, Mycoplasma pneumoniae and Aspergillus fumigatus have been mooted. NSG primarily affects younger patients (median, 42 years of age) (10). Family occurrence has not been reported. Clinical symptoms are nonspecific and include pleural pain, weight loss, cough, dyspnea and fever. Extrapulmonary involvement can mimic sarcoidosis (10). Radiological find-
ings vary; most often, nodular opacities are observed in the lung parenchyma, either solitary or multiple, with or without hilar and mediastinal lymphadenopathy (11,12). No specific laboratory biomarker for NSG diagnosis is available. ACE is usually normal (4). Pulmonary function tests are either normal or demonstrate a variety of abnormal patterns (13). The CD4/CD8 ratio in the bronchoalveolar fluid may be normal – in contrast to sarcoidosis (4).

The histopathological finding is central to, and indispensable for, the diagnosis of NSG. NSG should meet the following criteria: granulomas, necrosis and granulomatous vasculitis with no evidence to support an infectious etiology (7). The differential diagnosis includes granulomatous infection, nodular sarcoidosis and Wegener’s granulomatosis (granulomatosis with polyangiitis). The most difficult – and mostly impossible – to exclude is granulomatous infection that can cause necrotizing granulomatous inflammation and vasculitis resembling NSG. However, histological features typical of pulmonary sarcoidosis – non-necrotizing confluent granulomas surrounded by hyaline fibrosis and necrosis – are not characteristically seen in NSG. Still, some experts believe that NSG is essentially the same disease as sarcoidosis. Necrotizing granulomatous inflammation with vasculitis is also seen in Wegener’s granulomatosis. However, the presence of sarcoid-like granulomas and absence of the classic pattern of necrosis in Wegener’s granulomatosis, i.e. geographical areas of basophilic necrosis, favour NGS (10).

The clinical course of NSG is mostly benign with a tendency to spontaneous remission except for potentially lethal neurological lesions (14). Corticosteroids are the treatment of choice (4).

**Conclusion**

This work describes a rare systemic disease called necrotizing sarcoid granulomatosis (NSG). Emphasis is placed on histopathological findings and differentiation from other vasculitides or granulomatous diseases of the sarcoidosis type.

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