Case report

A crazy cause of dyspnoea: Pulmonary alveolar proteinosis

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In March 2012, a 37-year female patient presented to the emergency department with a 6 months history of progressive dyspnoea, fatigue, insomnia and generalized body pains. There was no accompanying cough or haemoptysis. She was a non-smoker with no background medical or surgical history. No risk factors for pulmonary disease could be identified from her occupational history. Prior to her admission she was treated with multiple courses of empirical antibiotics and bronchodilators without complete resolution of her symptoms.

Upon arrival to the hospital she was fully alert and orientated. Her vital signs on admission included a blood pressure of 125/79 mmHg, respiratory rate of 24 breaths per minute and a heart rate of 116 beats per min. She was afebrile with central cyanosis. Further examination showed oxygen saturation of 48% on room air. Chest examination revealed good air entry with no abnormal sounds. The rest of the physical examination was normal. Her full blood count, C-reactive protein, anti-nuclear antibodies and complement levels were all normal. An elevated LDH 307 U/L [120-230U/L] was detected on the liver function test. Anti-GM-CSF (granulocyte macrophage-colony stimulating factor) antibody levels could unfortunately not be done as this assay is not available in South Africa. Radiological investigations included a chest radiograph which demonstrated bilateral consolidation, and a high resolution computed tomography (HRCT) scan confirmed dense bilateral reticulonodular infiltrates involving mostly upper and mid lung regions. This picture was in keeping with the so-called 'crazy paving' pattern, as shown in figure 1.

The patient underwent a transbronchial biopsy in which histological findings showed alveolar lumina filled with eosinophilic proteinaceous material. Periodic acid Schiff staining was focally positive within the material. No infective organisms or granulomata were observed. Features were consistent with pulmonary alveolar proteinosis (PAP). The patient was treated with whole lung lavage. At follow-up visit the subject was asymptomatic and chest X-rays had normalized.

Discussion

Cough and dyspnoea are common symptoms observed by medical practitioners. It is sometimes difficult to distinguish between patients requiring minimal investigations and conservative treatment with those necessitating extensive evaluation and aggressive treatment. With this case, however, despite the lack of remarkable physical findings on chest examination, the hypoxemia and central cyanosis could not be ignored. In addition, the impressive radiologic findings demanded further invasive investigations.

PAP is a rare pulmonary disease with specific features of alveolar accumulation of surfactant comprising of proteins and lipids due to dysfunctional alveolar macrophages. It has an estimated incidence of 0·2 cases per million.[1] Three main categories of PAP are identified based on their aetiology: congenital, secondary and

acquired.[2]. Auto-immune (part of the acquired) accounts for almost 90% of PAP cases and is associated with GM-CSF.[1,2]

Physical examination findings are unremarkable but can include inspiratory crackles in 50% of patients, cyanosis in 25% and digital clubbing in a small percentage.[2] The clinical presentation of PAP is nonspecific. Radiological findings are however specific, with HRCT demonstrating patchy, ground-glass opacifications with superimposed inter and intralobular septal thickening that gives rise to the 'crazy-paving' pattern.[2] Whole lung lavage is the current standard treatment of choice. Other treatment options include: (i) inhaled aerosol GM-CSF, (ii) subcutaneous injected GM-CSF (iii) plasmapheresis and (iv) Rituximab, a monoclonal antibody directed against the CD20 antigen on B lymphocytes.[4,5] The natural history of PAP falls into one of three types: spontaneous resolution, persistent symptoms or progressive deterioration.[2,3]

The presentation of bilateral diffuse lung infiltrates allows for speculation of possible aetiologies such as infection, inflammation or malignancies. A key lesson here is that when a patient's condition does not improve despite appropriate therapy, the clinician must re-assess the path of action. This will require critical appraisal of original diagnosis and if needed a referral to a specialist centre.

Conflicts of interest

None exist

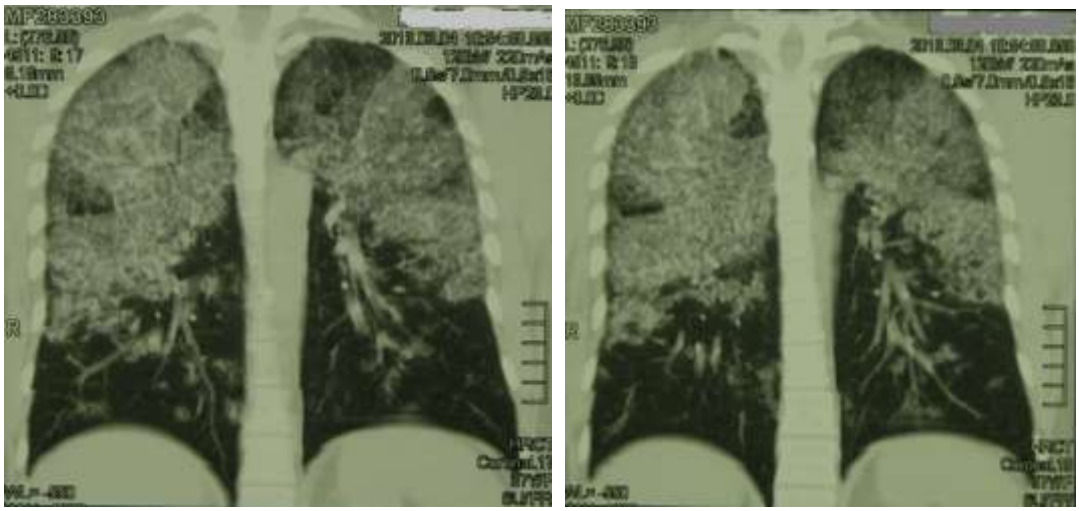

Figure 1. Diffuse bilateral areas of reticulonodular infiltrates with thickened septae, typical of the 'crazy-paving' pattern

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