Reminder of important clinical lesson

Multiple pulmonary micronodules in a patient with Crohn's disease

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Summary

Sarcoidosis is a terrific mimicker and can present in many different ways. The case of a middle-aged woman with Crohn's disease who attended the gastroenterology clinic for routine follow-up is presented. She had dry cough and breathlessness for a few weeks. A chest x-ray showed scattered multiple bilateral pulmonary micronodules. This finding on her chest x-ray posed a diagnostic challenge, especially in view of the fact that she was previously treated with immunosuppressants to control her Crohn's disease. A diagnosis of sarcoidosis was established by various tests including lung biopsy, which showed non-caseating granulomas. Within a few weeks of beginning systemic steroid treatment, improvement was noticed in symptoms and lung function tests.

BACKGROUND

Inflammatory bowel diseases (IBDs) are associated with various pulmonary pathologies including granulomatous interstitial lung disease.¹ A multiple micronodular appearance on chest radiographs in such patients raises the possibility of a wide variety of diagnoses including pulmonary Crohn's disease, mycobacterial and fungal infections, malignancy and hypersensitivity pneumonitis. A secure diagnosis may not be possible without the help of histological specimens and other supportive investigations.

CASE PRESENTATION

A 50-year-old primary school teacher attended the gastroenterology clinic for routine follow-up. She had minimal abdominal symptoms and was taking loperamide for intermittent diarrhoea. She mentioned experiencing mild non-productive cough and exertional breathlessness for a few weeks. There was no history of chest pain, haemoptysis, fever, paroxysmal nocturnal dyspnoea or pedal oedema.

She was diagnosed as having Crohn's disease 30 years ago. Her disease was relatively stable on regular 5-aminosalicylate preparations and occasional use of systemic steroids. Over the last 4 years, with increasing use of systemic steroids, izathioprine was tried without much success leading to use of infliximab 18 months ago. However, a few weeks later she experienced catastrophic rectal bleeding and underwent emergency subtotal colectomy and ileostomy. Subsequent to her surgery she did not require systemic immunosuppression. The macroscopic and microscopic features of the surgical specimen were considered typical for Crohn's disease.

Our patient was a lifelong non-smoker. She admitted using duck feather pillows and duvets and also noticing a damp roof in her bedroom with some black mould on it. She was not asthmatic or atopic and did not have eczema. She had never had the Bacillus Calmette-Guérin (BCG) vaccine and had no contact with tuberculosis (TB). On examination

her fingers were clubbed and she had bilateral crackles and no audible wheeze on chest auscultation.

INVESTIGATIONS

Oxygen saturation on room air was 92%. Arterial blood gas analysis revealed mild hypoxaemia (PaO₂ of 10.6 and PCO₂ of 4.4 kPa). A chest x-ray (figure 1) showed new onset bilateral multiple micronodular shadows that were not present 6 months ago. An induced sputum acid-fast bacillus (AFB) smear was negative. High-resolution CT showed bilateral diffuse multiple micronodules scattered in a random distribution only relatively sparing both bases (figure 2A,B). Moderately enlarged mediastinal lymph nodes were also noted. A Mantoux test was negative. A full lung function test revealed a forced expiratory volume in 1 s (FEV₁) of 1.1 litres (42% predicted), forced vital capacity (FVC) of 1.72 litres (55%) and FEV₁/FVC of 65%. The total lung capacity was 4.0 litres (79%) and transfer factor reduced at 5.8 ml/min/mm Hg (23%). Her C reactive protein level was raised at 134mg/L, corrected serum calcium at 2.7 mmol/litre (normal 2.20–2.60 mmol/litre) and serum angiotensin-converting enzyme (ACE) at 128 IU/litre (normal 20–54 IU/litre). Her white cell count and differentials were normal. Aspergillus and avian precipitans were negative and total IgE was normal. Fibreoptic bronchoscopy revealed normal macroscopic appearance of bronchi. Multiple transbronchial lung biopsies on histology showed multiple non-caseating granulomas (figure 3). Bacteriological studies of bronchoalveolar lavage (BAL) fluid and biopsy material including cultures for mycobacteria and fungi were negative.

OUTCOME AND FOLLOW-UP

Systemic steroids were given. Clinical improvement was noticed a few weeks later. After 3 weeks of treatment the FEV₁ improved to 1.8 litres (67%) and FVC 2.98 litres (95%). Total lung capacity improved to 4.7 litres (92%) and an

Figure 1 Plain chest x-ray showing bilateral diffuse micronodular shadows.

Figure 2 A. High-resolution CT (HRCT) showing random distribution of micronodules. B. HRCT showing some nodules along the fissure on the right side.

improved transfer factor of 11.2 (45%) was also recorded. The patient is still under regular follow-up in the respiratory clinic.

DISCUSSION

In this patient with longstanding Crohn's disease who was treated with immunosuppressants including anti-tumour necrosis factor (TNF), the finding of diffusely scattered pulmonary micronodules posed a diagnostic dilemma. The list of differential diagnoses included millary TB, fungal infec-

tions, atypical infections, sarcoidosis, metastatic disease, hypersensitivity pneumonitis, early pulmonary histiocytosis and pulmonary Crohn's disease. Ruling out infectious and some non-infectious causes helped in establishing the correct diagnosis of concomitant pulmonary sarcoidosis.

TB and atypical infections in this case could be excluded by absence of caseating granuloma and negative cultures from bronchoalveolar fluid and lung biopsy specimens. Bronchiolar granulomas associated with alveolitis may be seen in patients with hypersensitivity pneumonitis as well.²

Figure 3 A transbronchial lung biopsy showing well defined non-caseating granuloma showing macrophages and giant cells.

Although our patient had domestic exposure to duck feather and black moulds, negative serological studies along with the absence of any significant temporal association of symptom onset with exposure discounted the possibility of hypersensitivity pneumonitis. Pulmonary granulomas have been reported after the use of anti-TNF α (infliximab) in patients with seropositive rheumatoid arthritis, but those granulomas were caseating.³

Diffuse non-caseating granulomatous inflammatory changes were seen on lung biopsy in this case. Granulomatous interstitial lung disease has been reported in Crohn's disease.^{4–6} Bronchial involvement has also been reported in two cases, one showing non-caseating granuloma, and epithelioid-like cells on bronchial biopsy in the other.⁷ In all, 53 cases of IBD and concomitant sarcoidosis have been reported in the literature.^{8,9} In some case the presence of mediastinal lymphadenopathy suggested true sarcoidosis. It seems almost impossible to determine histologically whether bronchopulmonary granulomatosis seen in patients with Crohn's disease should be considered sarcoidosis or an extraintestinal manifestation of Crohn's disease. Crohn's disease and sarcoidosis have no known aetiology, though they share the same pathological and immunological features and are characterised by non-caseating epithelioid granulomas and accumulation of CD4 T lymphocytes at the site of disease activity. Besides histology, raised serum calcium and angiotensin-converting enzyme (ACE) levels, no response to the purified protein derivative (PPD) test and presence of mediastinal lymphadenopathy were helpful in establishing the diagnosis of pulmonary sarcoidosis.

Learning points

- ▶ Both inflammatory bowel disease (IBD) and sarcoidosis can cause granulomatous lung disease.
- ▶ IBD and sarcoidosis may exist concomitantly in some patients.
- ▶ Micronodules on chest radiograph has a wide differential possibility.
- ▶ A histological diagnosis should always be attempted.

Competing interests None.

Patient consent Obtained.

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