Not all nodules with PET hypermetabolic activity are malignant: a case of lung granuloma in ulcerative colitis

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DESCRIPTION

A 65-year-old man with a medical history significant for chronic obstructive pulmonary disease (COPD), ulcerative colitis (UC) and tobacco dependence was referred to a pulmonologist for evaluation of a 2.8 cm right lower lobe (RLL) lung nodule (figure 1A) found incidentally on CT of the chest. His review of systems was negative for dyspnoea, angina, haemoptysis, fever, night sweats, anorexia and weight loss. He required curative total proctocolectomy 8 years prior for UC refractory to corticosteroids. He was an active smoker and had a 35 pack-year smoking history. He worked as a cashier in a local supermarket and has been doing so for the past 25 years. Vital signs on evaluation revealed a pulse rate of 85, respiratory rate of 20, blood pressure of 120/65 and oxygen saturation of 94% in room air. His physical examination displayed decreased breath sounds throughout his lung fields, but no wheezing, rhonchi and crackles appreciated. His abdomen was soft and non-tender to palpation. Examination of his extremities revealed no finger clubbing or peripheral pitting oedema of his lower extremities. A decision was made to pursue a whole-body positive emission tomography scan due to a lack of previous chest imaging to determine the chronicity of those lung nodules and high suspicion for malignancy in the setting of long-term history of COPD and heavy tobacco dependence that showed increased metabolic uptake in the RLL nodule with a standardised uptake value maximum of 9.5 (figure 1B). Due to

concern for malignancy, a video-assisted thoracoscopic lung biopsy was performed that revealed numerous, discrete, non-necrotising granulomas (figure 2). Gram stain, Grocott's methenamine silver stain and Ziehl-Neelsen stain returned negative for bacterial, fungal and mycobacterial organisms. As he remained asymptomatic, decision was made to monitor his lung nodule with a serial CT scan. He returned 9 months later with repeat CT of the chest (figure 1C), demonstrating increased RLL lung nodule size from 2.8 cm to 5 cm. Oral prednisone therapy was initiated, and follow-up CT of the chest (figure 3) in 3 months showed significant improvement in the size of RLL nodule.

The differential diagnosis for lung nodules seen in inflammatory bowel disease (IBD) such as UC is non-caseating granuloma, organising pneumonia and necrobiotic nodule with a reported frequency of 13%, 6%–25%, 12%–14%, respectively.^{1,2} Age of onset is typically 40–70 years of age, where the majority of patients are previous or non-smokers. The pulmonary manifestations of UC are underdiagnosed due to the poor correlation with disease activity in 20% of patients. It may precede the bowel disease presentation by months or years in up to 10% of patients and even occur after total colectomy.¹ Up to 29% of patients with UC may develop or suffer worsening pulmonary involvement after total colectomy.³ The pathogenesis of pulmonary involvement in patients with IBD is likely due to the shared embryonic origin of the respiratory and gastrointestinal tracts, both of which originate from the primitive foregut that shares a similar columnar epithelium, epithelial exposure to similar antigens by inhalation and ingestion will cause inflammation and sensitisation of submucosal lymphoid tissue that plays a crucial role in host mucosal defence.^{1,4} Moreover, inflammatory mediators released by the bowel mucosa such as interleukin (IL)-1, IL-2, IL-6, and tumour necrosis factor-alpha can migrate to the lung and trigger endothelial cell adhesion, leucocyte migration/invasion, and increase the production of reactive oxygen species that trigger pulmonary abnormalities as part of the lung-gut cross-talk. Therefore, it is not uncommon for non-specific respiratory symptoms of dyspnoea or cough to be dismissed despite being the first and maybe the only presentation of underlying lung disease in any patients with IBD, where the focus is often related to their gastrointestinal symptoms. The diagnosis is often suspected based on abnormal spirometry or incidental radiographic findings after ruling out

Figure 1 CT of the chest. (A) Initial CT of the chest demonstrated a solitary, 2.8 cm, non-calcified, solid nodule in the medial segment of RLL with lobulated margin and no hilar/mediastinal lymphadenopathy. (B) CT-PET scan showed increased metabolic uptake in the RLL nodule without evidence of hypermetabolic activity elsewhere. (C) Repeat CT of the chest 9 months later revealed an increase in RLL lung nodule size from 2.8 cm to 5 cm, abutting the oblique fissure without any evidence of satellite lesions elsewhere or no hilar/mediastinal lymphadenopathy. PET, positive emission tomography; RLL, right lower lobe.

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Figure 2 Video-assisted thoracoscopic lung biopsy H&E stain. (A) Low power field showed densely consolidated lung parenchyma comprised of numerous, discrete, non-necrotising granulomas (blue arrow) with focal acute inflammation involving bronchiole structure and adjacent alveoli. (B) High power field revealed clusters of epithelioid histiocytes and frequent multinucleated giant cells (red arrow) within granuloma without the presence of suppurative granulomas, malignant cells, birefringent foreign material or vasculitis.

Figure 3 Follow-up CT of the chest in 3 months after oral prednisone therapy demonstrated significant improvement in the size of known right lower lobe nodule (blue arrow).

lung malignancies, infectious aetiologies from fungal or mycobacterial infections, and vasculitis such as granulomatosis with polyangiitis.⁴ As many as 37%–55% of patients will present with abnormalities in their spirometry or chest imaging.^{4,5} However, less than 10% of patients present with respiratory symptoms. The response rate towards corticosteroids is favourable even in the setting of quiescent UC and post-total proctocolectomy.⁴

Learning points

- The differential diagnoses of non-infectious and non-malignant lung nodules in patients with ulcerative colitis (UC) are broad and range from non-caseating granuloma, organising pneumonia and necrobiotic nodule.
- The pulmonary manifestations of UC are often under-recognised due to poor correlation with disease activity and may precede the bowel disease presentation by months or years, and even occur after total colectomy.
- Prognosis is often favourable in which corticosteroids are the cornerstone of treatment even in the setting of quiescent UC and post-total proctocolectomy.

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