Unusual Cause of Lung Nodules in an Adolescent

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A previously healthy 13-year-old female patient presented with a 9-month history of weight loss (20% body weight), lethargy, anorexia, and iron-deficiency anemia. The symptoms were associated with brief intermittent chest pain and palpitations but not with exertional dyspnea or a chronic cough. On examination she had mild conjunctival pallor. The patient's weight was 32 kg (below the 3rd percentile), height was 151 cm (at the 25th percentile), and body mass index (BMI) was 14 kg/m^2 (below the 3rd percentile). The patient had a resting tachycardia at 120 b/min with all other vital signs within normal ranges. Eye examination revealed bilateral intermediate uveitis. Cardiovascular and chest examination were un-remarkable. Blood investigations revealed low hemoglobin level of 100 g/l (reference range 110–145 g/L) with microcytic hypochromic anemia and an increased red-cell distribution width (RDW). The platelet count was high (800 × 10^9/L [reference range 150–450]). There was a mildly elevated total white cell count of 18 × 10^9/L with a predominant neutrophilia of 12.3 × 10^9 (reference range 2.4–9.5). The eosinophil count was also high at 1.2 × 10^9/L (reference range 0.2–0.8). She has elevated C - reactive protein (CRP) and erythrocyte sedimentation rate (ESR) at level of 7 mg/L (reference range, 0–5 mg/L), of 32 respectively. The patient had iron-deficiency anemia, low vitamin D levels of 9 ng/mL (reference range 50–100 ng/mL), and normal vitamin B12 and folate levels. Albumin levels were low at 26 g/L (reference range 38–54 g/L), with normal liver transaminases.

The patient underwent esophagogastroduodenoscopy (EGD) and colonoscopy. The EGD was normal, but colonoscopy revealed moderate pancolitis involving the left side of the colon. Histological examination of a colonic biopsy consistent with ulcerative colitis. Magnetic resonance enterography (MRE) showed mild circumferential mural thickening with hyperenhancement of the left colon. However, the visualized lung bases showed a few bilateral nodules. The chest computed tomography (CT) revealed multiple bilateral irregular pulmonary nodules with halo and feeding vessel signs [Figure 1 a and b].

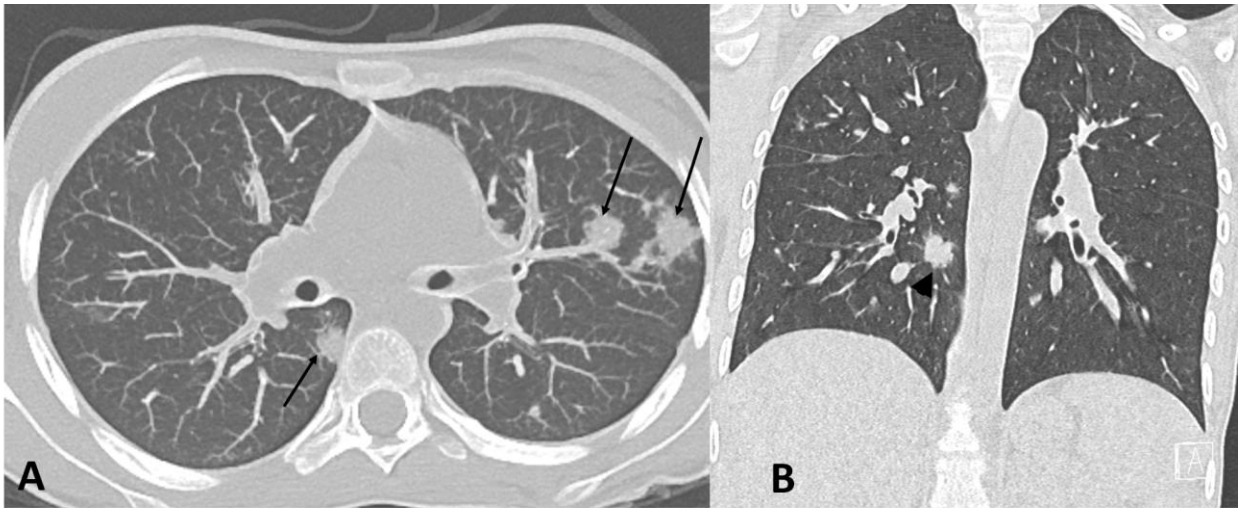

Figure 1: High-resolution CT scan of lungs with axial and coronal images (a and b) in lung-window settings- shows multiple bilateral nodular opacities, most of them were peripheral and subpleural (thin black arrows). (b)The nodules show ill-defined borders with ground-glass halo (Arrowhead).

Questions

1. What is the likely diagnosis?

2. How would you confirm the diagnosis?

3. How would you manage the patient?

Answers

1. Extra-intestinal manifestation of inflammatory bowel disease.

2. Computed tomography- guided lung biopsy.

3. Systemic or inhaled corticosteroids and or infliximab

Discussion

The nature of these nodules was of concern as to whether they were due to an infective or inflammatory process due to systemic vasculitis. Before starting immunosuppressive therapy, the patient underwent a CT-guided lung biopsy to rule out any infectious causes. Histology of the lungs revealed expanded alveolar spaces filled with fibroblastic plugs formed by spindled fibroblasts set in a matrix of loose collagen. The inter-alveolar septa were expanded by mixed inflammatory cells in areas showing perivascular accentuation. No fibrinoid necrosis, fibrin thrombi, or granulomas were observed. It was negative for fungal organisms. After excluding infectious causes and systemic vasculitis, we concluded that the lung findings were due to a rare extra-intestinal manifestation of inflammatory bowel disease suggestive of organizing pneumonia. The patient was started on oral prednisolone and mesalazine for the IBD. However, the symptoms continued along with elevated inflammatory markers; hence, an infliximab infusion was initiated. The infliximab infusion resulted in significant clinical and biochemical improvements. Since then, the patient has been on a regular 8-weekly infliximab infusion. Repeated chest CT revealed the resolution of the lung nodules [Figure 2].

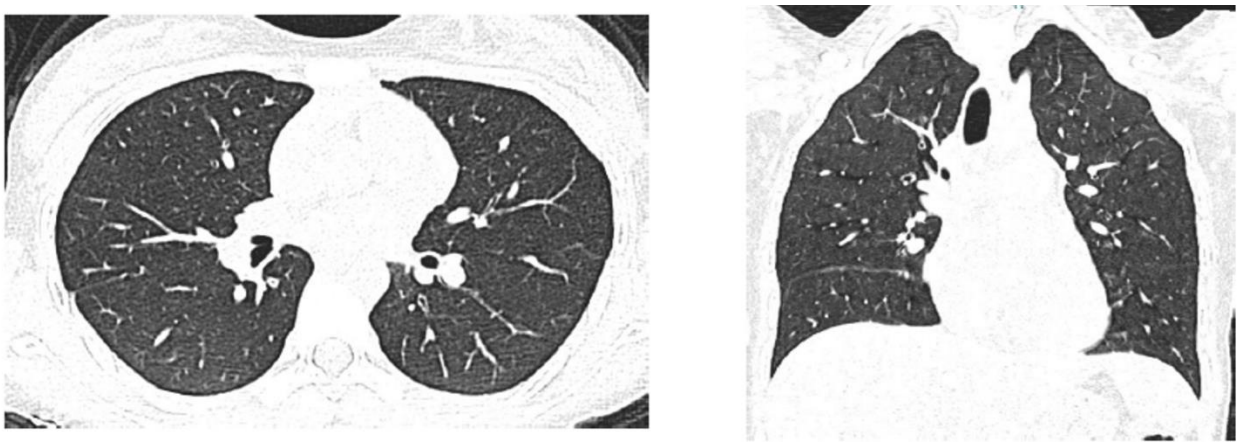

Figure 2: High-resolution CT scan of lungs with axial and coronal images in lung-window settings- shows interval resolution of previously seen multifocal lung nodules.

Pediatric inflammatory bowel disease (PIBD) is generally classified into three main subcategories: ulcerative colitis (UC), Crohn's disease (CD), and unclassified (IBDU).[1]

Up to 41% of patients with IBD may present with extra-intestinal manifestations, including skin manifestations (erythema nodosum), eye involvement (anterior uveitis), hepatic manifestations (autoimmune liver disease and fatty liver), and joint involvement (arthropathies). However, lung involvement is rare in PIBD.[2]

The respiratory manifestations of IBD can be classified into airway diseases, including large and small airways, parenchymal lung diseases, thromboembolic diseases, and enteropulmonary fistulas.[2,3] Patients with lung involvement may present with clear chest symptoms, or it can be subclinical and detected only by lung function tests or imaging.[2] Lung involvement can precede gut symptoms but can occur any time after diagnosis.[2,3]

Parenchymal lung disease is the most common respiratory manifestation of PIBD[3] and is found more frequently in patients with UC than in patients with CD, with a female predominance.[2] The most common parenchymal lung disease is bronchiolitis obliterans organizing pneumonia (BOOP), followed by eosinophilic pneumonia and nonspecific interstitial pneumonitis.[2]

Pulmonary involvement in IBD is likely due to intricate interaction between the gut and lungs, through what is known as the gut-lung axis. They both share same mucosal immunologic features and mutual need for microbial homeostasis suggest that this cross talk is mediated by the mucosal immune system's interaction with the microbiotic environment. Recent studies showed that alteration of gut microbiota may activate immune cells in the intestinal mucosa which may cause inflammatory response in the lung when exposed to common allergens.[4]

Lung involvement is more common in adults with CD; however, few studies have reported such lesions in children with UC. It could be underreported due to decreased awareness and, additionally, due to the heterogeneity of the clinical presentations.[3,5] These patients tend to present with general symptoms, including malaise, fever, arthralgia, and weight loss. Additionally, respiratory symptoms, such as dry cough, shortness of breath, and chest tightness, have been reported.[6] Radiological investigations, especially chest CT, play an important role in diagnosing IBD-related lung involvement. BD-related parenchymal lung diseases responded well to systemic or inhaled corticosteroids, or both, or infliximab.[2,3]It is important to rule out other diagnoses with similar radiological manifestations, such as tuberculosis, aspergillosis, or granulomatosis with polyangiitis (Wegener granulomatosis).

Early recognition and treatment of pulmonary involvement in IBD are essential to prevent long-term sequelae.

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