A curious presentation of Crohn's disease with pulmonary involvement: a case report

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Abstract

Crohn's disease (CD) is a chronic inflammatory bowel disease often presenting with extraintestinal manifestations. However, pulmonary involvement in CD is quite rare. We here report a case of CD with pulmonary manifestation as the first presenting sign. Thus, immune-mediated inflammatory disorders such as CD should always be kept in the differential list in case of unusual clinical symptoms or radiological signs of idiopathic pulmonary presentations. (Acta gastroenterol. belg., **2023,** 86, **98-101**).

Keywords: Crohn's disease, inflammatory bowel disease, extraintestinal manifestation, pulmonary disease, pulmonary manifestation of inflammatory bowel disease, biological.

Introduction

Crohn's disease (CD) is a granulomatous systemic disorder mainly affecting the gastrointestinal tract, although in 20-40% of patients extraintestinal manifestations (EIM) may be present (1). Uveitis, conjunctivitis, arthritis, erythema nodosum, pyoderma gangrenosum, and primary sclerosing cholangitis are the most common EIMs. Pulmonary involvement with CD is extremely rare with an estimated overall prevalence of 0.4% (2). The presentation of bronchopulmonary manifestations in CD is variable, as all segments of the respiratory tract can be affected. Presence of granulomas on pathology could be an indication for CD (3), but the broad differential diagnosis may be challenging for physicians. We report a case with pulmonary manifestation as a first presentation of CD to illustrate this.

Case history

A 73-year-old woman with a past medical history of gastroesophageal reflux disease (GERD) and liver hemangiomas presented in a regional hospital with intermittent complaints of chills, vomiting and epigastric pain. She had no fever or weight loss. There was no history of smoking or alcohol use. She was on pantoprazole 20 mg once a day. Gastroscopy revealed a small hiatal hernia with signs of reflux esophagitis grade A. Biopsies for Helicobacter pylori were negative. An ultrasound of the abdomen showed two known liver hemangiomas.

To rule out respiratory infection a chest X-ray was done. This showed an opacity in the right upper lobe that warranted further exploration. Chest computed tomography (CT) confirmed a mass of 24 mm with calcifications in the right upper lobe close to the pleura. There was no history of asbestos exposure or known contact with tuberculosis (TB). By this time her initial complaints had completely resolved on pantoprazole 40 mg once a day. Her labs showed no signs of inflammation. Due to suspected lung cancer, carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE) were determined, but returned normal. CT of the brain and the abdomen showed no signs of malignancy, but an incidental finding of terminal ileitis was seen. Pulmonary function tests were within the normal range. Positron emission tomography CT (PET-CT) showed intense activity in the known lesion (25.7 mm in diameter) in the right upper lobe, with central excavation, which was not previously visible on the initial chest CT. There was a secondary hypermetabolic nodule seen in the left upper lobe. Bronchoscopy was unremarkable, except for some strings of blood in the apex of the right upper lobe. A bronchoalveolar lavage for cytologic analysis, bacterial cultures, fungal cultures, Ziehl-Nielsen staining, and polymerase chain reaction (PCR) for TB was negative. A CT-guided percutaneous lung biopsy was performed and showed extensive fibrosis with elastosis, mild chronic inflammation, bleeding in resorption and some multinucleated giant cells: suggestive of an old pulmonary infarction. As the pathology findings could not explain the intense hypermetabolic activity on PET-CT the diagnosis remained unclear.

Because of the inconclusive pathology together with the central excavation seen on PET-CT a second CT-guided lung biopsy was performed. This time it showed lung parenchyma with epithelioid granulomas and a Langhans giant cell, suggestive of a granulomatous inflammation such as TB or sarcoidosis. Ziehl-Nielsen staining, culture and PCR for TB on the tissue remained negative. Autoimmune disease was excluded. Because of normal serum levels of angiotensin-converting enzyme (ACE) and the radiologic image sarcoidosis seemed less likely. Since the patient was asymptomatic a follow-up CT of the chest after 3 months was planned.

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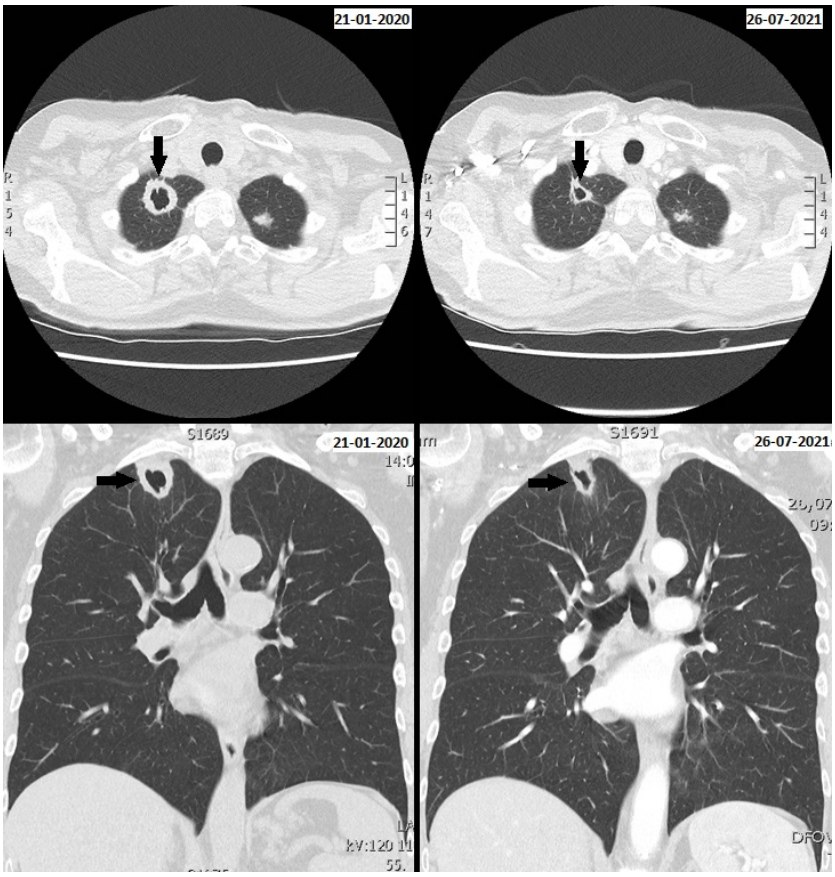

Figure 1. — Left side: Chest CT before treatment showing the mass in the right upper lobe with central excavation (arrow). Right side: Chest CT showing reduction of the mass in the right upper lobe (arrow) after one year of treatment with infliximab.

Due to the coincidental finding of ileitis terminalis on CT, an ileocolonoscopy was performed. This showed ulcerations in the terminal ileum, a deformed and ulcerated ileocecal valve and focal sigmoiditis. Ileal biopsies showed mild, chronic inflammation without granulomas. Colonic biopsies were unremarkable. A magnetic resonance enterography (MRE) revealed six consecutive segmentary bowel thickenings of the terminal ileum with skip areas over a total length of 40 cm, consistent with CD. Because the patient was asymptomatic , the decision was taken not to treat.

After 6 months of intensive work-up the patient still had no clear diagnosis. The differential diagnosis remained sarcoidosis or possible pulmonary disease as an EIM of CD. Chest CT after 3 months and 6 months showed no changes in the pulmonary nodules. However, one year later enlargement of the nodule in the left upper lobe was noticed for which the patient was referred to our hospital. The patient at that time was still asymptomatic. leocolonoscopy was repeated and showed again ulcerations in the terminal ileum, but no signs of inflammation in the colon. Biopsies in the ileum showed only mild, active ileitis without signs of chronicity. Fecal calprotectin was elevated to 1084 mg/kg. After discussion with the patient, a course of budesonide 9 mg was started and tapered over 3 months. Following budesonide, fecal calprotectin dropped to 188 mg/kg. Anti-TNF (infliximab) was started. Chest CT one year after treatment initiation showed a reduction in diameter of the pulmonary mass from 25.7 mm to 18 mm with more central excavation. The mass in the left upper lobe remained unchanged. Fecal calprotectin decreased further to 169 mg/kg. The patient is currently doing well under infliximab every 8 weeks.

Discussion

CD is an inflammatory condition of unknown etiology characterized by transmural, noncaseating granulomatous inflammation of the gastrointestinal tract, but can involve nearly any organ in the body. Up to 50% of patients with IBD experience at least one EIM, which can present even before IBD is diagnosed (3).

Pulmonary involvement is rare. Several mechanisms have been proposed by which the lungs may become involved in CD. These include the same embryological origin of lung and gastrointestinal tract, similar immune systems, and adverse pulmonary effects of CD drugs (2). In most cases the development of lung involvement parallels that of intestinal disease activity or occurs after the onset of gastrointestinal symptoms. In this patient, the incidental finding of pulmonary manifestation lead to

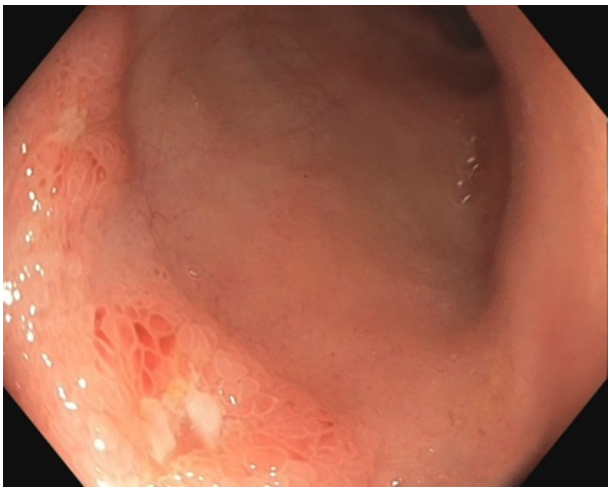

Figure 2. — Image of ileocolonoscopy before treatment showing ulcerations in the terminal ileum.

the diagnosis of CD. This is rare and only a few cases have been reported in literature (4,5,6). A case series by Camus et al. (4) reported 5 patients out of 33 cases where pulmonary manifestations predated the bowel disease by several months up to several years. Eliadou et al. (6) recently found 14 cases of IBD with non drug-related granulomatous lung disease, but in only 3 of them the pulmonary manifestations lead to the diagnosis of CD.

Pulmonary EIM of CD can be very difficult to diagnose and patients often have to undergo complex and invasive investigations, which was also the case in our patient. There is a wide array of different lung manifestations, ranging from subclinical alterations, airway diseases, lung parenchymal diseases, pleural diseases, and drug-related diseases (2). The most common clinical symptoms are progressive dyspnea, dry cough, fever, flu-like symptoms, and chest pain (7). Our patient, however, did not present with any respiratory symptoms. Imaging may show bronchial wall thickening and bronchiectasis, but also multifocal patchy consolidations, ground-glass opacities or lung nodules may be seen (8). In our case it was an incidental finding of a pulmonary nodule, mandating a work-up to rule out malignancy. The progression into a excavating lesion on follow-up PET-CT made an infectious or inflammatory etiology more likely.

Unfortunately, there are no specific pathologic findings distinguishing pulmonary EIM of CD from other etiologies. Casey et al. (9) reviewed 11 lung biopsies from patients with CD and found variable histologic appearances, most commonly chronic bronchitis and bronchiolitis with non necrotizing granulomatous inflammation. In our case the patient underwent two lung biopsies. Only the second biopsy showed signs of granulomatous inflammation, which was still difficult to distinguish from sarcoidosis.

The prognosis of pulmonary CD is favorable with a high response rate to therapy (9). Most of the respiratory changes respond well to steroids, but patients may require additional immunomodulators or biologicals (3). We decided to start budesonide instead of systemic steroids, to avoid side effects of the latter in this elderly patient, and to allow reimbursement with biological therapies thereafter. Eight cases of symptomatic pulmonary EIM with CD treated with infliximab were reviewed by Hayek et al. (10). All of them responded well to infliximab, resulting in clinical and radiologic resolution of the pulmonary EIM. In our patient, the largest nodule reduced in size after one year of treatment with infliximab.

In conclusion, pulmonary manifestations of CD are rare and present in a broad spectrum. As a consequence they might be associated with a diagnostic challenge necessitating an extensive work-up. Thus, CD should be a differential diagnosis in cases of unusual clinical symptoms or radiological signs of idiopathic pulmonary presentations.

Conflict of interest

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