Respiratory involvement in Crohn's disease: a case report

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Abstract

Inflammatory bowel disease (IBD) predominantly affects the gastro-intestinal tract. There is however a large array of extra intestinal manifestations (EIM) associated with these diseases. A lesser known EIM is pulmonary involvement, which has been first described in 1973. Since the introduction of HRCT more attention is guided towards this specific involvement. Awareness of pulmonary involvement in IBD-patients may lead to better screening, guide appropriate therapy, and ultimately result in better patient care. When untreated, serious and persisting complications, such as stenosis or strictures of the large airways, as well as bronchiectasis or bronchiolitis obliterans might occur. (Acta gastroenterol. belg., **2023,** 86, **367-370**).

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

Introduction

Both Crohn's disease (CD) and Ulcerative Colitis (UC) are inflammatory bowel diseases. Several extra-intestinal symptoms have been widely discussed as extra-intestinal manifestations of IBD. Some flare with the disease (erythema nodosum, iritis and peripheral arthritis) while others appear to be detached from bowel inflammation (spondylitis ankylosans, primary sclerosing cholangitis). The occurrence of lung involvement is rare in IBD-patients and poorly understood.

Case report

A 16-year-old-patient presented on the outpatient consultation with symptoms of altering bowel patterns and increasing abdominal discomfort since a few weeks. There was a loose stool consistency with intermittent diarrhea. No blood or mucus contamination was noticed. Nocturnal defecation was absent. There were no complaints of extra-intestinal manifestations (uveitis, arthritis, dermatosis, sicca-complaints). Anorexia was present since a few days resulting in a 2 kg loss of bodyweight. The patient was a nonsmoker and did not present with dyspnea, upon inquiry he did however experience dyspnea on exertion. He did not have a cough nor phlegm. Clinical examination revealed tenderness during left fossa palpitation. Peritoneal resistance was absent. A blood analysis was performed, showing a moderate irondeficiency anemia with inflammation (Hb: 12.2 g/100 ml (ref. 13-16 g/100 ml), transferrin saturation: 11% (ref. 20-50%), ferritin: 172 µg/L (ref. 20-200 µg/L), CRP: 53.2 mg/L (ref. <5 mg/L)). A stool sample was analyzed which was positive for blood (iFOB), calprotectin levels were elevated (5651 mg/kg (ref. <50 mg/kg)).

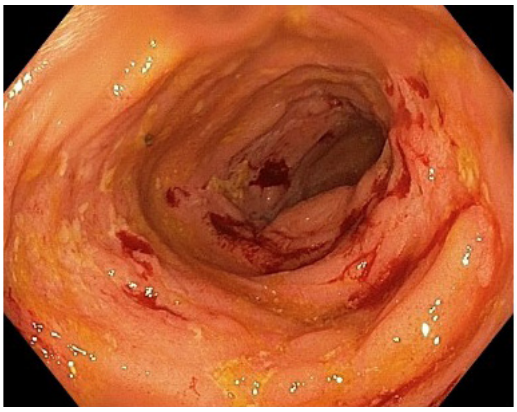

Figure 1. — Endoscopic view: Ileum with ileitis

The patient was admitted to our ward. IV-infusion with administration of antibiotics Levofloxacine-Ornidazol (Tavanic®-Tiberal®) was started. A colonoscopy was performed the next day, exposing an ulcerative ileitis and pancolitis (Figure 1), compatible with Crohn's disease, confirmed by histopathology.

A chest X-ray (Figure 2) as part of the clinical path in our IBD-clinic, was suggestive for bronchiectasis. A sequential CT-scan revealed micronodular bilateral lung enhancement (centrolobular type), accompanied by 'tree-in-bud sign' (Figure 3a), indicative for small air-way inflammation/obstruction, primarily in the lower lungs. Pulmonary function tests (PFTs) were performed and showed a forced vital capacity (FVC) of 79% of predicted value. Ple-thysmography also appeared abnormal, residual volume (RV) was at 232% of the predicted value, vital capacity (VC) was reduced to 69% of normal. Total lung capacity (TLC) was not altered (102% of predicted value), resulting in an increased RV/TLC. Diffusing capacity for carbon monoxide (DLCO) was 79% of predicted. Bronchoscopic alveolar lavage

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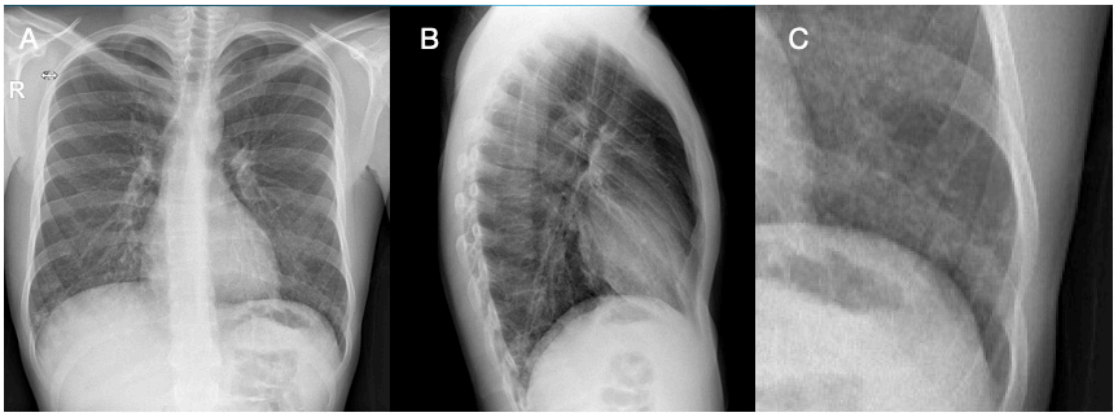

Figure 2. — (A-B) Chest x-ray (f/p) suggestive for bronchiectasis in both lower lungs.
(C) Close-up of the bronchiectasis of the left lower lung.

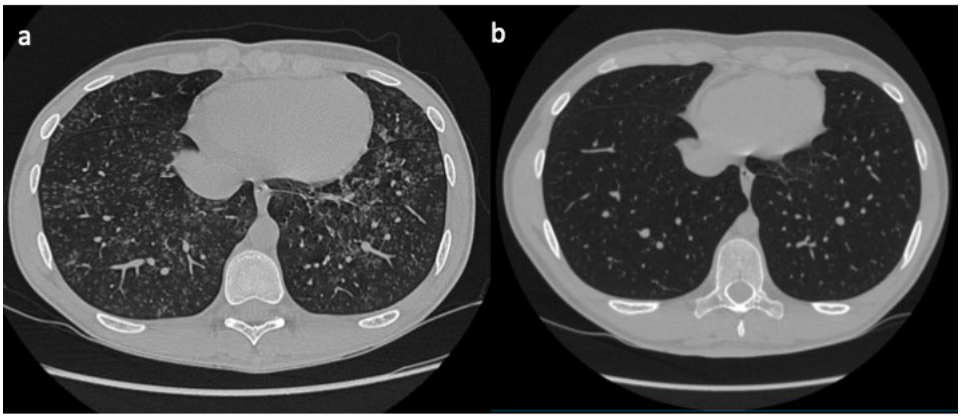

Figure 3. — (a) CT thorax at diagnosis showing micro nodular enhanced lung drawing of the centrilobular type in the midfields (a), Tree-in-bud phenomenon is present. (b) Resolution of pathologic findings 2 months after initial treatment.

revealed 50% lymphocytes and 50% macrophages, compatible with diffuse parenchymal lung disease (DPLD) - granulomatous bronchiolitis - associated with IBD. A 'top-down' strategy was chosen due to the young age, severity of mucosal defects and the pulmonary involvement. Adalimumab (Humira®) was administered together with antibiotics and corticosteroids (CS) in a rapid taperschedule (32mg during 10 days followed by a decrease of 8 mg every 2 weeks till cessation). A second CT thorax (Figure 3b) performed 2 months later, showed complete remission of the aforementioned pulmonary lesions. PFTs improved as well (FVC recovered to 88%, VC increased to 85%, RV decreased to 158%) signifying less airtrapping, DLCO appeared completely normal at 100%. A relook colonoscopy after one year, showed mucosal healing. The patient had no more respiratory symptoms nor gastro-intestinal symp-toms one year post-diagnosis. Current medication is limited to Humira 40 mg once every 2 weeks with a target trough level target of 4-8 µg/mL.

Discussion

Extra-intestinal manifestations are frequently associated with IBD, incidence rates range from 21-41% (1). CD has a higher incidence rate of these manifestations then UC (1). It is of importance to recognize and treat them early to avoid complications in future. Overt pulmonary involvement in IBD is unusual and previously reported at 0.4% (2). The pathogenesis of IBD-associated pulmonary disease might be found in the common embryogenic origin of the intestinal tract and the lungs. Both originate from the primitive foregut, containing similarities in their submucosal lymphoid tissue. The biliary tract (which also originates from the primitive gut) is also a relatively frequent EIM in IBD, making this claim even more likely (3). Subsequently, higher prevalence of other EIM involvement is reported in this subgroup of patients with pulmonary involvement (1,3).

A study shows that pulmonary function tests are abnormal in 58% of patients, of whom 33% are subclinical. HRCT appears to be abnormal in 52% of patients, whilst only 58% of them had respiratory symptoms (4). Localization and type of pulmonary involvement remains con-stant within one patient. Incidence of respiratory manifestations appears to be higher in UC compared to CD (1,3,5,6). Severity of these manifestations is correlated with disease activity and steroid treatment response. These respiratory symptoms usually start and frequently

flare when gut inflammation is present (4). Some reports however show that the abnormal inflammatory responses in IBD may also shift from the bowel to the lung. This intriguing shift of inflammation localization is most prominent in UC patients who underwent a colectomy in the past and still experience pulmonary flares (3,7). As such colectomy is not indicated as a method to relieve respiratory symptoms.

Symptoms and diagnosis

Patients may present with nonspecific respiratory symptoms, most commonly cough and breathlessness (4,5). Although nonspecific, these symptoms already hint towards the site of inflammation. While upper airway involvement is accompanied with hoarseness, stridor and cough. Lower bronchial tract involvement, associated with COPD, is usually accompanied by dyspnea (6).

PFTs are a great tool in the work up when suspicion of pulmonary involvement is present. The most prevalent abnormalities in lung function are a decreased DLCO (mean values 79.8% vs 96.3%, p=0.004) and an elevation in RV/TLC ratio (36.5 vs 30.8 p=0.013) (4). A slightly greater, but significant, reduction in PFTs is seen in active CD and UC com-pared to inactive disease (4). Other reports suggest that PFTs may not generally correlate with IBD activity (8). A methacholine challenge test can easily detect bronchial hyperreac-tivity, indicative for pulmonary inflammation, even without symptoms or other test abnormalities. In one study 25% of asymptomatic patients had subclinical bronchial hyperreactivity, which is significantly more compared to the general population (P = 0.026) (9).

Due to radiation exposure and the young age of most IBD patients, pulmonary imaging should only be used in symptomatic patients, or when a high index of suspicion (abnormal PFTs or symptoms) of respiratory involvement is present (5,9). HRCT-thorax has been shown to be the imaging modality of choice for the detection and assessment of pulmonary involvement in IBD (5). HRCT alterations have a prevalence range between 22-89%, more frequent than not this is a subclinical observation. At present it is uncertain if these subclinical alteration have any clinical significance although prevention of irreversible sequelae is of importance (5,10,11). The most common findings on HRCT are bronchial wall thickening, bronchiectasis, lung opacities, emphysema and groundglass alterations (5). To achieve a definitive diagnosis bronchoscopy and/ or thoracoscopic wedge biopsy is frequently neces-sary (12). Bronchoalveolar lavage cell profile is generally neutrophilic, although lymphocytic predominance has also been observed (6).

The respiratory tract may be involved at any level with a broad spectrum of alterations in-cluding bronchiectasis, tracheal stenosis, chronic bronchitis, asthma, bronchiolitis and COPD (5,12). Airway inflammation is the most prevalent respiratory involvement in IBD and is frequently present during diagnosis (8,13,14). Asthma appears to be more frequent and severe in the IBD population than one would expect (7.1-7.8% compared to 5% in general population) (11). Various forms of interstitial lung disease (ILD) may develop in IBD patients. Bronchiolitis obliterans is the most common type of ILD in IBD patients, while other types of ILD are rather unusual (6). Of note is that sulphasalazine and mesalazine, are known to induce drug-related ILD. Distinction between IBD related or medication related ILD may be difficult. Stopping these drugs, might be useful to differentiate between both entities, this however comes at the risk of aggravating intestinal inflammation (6).

Treatment

Pulmonary EIM are extremely rare, due to the scarcity of this manifestation randomized studies comparing different treatment protocols are missing. Early treatment however is of importance to minimize irreversible sequelae of inflammation. These sequelae, strictures of the large airways, bronchiectasis or bronchiolitis obliterans, sometimes require surgical in-tervention (6).

When respiratory symptoms are mild, local treatment in the form of nebulized steroids are sufficient. In the presence of more severe lung involvement, oral steroids may be associated. Tracheal and bronchial involvement respond better to CS than lung involvement. Although CS are known to alleviate the disease burden of IBD and the associated lung manifestation, it is advised to restrict the usage to disease flares due to associated side effects (6). More recently reports of anti TNF-alfa guided treatment seem to be emerging (15). Adalimumab and Infliximab appear to be effective for achieving initial and durable responses (15). Extensive screening for infection should be conducted before starting these biologicals. At present times more data is needed to determine the place of these rather new biologicals in this rather rare EIM of IBD.

Conclusion

In case of respiratory symptoms a high level of suspicion of pulmonary involvement is necessary when treating IBD patients. When dyspnea, cough or phlegm is present we suggest PFTs. If abnormal, an inspiratory and expiratory HRCT-thorax is indicated to reveal any abnormalities. CS are the go to agent to treat the airway or lung disease. Tracheal and bronchial involvement respond better than lung involvement to CS. A short course of oral corticosteroids may be indicated for severe symptoms. In the case of worsening symptoms or severe adverse events to CS, administration of biologicals such as Infliximab or Adalimumab may favor outcome. When an infectious process is present, antibiotics should be associated. It is imperative to administer treatment early to minimize irreversible sequelae of inflammation. These sequelae, strictures of large airways, bronchiectasis or bronchiolitis obliterans sometimes require surgical intervention.

Conflicts of interest

There are no financial conflicts of interest to disclose.

References

1. STORCH I., SACHAR D., KATZ S. Pulmonary manifestations of inflammatory bowel disease. *Inflamm Bowel Dis.*, 2003,**9**(2):104-15.
2. ROGERS BH., CLARK LM., KIRSNER JB. The epidemiologic and demographic characteristics of inflammatory bowel disease: an analysis of a computerized file of 1400 patients. *J Chronic Dis*., 1971,**24**(12):743-73.
3. CAMUS P., PIARD F., ASHCROFT T., GAL AA., COLBY TV. The lung in inflammatory bowel disease. *Medicine* (Baltimore), 1993,**72**(3):151-83.
4. SONGÜR N., SONGÜR Y., TÜZÜN M., DOGAN I., TÜZÜN D., ENSARI A., HEKIMOGLU B. Pulmonary function tests and high-resolution CT in the detection of pulmonary involvement in inflammatory bowel disease. *J Clin Gastroenterol*., 2003,**37**(4):292-8.
5. COZZI D., MORONI C., ADDEO G., GINEVRA D., LANZETTA M., CAVIGLI E., *et al.* Radiological Patterns of Lung Involvement in Inflammatory Bowel Disease. *Gastroenterol Res Pract*., 2018: 5697846.
6. CAMUS P., COLBY TV. The lung in inflammatory bowel disease. *Eur Respir J*., 2000,**15**(1):5-10.
7. RAJ AA., BIRRING SS., GREEN R., GRANT A., DE CAESTECKER J., Pavord ID. Prevalence of inflammatory bowel disease in patients with airways disease. *Respir Med*., 2008,**102**(5):780-5.
8. HERRLINGER KR., NOFTZ MK., DALHOFF K., LUDWIG D., STANGE EF., FELLERMANN K. Alterations in pulmonary function in inflammatory bowel disease are frequent and persist during remission. *Am J Gastroenterol*., 2002,**97**(2):377-81.
9. MANSI A., CUCCHIARA S., GRECO L., SARNELLI P., PISANTI C., FRANCO MT. *et al.* Bronchial hyperresponsiveness in children and adolescents with Crohn's disease. *Am J Respir Crit Care Med.*, 2000,**161**(3 Pt 1):1051-4
10. DESAI D., PATIL S., UDWADIA Z., MAHESHWAR S., ABRAHAM P., JOSHI A. Pulmonary manifestations in inflammatory bowel disease: a prospective study. *Indian J Gastroenterol.*, 2011,**30**(5):225-8.
11. BERNSTEIN CN., WAJDA A., BLANCHARD JF. The clustering of other chronic inflammatory diseases in inflammatory bowel disease: a population-based study. *Gastroenterology*., 2005,**129(**3):827-36.
12. LU DG., JI XQ., LIU X., LI HJ., ZHANG CQ. Pulmonary manifestations of Crohn's disease. *World J Gastroenterol.*, 2014,**20**(1):133-41.
13. DOUGLAS JG., MCDONALD CF., LESLIE MJ., GILLON J., CROMPTON GK., MCHARDY GJ. Respiratory impairment in inflammatory bowel disease: does it vary with disease activity? *Respir Med*., 1989,**83**(5):389-94.
14. BONNIERE P., WALLAERT B., CORTOT A., MARCHANDISE X., RIOU Y., TONNEL AB. *et al.* Latent pulmonary involvement in Crohn's disease: biological, functional, bronchoalveolar lavage and scintigraphic studies. *Gut*., 1986,**27**(8):919-25.
15. SHIN D., PARK BK., SEO J., WON SY., LEE MK., HONG YK., CHO YS. Pulmonary Extraintestinal Manifestation of Crohn's Disease Treated Successfully with Adalimumab. *Korean J Gastroenterol.*, 2018,**72**(3):141-45.