

## Tracheobronchial nodules and pulmonary infiltrates in a patient with Crohn's disease

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### Abstract

Crohn's disease is a granulomatous systemic disorder of unknown etiology. Obvious pulmonary involvement is exceptional. Tracheal involvement in Crohn's disease is even more unusual, only a few cases have been reported to date. We herein report a rare case of tracheobronchial nodules and pulmonary infiltrates in both lungs as a complication of Crohn's disease. A 42-year-old man underwent pancolectomy for multiple broken colon caused by Crohn's disease. Forty days later pulmonary symptoms and radiologic abnormalities were noted. A search for bacterial (including mycobacteria) and fungal in the repeated sputum proved negative. The treatment consisted of intravenous antimicrobials for one month, but there was no improvement in pyrexia or cough and radiologic abnormalities. Fiberoptic bronchoscopy (FOB) was performed and revealed nodes in the trachea and the right upper lobe opening. Histopathology of tracheobronchial nodules and bronchial mucosa biopsy specimen both showed granulomatous inflammation with proliferation of capillaries and inflammatory cells. Oral steroid and salicylazosulfapyridine were commenced and

led to marked improvement in symptoms and an almost complete resolution of his chest radiograph. Repeated FOB showed that nodes in the trachea disappeared and the ones in the right upper lobe opening diminished obviously. Crohn's disease can be associated with several respiratory manifestations. The form of tracheal and bronchopulmonary involvement in Crohn's disease is rare and responded well to steroids.

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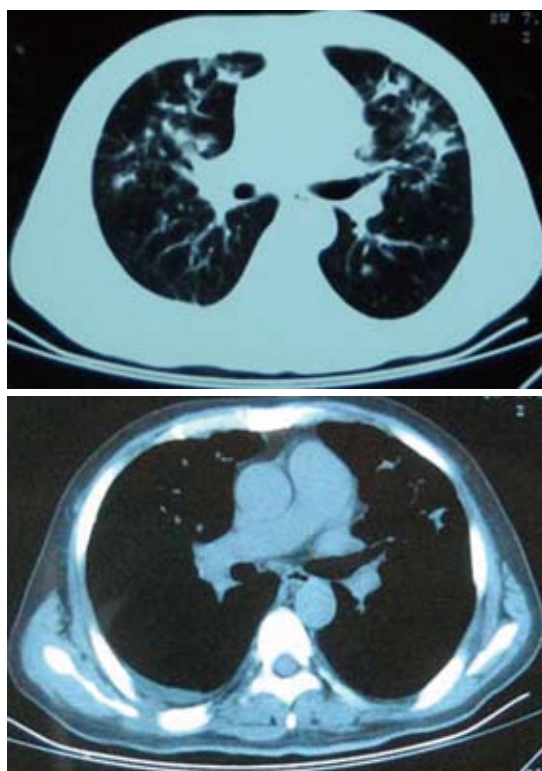
**Key words:** Crohn's disease; Inflammatory bowel disease; Lung; Extracolonic involvement

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### INTRODUCTION

Crohn's disease has long been recognized to cause both intestinal and extraintestinal complications. Extra-intestinal manifestations occur in at least 25% of Crohn's disease patients<sup>[1]</sup>. Although some papers have reported respiratory tract involvement in Crohn's disease, such as tracheobronchitis<sup>[2]</sup>, tracheobronchial stenosis<sup>[3]</sup>, upper bronchial pseudotumors and stenosis<sup>[4]</sup>, granulomatous bronchiolitis<sup>[5]</sup>, reports of involvement in both respiratory tract and lung parenchyma in Crohn's disease are very rare. We describe a patient with Crohn's disease who presented with tracheobronchial nodules and pulmonary infiltrates.



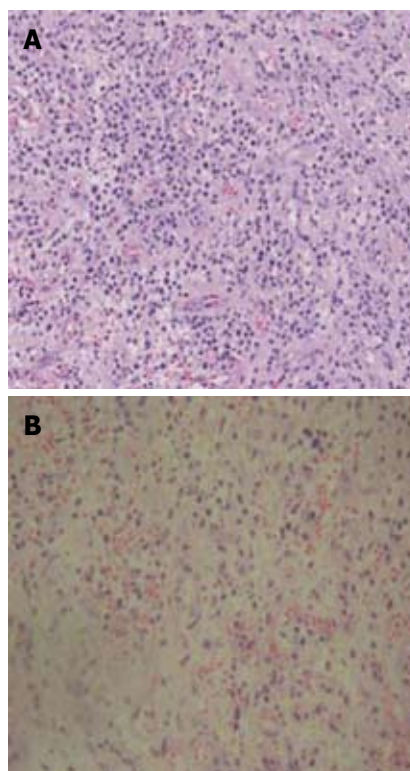
**Figure 1** Computed tomography scan of the thorax (January 19, 2009), showing multiple patchy shadows in both lung fields with a little right pleural effusion.



**Figure 2** Fiberoptic bronchoscopy (March 9, 2009), showing nodes in the right upper lobe opening.

## CASE REPORT

A 42-year-old man was admitted to our department because of a slow onset of cough and pyrexia in January 19, 2009. Forty days prior to this presentation, severe abdominal pain and diarrhea led to his referral to abdominal computed tomography (CT) that revealed free gas under the diaphragm. The patient underwent celiotomy. During operation, multiple broken colon was identified and pancolectomy was performed. The pathology of resected specimen revealed Crohn's disease of colon. His symptoms were resolved after the operation. On admission, he was expectorating about 20 mL of grossly frothy sputum



**Figure 3** Transfiberoptic bronchoscopy mucosal biopsy, showing polypoid hyperplasia of granulation tissue and hyperplasia of capillary with inflammatory cells (hematoxylin and eosin stain,  $\times 200$ ). A: Tracheobronchial nodules; B: Left lingular lobe.

per day and he had a pyrexia of 37.7 °C. Laboratory data on admission were: white cell counts  $8.5 \times 10^9/L$ , 63% segmented neutrophils, a moderate increase of erythrocyte sedimentation rate (30 mm in the first hour). A CT scan of the chest revealed bilateral lung patchy shadows (Figure 1). Initial treatment consisted of intravenous azithromycin (0.5 g, once a day) with aztreonam (2.0 g, twice a day) for 2 wk. A search for bacterial (including mycobacteria) and fungal in the repeated sputum proved negative. The purified protein derivative skin test and cytoplasmic-antineutrophil cytoplasmic antibodies (c-ANCA) were also negative. Intravenous cefoperazone/sulbactam (3.0 g, twice a day) was substituted for 2 wk, but there was no improvement in pyrexia or cough, and his chest CT revealed no dissipation. On day 36 after admission, the patient underwent fiberoptic bronchoscopy (FOB) which showed nodes in the trachea and the right upper lobe opening (Figure 2). Transbronchial lung biopsy was performed in tracheobronchial nodules and left lingular lobe. Histopathology of tracheobronchial nodules and bronchial mucosa biopsy specimen both showed granulomatous inflammation with proliferation of capillaries and inflammatory cells (Figure 3). Fibercoloscopy was performed in the following day, which showed cobblestones in the residual sigmoid colon. On day 55, antibiotic treatment was discontinued and the patient was started on prednisone 50 mg daily and salicylazosulfapyridine (SASP) (1.0 g, four times a day) for a presumptive



**Figure 4** Computed tomography scan of the thorax (April 5, 2009), showing multiple patchy shadows in both lung fields almost disappeared.

diagnosis of Crohn's disease related tracheobronchial nodules and tracheobronchitis associated with pulmonary infiltrates. Within 48 h, the patient's temperature turned normal. There was improvement in cough and the volume of sputum being expectorated a week later. A follow-up CT 3 wk later showed disappearance of the bilateral patchy shadows (Figure 4). He underwent repeated FOB in the following day which showed that nodes in the trachea disappeared and the ones in the right upper lobe opening diminished obviously (Figure 5).

## DISCUSSION

Crohn's disease is a granulomatous inflammation of unknown etiology that mainly affects the small bowel, although extracolonic manifestations are common. Extraintestinal manifestations occur in at least 25% of Crohn's disease patients, most commonly in the skin and genitourinary system<sup>[6]</sup>. It has been rarely reported in the lung. The overall prevalence of concomitant bronchopulmonary manifestations is as low as 0.4%<sup>[7]</sup>. Several forms of involvement of the lung parenchyma are recognized<sup>[8-11]</sup>. Diffuse, nongranulomatous interstitial inflammatory lymphoid infiltration has also been described in Crohn's disease<sup>[12]</sup>.

The clinical features of extraintestinal involvement in our patient seem to be interesting for several reasons. Both tracheal-bronchus and lung parenchyma are involved. Transfiberoptic bronchoscopy biopsy of the tracheobronchial nodules and bronchial mucosa in the



**Figure 5** Fiberoptic bronchoscopy (April 6, 2009), showing nodes in the right upper lobe opening diminished obviously.

left lingular lobe revealed a benign, nongranulomatous inflammation with proliferation of capillaries and inflammatory cells. Although tracheobronchial involvement in Crohn's disease has been described in literature, the extent of involvement seen in the current patient with nodules in trachea and right upper lobe bronchus, seems quite unusual. There are few previous reports of tracheobronchial nodules. Crohn's disease can involve the lung parenchyma, the tracheobronchial tree, and the pleura<sup>[13]</sup>. The patient underwent colectomy prior to admission. The pulmonary manifestations of Crohn's disease in some patients may only become clinically remarkable after surgery<sup>[14]</sup>. Colectomy may aggravate respiratory symptoms<sup>[15]</sup>. However, the pathogenesis of Crohn's disease-related airway disease remains unknown. It may involve an inflammatory component because a large proportion of these patients are responsive to steroid therapy. The lung and the gastrointestinal tract have a similar embryological origin (a potential source of common antigenicity), and some authors considered a breakdown in the intestinal barrier and entry of dietary antigens as the cause of extracolonic involvement in Crohn's disease<sup>[16]</sup>. One proposed mechanism is that many of the extraintestinal manifestations of Crohn's disease, including lung disease, are secondary to circulating inflammatory mediators released by the inflamed bowel mucosa<sup>[17]</sup>. These inflammatory mediators may survive in the pulmonary system for a long time, causing smoldering injuries. This explains the development of pulmonary disease after colectomy in some of the patients with Crohn's disease.

Clinically, when assessing the relationship between respiratory disease and Crohn's disease, one should always keep in mind that the two conditions may have occurred together simply by chance, and therefore other differential diagnoses should be made, such as sarcoidosis, a systemic vasculitis (Wegener's granulomatosis or Churg-Strauss disease), or a prior pulmonary process. In the current patient, the diagnosis of Crohn's disease was initially clearly established on histological grounds of the resected bowel specimen. Although sarcoidosis and Crohn's disease may coexist in the same patient<sup>[18]</sup>, the absence of typical sarcoid granulomata in tracheobron-



chial biopsies, and the lack of evidence for extrapulmonary sarcoid involvement led the authors to rule out sarcoidosis. In view of the absence of histological findings suggestive of Wegener's granulomatosis, the lack of c-ANCA and no extrapulmonary involvement, the diagnosis of Wegener's granulomatosis was unlikely. Post-obstructive pneumonia results from airway obstruction, commonly due to lung cancer. A mismatch in scope of bilateral and diffuse lung infiltrates with tracheobronchial nodules excluded a diagnosis of post-obstructive pneumonia.

The initial lesion of tracheobronchial Crohn's disease seems to be mucosal inflammation, with symptoms of cough and pyrexia<sup>[19]</sup>. Mucosal inflammation may be accompanied by bronchial suppuration. Biopsy shows either severe nonspecific chronic inflammation or non-caseating tuberculoid granulomas. These appearances have been associated with those in the bowel, and it is possible that the gut and the lung are both affected because they share common antigens. The lung and gastrointestinal tract contain submucosal lymphoid tissues and play crucial roles in host mucosal defense. The similarity in the mucosal immune system causes the same pathogenetic changes. The clinical courses between upper airway and gastrointestinal tract disease are not entirely parallel<sup>[20]</sup>. It was thought that the tracheobronchial nodules and pulmonary infiltrates were both caused by Crohn's disease, because the pathological finding resembled that of the colon. In addition, they almost vanished as good response to steroids while multiple antibiotic regimens failed to produce clinical improvement.

Drug-induced disease must be kept in mind in patients taking sulfasalazine, mesalamine, methotrexate, and anti-tumor necrosis factor- $\alpha$ . Sulfasalazine and 5-aminosalicylic acid derivatives have been reported to cause interstitial pneumonitis, eosinophilic pneumonia, or bronchiolitis obliterans organizing pneumonia in rare cases<sup>[21,22]</sup>. Other commonly used medications in inflammatory bowel disease patients include 6-mercaptopurine, azathioprine, and methotrexate. These drugs may also cause pneumonia *via* opportunistic infections, or acute pneumonitis or pulmonary fibrosis<sup>[23]</sup>. Lung abnormalities observed in our patient were unrelated to pharmacological treatment.

Patients with pulmonary involvement of Crohn's disease can be cured with glucocorticoid and SASP, for they are strikingly steroid-responsive frequently. Pulmonary manifestations almost vanished after receiving oral prednisone and SASP in the present case. In all patients with airway disease, marked and long-lasting responses were seen following systemic or inhaled administration of steroids. These findings were not commonly observed for patients with chronic bronchitis without Crohn's disease. Intravenous steroids were required in the initial management of life-threatening complications such as asphyxiating subglottic stenosis or extensive interstitial lung disease. Bronchial lavages with methylprednisolone

were effective in some patients with severe airway inflammation. Bronchoscopic dilatation or stent placement should be considered in cases of tracheal stenosis due to Crohn's disease refractory to steroid treatment<sup>[24]</sup>. Other interventional pulmonology techniques, such as bronchoscopic resection or ablation, could not be generally indicated for treatment modalities potentially contraindicated because of the risk of stenosis or fistula.

In summary, this case illustrates a rare form of tracheal and bronchopulmonary involvement in Crohn's disease with nodes and multiple patchy shadows in both lung fields. As is the case with other forms of pulmonary involvement in Crohn's disease, this manifestation responded well to steroids. It is believed that early investigation and vigorous treatment of bronchopulmonary involvement of Crohn's disease is essential.

## REFERENCES

- 1 **Ephgrave K.** Extra-intestinal manifestations of Crohn's disease. *Surg Clin North Am* 2007; **87**: 673-680
- 2 **Iwama T, Higuchi T, Imajo M, Akagawa S, Matsubara O, Mishima Y.** Tracheo-bronchitis as a complication of Crohn's disease--a case report. *Jpn J Surg* 1991; **21**: 454-457
- 3 **Kuźniar T, Sleiman C, Brugière O, Groussard O, Mal H, Mellot F, Pariente R, Malolepszy J, Fournier M.** Severe tracheobronchial stenosis in a patient with Crohn's disease. *Eur Respir J* 2000; **15**: 209-212
- 4 **Henry MT, Davidson LA, Cooke NJ.** Tracheobronchial involvement with Crohn's disease. *Eur J Gastroenterol Hepatol* 2001; **13**: 1495-1497
- 5 **Vandenplas O, Casel S, Delos M, Trigaux JP, Melange M, Marchand E.** Granulomatous bronchiolitis associated with Crohn's disease. *Am J Respir Crit Care Med* 1998; **158**: 1676-1679
- 6 **Calder CJ, Lacy D, Raafat F, Weller PH, Booth IW.** Crohn's disease with pulmonary involvement in a 3 year old boy. *Gut* 1993; **34**: 1636-1638
- 7 **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**: 743-773
- 8 **Shulimzon T, Rozenman J, Perelman M, Bardan E, Ben-Dov I.** Necrotizing granulomata in the lung preceding colonic involvement in 2 patients with Crohn's disease. *Respiration* 2007; **74**: 698-702
- 9 **Casey MB, Tazelaar HD, Myers JL, Hunninghake GW, Kakkar S, Kalra SX, Ashton R, Colby TV.** Noninfectious lung pathology in patients with Crohn's disease. *Am J Surg Pathol* 2003; **27**: 213-219
- 10 **Golpe R, Mateos A, Pérez-Valcárcel J, Lapeña JA, García-Figueiras R, Blanco J.** Multiple pulmonary nodules in a patient with Crohn's disease. *Respiration* 2003; **70**: 306-309
- 11 **Lucero PF, Frey WC, Shaffer RT, Morris MJ.** Granulomatous lung masses in an elderly patient with inactive Crohn's disease. *Inflamm Bowel Dis* 2001; **7**: 256-259
- 12 **Hotermans G, Benard A, Guenanen H, Demarcq-Delerue G, Malart T, Wallaert B.** Nongranulomatous interstitial lung disease in Crohn's disease. *Eur Respir J* 1996; **9**: 380-382
- 13 **Tagle M, Barriga J, Piñero A.** Crohn's disease associated with focal pulmonare lesion. *Rev Gastroenterol Peru* 2003; **23**: 293-296
- 14 **Kelly MG, Frizelle FA, Thornley PT, Beckert L, Epton M, Lynch AC.** Inflammatory bowel disease and the lung: is there a link between surgery and bronchiectasis? *Int J*

- Colorectal Dis* 2006; **21**: 754-757
- 15 **Ceyhan B.** Inflammatory bowel disease and lung. *Tuberk Toraks* 2006; **54**: 292-298
  - 16 **Baughman RP,** Lower EE, du Bois RM. Sarcoidosis. *Lancet* 2003; **361**: 1111-1118
  - 17 **Bulger K,** O'Riordan M, Purdy S, O'Brien M, Lennon J. Gastrointestinal sarcoidosis resembling Crohn's disease. *Am J Gastroenterol* 1988; **83**: 1415-1417
  - 18 **McCormick PA,** O'Donoghue DP, FitzGerald MX. Crohn's colitis and sarcoidosis. *Postgrad Med J* 1986; **62**: 951-953
  - 19 **Lemann M,** Messing B, D'Agay F, Modigliani R. Crohn's disease with respiratory tract involvement. *Gut* 1987; **28**: 1669-1672
  - 20 **Asami T,** Koyama S, Watanabe Y, Miwa C, Ushimaru S, Nakashima Y, Nokubi M. Tracheobronchitis in a patient with Crohn's disease. *Intern Med* 2009; **48**: 1475-1478
  - 21 **Parry SD,** Barbatzas C, Peel ET, Barton JR. Sulphasalazine and lung toxicity. *Eur Respir J* 2002; **19**: 756-764
  - 22 **Pérez C,** Errázuriz I, Brockmann P, González S, Cofré C. Eosinophilic pneumonia caused by mesalazine. Report of one case. *Rev Med Chil* 2003; **131**: 81-84
  - 23 **Bernal I,** Domènech E, García-Planella E, Cabré E, Gassull MA. Opportunistic infections in patients with inflammatory bowel disease undergoing immunosuppressive therapy. *Gastroenterol Hepatol* 2003; **26**: 19-22
  - 24 **Plataki M,** Tzortzaki E, Lambiri I, Giannikaki E, Ernst A, Siafakas NM. Severe airway stenosis associated with Crohn's disease: case report. *BMC Pulm Med* 2006; **6**: 7

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