Eur Respir J 2000; 15: 209–212
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European Respiratory Journal
ISSN 0903-1936

CASE STUDY

Severe tracheobronchial stenosis in a patient with Crohn's disease

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ABSTRACT: Tracheobronchial involvement in Crohn's disease is rare, usually associated with symptoms of tracheobronchitis, and typically responds well to steroids. The authors report a case of a 29-yr old patient with Crohn's disease, who presented with dyspnoea, fever, and a productive cough. Computed tomography of the chest revealed extensive nodular tracheobronchial stenosis, that was accompanied by severe mucosal inflammation at bronchoscopy. High-dose oral steroids diminished the mucosal inflammation, but had limited efficacy on the underlying tracheobronchial stenosis. It is speculated that this relative ineffectiveness of steroids may be due to the persistence of the untreated inflammatory process.
Eur Respir J 2000; 15: 209–212.

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Keywords: Crohn's disease
tracheobronchial stenosis

Received: April 17 1998
Accepted after revision May 25 1999

T. Kuźniar was a recipient of a stipend from the Association of the Medical Doctors of Polish Origin in France.

Crohn's disease (CD) is a chronic granulomatous inflammatory bowel disease, which may occasionally affect extraintestinal organs [1, 2]. Pulmonary involvement is most often subclinical, reflected by an increased lymphocyte count in the bronchoalveolar lavage fluid (BALF) [3], and/or lung function test abnormalities [4, 5]. Overt and clinically significant lung involvement is rare, and may take the form of chronic bronchitis, bronchiectasis, granulomatous interstitial pneumonitis, bronchiolitis obliterans, fibrosis, alveolitis, or pleuritis [6–8]. Tracheal involvement in CD is even more unusual, and consists of mucosal inflammation [9–12]. This report describes the case of a young patient with CD, who presented with extensive tracheal wall thickening, and a severe tracheobronchial stenosis. These features have only rarely been clearly documented to date [6].

Case study

A 29-yr old Caucasian male patient presented in October 1996 with dyspnoea and a 2 day history of fever and purulent sputum. Since 1979, he had suffered from typical CD which had been diagnosed on clinical, endoscopic and histological grounds. He underwent colectomy with ileorectal anastomosis in 1980. In the following years, he suffered from repeated exacerbations of ileal and perianal CD, and underwent total colectomy with permanent ileostomy in 1987. He had no digestive symptoms thereafter and received no specific treatment. His respiratory symptoms developed in 1982, in the form of a productive cough. In 1987, he was started on inhaled beclomethasone, 1500 $\mu g \cdot day^{-1}$, which he took continuously until 1996. Beclomethasone initially controlled the production of sputum. However, since 1991 and despite maintenance inhaled steroid treatment, the patient experienced a steady increase in the volume of sputum, which amounted to 150–200 mL daily in 1996.

The day before admission, the patient developed fever and a marked increase in the volume of purulent sputum. On admission, a severe dyspnoea was noted. On physical examination, the patient had polypnoea and bilateral rales and coughed up purulent, blood-tinged sputum. His temperature was 37.9°C and his arterial oxygen saturation (Sa,O_2) was 96% (room air). Laboratory investigations showed normal serum values of electrolytes, glucose, liver function tests, urea and creatinine. Other laboratory tests showed an erythrocyte sedimentation rate of 26 $mm \cdot 1h^{-1}$, and C-reactive protein 84 $mg \cdot L^{-1}$ (Normal: <6). Complete blood count revealed slight microcytosis, with normal white blood cell count. Serum protein was normal. An human immunodeficiency virus (HIV) test was negative. The anti-nuclear antibodies were absent, but the perinuclear antineutrophil cytoplasm antibodies (p-ANCA) were present. A salivary gland biopsy was normal. There were no significant abnormalities on the chest radiograph. Pulmonary function tests showed an obstructive pattern and are shown in table 1; there was no improvement in forced expiratory volume in one second (FEV_1) following inhalation of β_2-agonist.

The fibreoptic bronchoscopy (FOB) was performed on admission, and showed marked inflammation of tracheal and bronchial mucosa, with abundant purulent secretions. There were extensive tracheal and bronchial deformities,

Table 1. – Pulmonary function tests' values

Parameter	September 1996	November 1996	January 1999
VC L	2.71 (56)	4.17 (87)	4.45 (93)
FEV_1	1.54 (38)	2.88 (71)	3.10 (77)
FEV_1/VC %	52	69	70
$FEF_{25–75}$ L	0.96 (20)	2.18 (46)	2.13 (45)
P_{a,O_2} kPa	11.2	13.3	15.0
P_{a,CO_2} kPa	5.4	5.2	5.6

Data in parentheses are percentage of predicted value. Measurements in September 1996 were taken on admission; those in November 1996 were after 6 weeks of oral and inhaled steroids; and those in January 1999 were after 28 months of therapy. VC: vital capacity; FEV_1: forced expiratory volume in one second; $FEF_{25–75}$%: forced mid-expiratory flow; P_{a,O_2}: oxygen tension in arterial blood; P_{a,CO_2}: carbon dioxide tension in arterial blood.

with a stenosis of both mainstem bronchi to <40% of the normal diameter. There was no expiratory collapse. Histological examination of several biopsies of the stenosed areas showed an intense inflammatory process, mucosal hyperplasia with dense lymphocytic, and plasma cell infiltrate in the submucosa (fig. 1). Immunohistochemical tests identified the lymphocytes as both T- and B- cells. The BALF, performed during the FOB, was almost exclusively neutrophilic (97%). An extensive search for bacterial (including mycobacteria), fungal and parasitic infectious agents in the BAL was negative.

A computed tomographic scan (CT) of the thorax showed extensive airway deformities (figs. 2 and 3). The wall of the lower third of the trachea was markedly increased in thickness. The deformities extended peripherally to form nodular stenoses in the two mainstem bronchi. Mucoid impaction in small bronchi, as well as alveolar micronodules in the lower right lobe were noted (not shown).

The patient was initially treated with antibiotics (amoxicillin-clavulanate) for 10 days, along with oral steroids (starting dose, 80 mg·day^{-1} prednisone), and nebulized budesonide (1000 μg, *q.i.d.*). This resulted in prompt symptomatic improvement with disappearance of purulent sputum after ~1 week. After 6 weeks, the patient was symptom-free, and had marked improvement in lung function

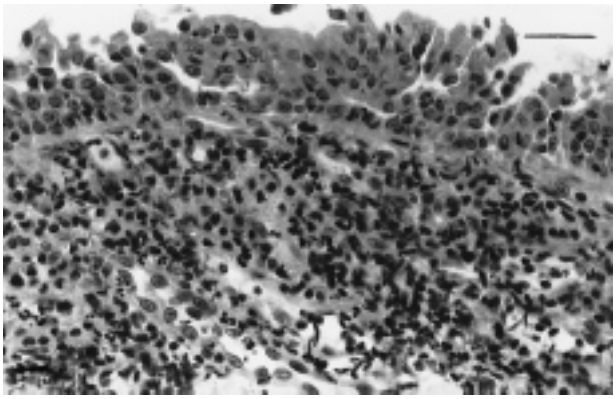

Fig. 1. – Bronchial biopsy: dense and diffuse submucosal infiltrate of lymphocytes and plasma cells (haematoxylin and eosin stain).

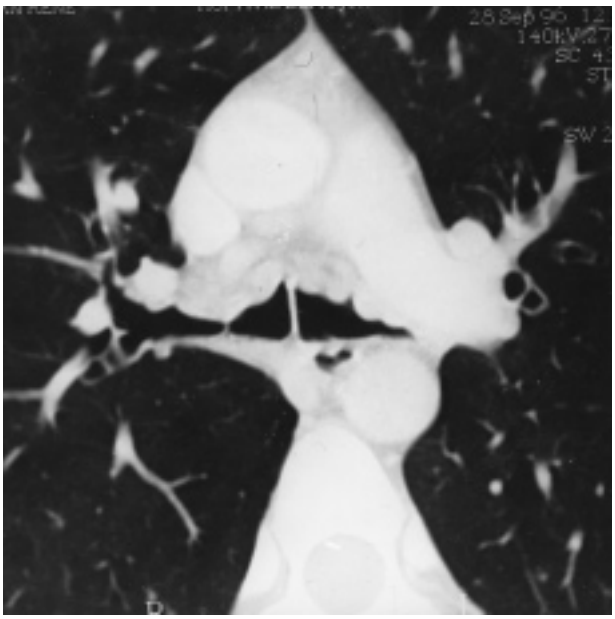

Fig. 2. – Computed tomography scan of the thorax showing nodular stenoses of the two mainstem bronchi (2 weeks after the admission).

(table 1). A follow-up CT showed a slight decrease in tracheal wall thickness, with the persistence of tracheal and bronchial deformity, and a complete clearing of parenchymal abnormalities. A control FOB performed at 4 months (fig. 4) showed the disappearance of mucosal inflammation but persistence of slit-like stenoses of trachea and bronchi. Oral steroids were subsequently tapered to 20 mg of prednisone per day at 6 months, 7.5 mg of prednisone per day at 10 months and were withdrawn at 13 months. Twenty-eight months after initial presentation the patient is receiving inhaled budesonide at the dose of 3000 μg·day^{-1}. At a control visit at 12 months, there were no changes in CT and FOB appearances of the stenotic area, but the mucosal inflammation has not recurred.

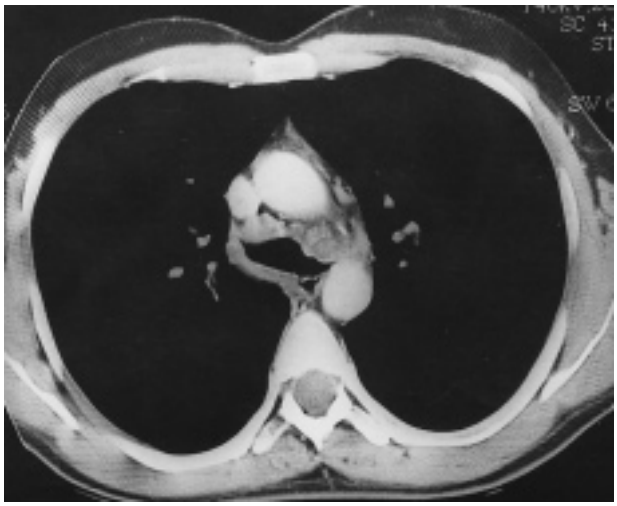

Fig. 3. – Computed tomography scan of the thorax showing an increase in the thickness of the tracheal wall and mediastinal lymph node enlargement (2 weeks after the admission).

Table 2. – Literature data on upper airway and tracheobronchial involvement in patients with Crohn's disease

Sex	Type of involvement	Route and response to steroids	[Ref.]
F (34)	tracheobronchitis with AO	OCS – dramatic improvement	[6]
M (37)	tracheobronchitis without AO	OCS and ICS – dramatic improvement	[9]
F (24)	tracheobronchitis with AO	OCS – dramatic improvement	[10]
F (19)	tracheobronchitis without AO	OCS – marked improvement	[10]
F (59)	tracheobronchitis without AO		[11]
M (26)	tracheobronchitis without AO	OCS – dramatic improvement	[12]
M (25)	laryngitis with AO	OCS – complete clearance of symptoms, then steroid-dependence	[24]
F (22)	laryngitis with AO	OCS – some initial improvement, then upper airway obstruction requiring tracheotomy	[24]
M (29)	tracheobronchitis with AO	ICS, OCS – improvement of tracheobronchitis, persistence of tracheobronchial deformity	[present case]

Data in curved parentheses are patient age. F: female; M: male; AO: airway obstruction; OCS: oral steroids; ICS: inhaled steroids.

Discussion

The authors report the case of a young patient with CD, who developed tracheobronchial inflammation and stenosis several years after the onset of his intestinal disease and colectomy. While clinically significant pulmonary involvement of CD is rare, subclinical respiratory involvement has well been described [4, 5, 13]. In inflammatory bowel disease (IBD) in general, many forms of bronchial involvement typically develop after colectomy [14]. This feature is especially true in patients with ulcerative colitis [6, 11].

In the present case the authors discussed other disease processes that may produce a close clinical, endoscopic, and radiological picture. Relapsing polychondritis was excluded on the basis of clinical, radiological and histological findings [15]. Tracheal tuberculosis was also excluded due to absence of *mycobacteria* in repeated sputum and BAL cultures, and a clinical improvement over twelve months of steroid therapy. Although sarcoidosis and CD may coexist in the same patient [16, 17], the absence of typical sarcoid granulomata in bronchial biopsies, and the lack of evidence for extrapulmonary sarcoid involvement led the authors to rule out sarcoidosis. The absence of cutaneous pustules excluded a diagnosis of Sweet′s syndrome [18]. Tracheobronchial involvement in Wegener′s granulomatosis may present as ulcerating tracheobronchitis or tracheal/bronchial stenosis [19, 20]. The extent of tracheal and bronchial lesions observed in the current patient, the absence of histological findings suggestive of Wegener′s granulomatosis, the lack of cytoplasmic-antineutrophil cytoplasmic antibodies (c-ANCA), no extrapulmonary involvement and slow progression without specific treatment all made, in the authors′ opinion, the diagnosis of Wegener′s granulomatosis unlikely. Of note is that detectable perinuclear (p)-ANCA are a frequent finding in patients with ulcerative colitis and may occur in up to 20% of patients with CD [6, 21]. Ulcerative colitis may also affect the upper respiratory tract [6, 11, 22, 23]. In the current patient, however, the diagnosis of Crohn′s disease was initially clearly established on histological grounds of the resected bowel specimen.

Although the literature gives several descriptions of tracheobronchial involvement in CD (table 2), the extent of involvement seen in the current patient, with bronchial wall thickening, stenosis of the trachea and both mainstem bronchi seems quite unusual [6]. The initial lesion of tracheobronchial CD seems to be mucosal inflammation, with symptoms of cough and dyspnoea [6, 10–12]. In one case, the friable and haemorrhagic granulation tissue severely obstructed the tracheal lumen [6]. Mucosal inflammation may be accompanied by bronchial suppuration. Inflammation and attending obstruction may be so extensive, that this may lead to acute respiratory failure, requiring intubation and mechanical ventilation [9]. All these symptoms usually respond to inhaled and/or oral steroids [6, 9–12].

The current patient may represent a more advanced and chronic stage of the same disease process. As an appropriate dose of inhaled and/or systemic steroids may rapidly improve symptoms of tracheobronchial involvement of

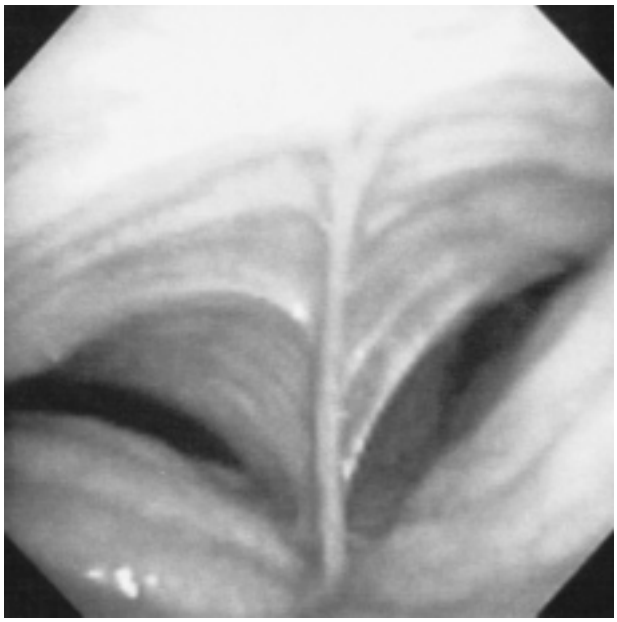

Fig. 4. – Endoscopic view of tracheal bifurcation after 4 months of treatment with systemic and inhaled steroids that showed marked improvement of tracheobronchial inflammation, but a slit-like narrowing of the two mainstem bronchi (front in the bottom of the picture).

CD [6, 9–12], it seems necessary to search for such an involvement in all patients with CD and persistent respiratory symptoms. It is possible, that the initial dosage of inhaled steroids (1500 μg budesonide per day) that the patient had been receiving since 1987 was insufficient to control symptoms and prevent complications of the ongoing airway inflammation. Higher dosage of budesonide (4000 $\mu g \cdot day^{-1}$), supplemented with oral steroids resulted in rapid symptomatic improvement. The systemic effects of this mode of treatment remain, however, to be evaluated.

In summary, this case illustrates an advanced stage of tracheal and bronchopulmonally involvement in Crohn′s disease with marked tracheobronchial obstruction, due to the extensive bronchial deformities. This developed despite long-term, but possibly too low-dosed inhaled steroids. Higher dose inhaled steroids associated with oral steroids, which were reported to be rapidly effective in cases of bronchopulmonary CD [6], diminished the associated mucosal inflammation, but could not restore normal tracheobronchial patency. It is believed that the need exists for early investigation and vigorous treatment of airway involvement of Crohn′s disease.

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