

Granulomatous bronchiolitis of Crohn's disease successfully treated with inhaled budesonide

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ABSTRACT

A 39-year-old white woman with longstanding Crohn's disease presented with the rare complication of granulomatous bronchiolitis. Rapid resolution after inhaled budesonide is highlighted, as this is the first case described in the literature successfully treated without the need for systemic therapy. This less toxic approach to therapy is warranted in granulomatous bronchiolitis of Crohn's disease to avoid unwanted side effects of steroids and infliximab.

A 39-year-old white woman had been diagnosed with Crohn's disease (CD) at the age of 15. She had been treated with high-dose prednisone with disabling side effects including weight gain, alopecia and herpes zoster outbreaks. Mesalamine was tried but resulted in a severe febrile reaction. Subsequently, she was managed with a total colectomy and most recently with 6-mecaptopurine at a dose of 50–75 mg/day prior to her presentation. Her CD had been relatively quiescent on this therapy. There was no prior history of any lung disorder including asthma, bronchitis or pneumonia.

Four months before presentation she noted a dry non-productive cough and progressive dyspnoea. A course of moxifloxacin, albuterol metered dose inhaler and salmeterol/fluticasone dry powder inhaler (500/50) did not improve her symptoms. A second course of azithromycin also did not alter her symptoms. A complete blood count revealed her usual baseline anaemia (haemoglobin 10 g/dl, haematocrit of 30%) with a normal white blood cell count ($6.7 \times 1000/\mu\text{l}$) without eosinophilia. The chest radiograph was normal without evidence of infiltrate, adenopathy or effusion. Pulmonary function tests including methacholine challenge were normal. A CT scan of the chest revealed patchy micronodular densities and mild bronchiectasis at the lung bases bilaterally. A PPD test was negative. Hypersensitivity antibodies were negative to a standard panel of antigens. Fiberoptic bronchoscopy revealed normal-appearing airways and only modest thin secretions. Bronchoalveolar lavage revealed normal CD8/CD4 ratios, no eosinophils and negative stains and cultures for acid-fast bacilli (AFB), fungi and bacteria. An open lung biopsy was advised and declined by the patient. Progressive coughing jags resulted in severe chest wall pain. A second high-resolution CT scan of the chest 4 months after the first revealed a new left ninth rib fracture and worsening parenchymal infiltrates (fig 1). A video-assisted thoroscopic biopsy was performed and all stains were negative for AFB, fungal or bacterial elements. Tissue

examination revealed a mild peribronchial lymphocytic infiltrate. Focally, the airways showed loosely organised granuloma (fig 2). There was minimal alveolar or interstitial inflammation or fibrosis. Features of asthma (goblet cell metaplasia, sub-epithelial fibrosis) were absent.

Because of prior severe side effects to systemic steroids, nebulised budesonide (0.5 mg/2 ml) twice daily was begun. The patient noted a gradual improvement in her symptoms with progressive resolution of her cough and dyspnoea over a 2-week period. After 1 month she reported being back to her usual respiratory health. Treatments were reduced to once daily for two further months and were then discontinued. A CT scan performed 3 months after initiation of treatment showed complete resolution of the parenchymal abnormalities. She remains symptom-free 3 years later with no additional treatment.

DISCUSSION

Pulmonary involvement in CD, while rare, has been reported in the literature since the mid-1970s.^{1,2} To date, only 25 cases of CD with suspected pulmonary involvement have been described in the literature.³ The development of both large and small airways involvement in this disorder often results in symptomatic cough and dyspnoea prompting pulmonary consultation.^{3,4} Subclinical alveolitis suggested by increased numbers of T lymphocytes in the bronchoalveolar lavage fluid may be latently present as well in CD,^{5,6} and small airways dysfunction has been demonstrated using methods based on the density dependence of airflow.⁷ Vandenplas *et al* first reported isolated biopsy-confirmed granulomatous bronchiolitis in 1998.⁸ Treatment with systemic steroids has generally been advocated and successful in the few cases reported.^{2,4,8} In more recent reports infliximab has been used to treat the pulmonary manifestations of CD.^{8,9}

With the introduction of inhalable budesonide, the possibility of delivering effective doses of steroid to the distal airways to modify granulomatous bronchiolitis of CD became possible with the advantage of significantly less systemic absorption. To our knowledge, this is the first case of granulomatous bronchiolitis of CD to be successfully treated by inhaled steroids. It is of interest that relatively high doses of inhaled fluticasone propionate with which the patient was indeed compliant were unsuccessful in treating her granulomatous bronchiolitis. Many potential explanations exist for this observation. Differences in lung steroid deposition achieved by nebulised budesonide may have been greater than that achieved by

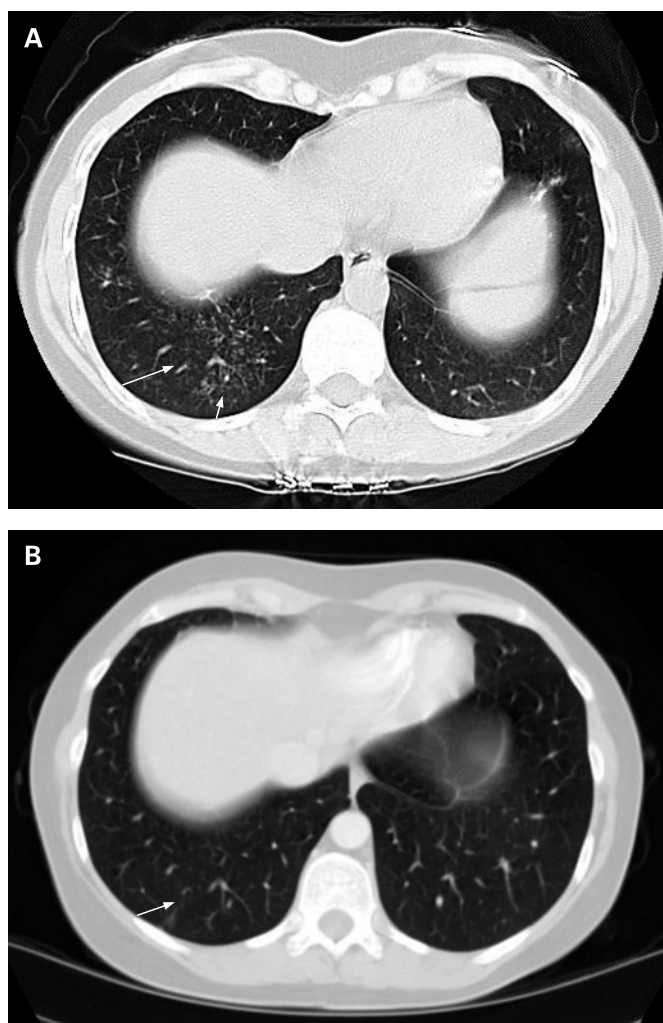


Figure 1 (A) Representative CT scan of the right lung base showing multiple patchy micronodular densities (arrows) prior to biopsy and treatment. (B) Same region of the right lower lobe 3 months after treatment with inhaled budesonide. Note resolution of the micronodular densities (arrow).

fluticasone (8–20% for dry powder diskus inhaler versus 58–70% with nebulised budesonide in adults).^{10 11} Other factors that may have influenced deposition in this patient include inconsistent flow rate generation that could alter upper airway versus lower airway deposition with the diskus mode of delivery, and efficacy may have been different between the two inhaled steroids in that budesonide can be reversibly esterified into lipophilic fatty esters that can serve as a local depot of regenerable budesonide that may extend its local effects.¹¹ That such an approach could work in a relatively short time

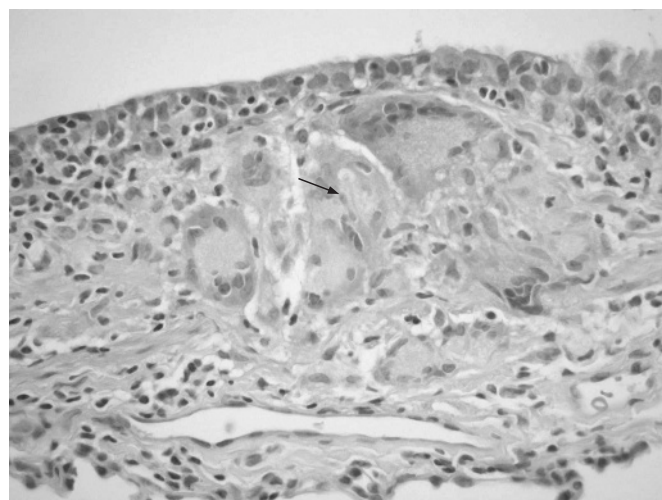


Figure 2 Video-assisted thoroscopic biopsy specimen of right lower lobe. Note poorly formed epithelioid granulomas with multinucleated giant cells in the walls of the terminal bronchioles (arrow).

frame is encouraging and likely to spare significant systemic side effects often associated with both steroids and anti-tumour necrosis factor antibodies. This treatment approach should be tried in all such cases of isolated airway involvement in CD or ulcerative colitis before resorting to more problematic systemic therapies.

Competing interests: None.

Patient consent: Obtained.

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