Pulmonary actinomycosis complicating infliximab therapy for Crohn’s disease

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Acute and convalescent sera for Mycoplasma pneumoniae and Legionella pneumophila showed no rise in titre. *Actinomyces graevenitzii* was cultured from the bronchial lavage fluid; cultures for tuberculosis, fungi and viruses were negative.

**DISCUSSION**

Pulmonary actinomycosis is a relatively rare disease usually caused by *Actinomyces israelii*, but other pathogenic species have been reported. It usually presents as an indolent pneumonia with fever, weight loss, cough, sputum and chest pain. There are no specific radiographic manifestations but lesions that involve the chest wall and pleura with destruction of adjacent bones are highly suggestive. The symptoms and clinical and radiological signs often mimic malignancy or tuberculosis, and miliary presentations of the disease have been reported. Ariel et al described five patients with endobronchial actinomycosis presenting in a subacute fashion. Endobronchial infection is thought to be due to implantation of infected aspirated material or lympho-haematogenous spread to the peribronchial region.

Actinomycosis has occasionally been reported in association with immunosuppressed states including post solid organ transplantation, with HIV/AIDS and following chemotherapy, but most often no defects in immunity can be identified in patients with this infection. It remains unclear which host defence mechanisms are important in preventing or controlling actinomycosis and the degree to which the incidence of infection is increased in immunocompromised patients, if at all. Dental procedures and aspiration of oropharyngeal contents are recognised risk factors for pulmonary actinomycosis, but these were absent in our patient. Actinomycosis has also occasionally been reported to complicate the diagnosis of CD of the small bowel; however, our patient had had multiple resections with no evidence of opportunistic infections in his resected specimens. There have not been any reports to date of actinomycosis complicating treatment with infliximab or other TNF inhibitors.

Infliximab is a chimeric IgG1 monoclonal anti-TNF antibody. It was the first anti-TNF agent to be approved by the FDA for induction and maintenance therapy in patients with moderate to severe CD refractory to conventional treatments. It has multiple suppressive effects on the immune response. After a single infusion in patients with steroid refractory ileocolonic CD, almost no neutrophils could be detected in colonic biopsy specimens and there was also a decrease in mononuclear cells. Aberrant colonic epithelial HLA-DR expression completely disappeared, and the percentage of intercellular adhesion molecule 1, lymphocyte function-associated antigen 1-expressing and interleukin (IL)-4 and TNF positive lamina propria mononuclear cells sharply decreased. Infliximab also decreases the proinflammatory cytokines IL-1 and IL-6 and adhesion molecules E-selectin and intercellular adhesion molecule-1.

**Abbreviations:** CD, Crohn’s disease; IL, interleukin; TNF, tumour necrosis factor; WBC, white blood cells
Infliximab has also received FDA approval for the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis, and recent trials have demonstrated significant efficacy in the treatment of psoriasis and ulcerative colitis.\textsuperscript{11,12} Infections associated with infliximab treatment have included tuberculosis (\textit{Mycobacterium tuberculosis} and \textit{M avium}), leprosy, cryptococcosis, coccidioidomycosis, histoplasmosis, aspergillosis, candidiasis, \textit{Pneumocystis carinii} (\textit{jiroveci}) pneumonia, listeriosis and legionellosis.\textsuperscript{13} Although our patient presented with pulmonary symptoms, other patients receiving anti-TNF agents may present with extrapulmonary manifestations.\textsuperscript{13}

In summary, we have described the first case of pulmonary actinomycosis in association with infliximab therapy for CD. The patient presented acutely, rather than in the chronic manner typical of the disease in the lungs of normal non-immunosuppressed individuals. This atypical presentation may have been due in part to the suppressive effects of infliximab on his normal inflammatory response. His response to high-dose intravenous penicillin was excellent and infliximab was restarted after a 4-month hiatus without consequence. Infliximab and other TNF inhibitors have shown promising therapeutic effects in an increasing number of conditions. Physicians caring for these individuals need to be aware of the entire spectrum of associated infectious complications and, in particular, need to maintain a high index of suspicion because of their often systemic and atypical presentation.

\textbf{REFERENCES}


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