Pulmonary actinomycosis coexisting with intestinal tuberculosis as a complication of adalimumab treatment for Crohn's disease

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To the Editor,

Tumor necrosis factor alpha (TNF-α) blocking agents are highly effective in inducing and mantaining remission in Crohn's disease (CD) (1). However, due to the profound supression of T-cell mediated immunity, opportunistic infections still remain a major concern in this group of patients (2). We would like to draw attention to the unique case of a young patient with a imunomodulator therapy-resistant Crohn's disease treated with adalimumab who developed pulmonary actinomycosis and intestinal tuberculosis despite adequate screening for latent tuberculosis.

A 23-year old male patient, initially diagnosed with ileal CD at the age of 17 and maintained on azathioprine therapy with good outcome, was admitted with a severe flare of CD. After exclusion of tuberculosis on the basis of chest X-ray, negative PPD test and Quantiferon assay, induction therapy with adalimumab was initialised. After third dose of adalimumab he was hospitalized due to dry cough and diarrhea. X-ray and CT scan of the chest revealed an inflammatory infiltrate in the apical segment of the left lower lobe of the lung without signs of tissue destruction (Fig. 1). The bronchoscopy was performed and cytological evaluation of specimen was positive for Actinomyces meyeri and negative for mycobacteria.

Additionally, the stool cultures were positive only for Mycobacterium tuberculosis (Fig. 2). The radiological (CT) and endoscopic investigations (colonoskopy) did not reveal any morphological signs of intestinal tuberculosis. The patient was treated with penicillin for 6 weeks and parallel with antituberculous therapy (combination of isoniasid, rifampicin and etambutol) with excellent response to the treatment. Adalimumab therapy was restarted and intensified up to 40 mg weekly with good control of disease activity. During this period he was followed up by gastroenterologist and a pulmologist with no signs of any complications. The CD was remained in deep remission.

Anti-TNF-α therapy, although highly effective in the setting of CD, still bears a risk of serious opportunistic infections (3). This is the first report of pulmonary actinomycosis as a complication of adalimumab therapy in a patient with CD and is, to the authors' knowledge, the first case of combined pulmonary actiomycosis and intestinal tuberculosis in a CD patient treated with anti TNF-α agents. There are several different species of Actinomyces and although the disease in humans is predominantly caused by Actinomyces israelii many different species can cause disease in humans including Actinomyces meyeri (4). Pulmonary actinomycosis accounts for around 15% of all cases and most commonly leads to chronic pneumonia (4,5).

Clinically, patients usually present with a fever, cough, weight loss and chest pain (4). In contrast to other Actinomycetae, in infections caused by Actinomyces meyeri the lungs are involved in 50% of cases (5). The reason for this difference is not clear but it might reflect a higher propensity of Actinomyces meyeri for dissemination. Thus, one must bear in mind that in immunocompromised hosts non-resolving or slow-resolving pneumonia can be a consequence of Actinomyces infection. Tuberculosis is also well known oportunistic infection in patients treated with anti-TNF-α agents. It is a standard procedure to screen patients for latent tuberculosis prior to starting treatment with these agents (5). However, despite negative screening tests for tuberculosis, which were done according to the guidelines for opportunistic infections in CD, our patient developed pulmonary actinomycosis and intestinal tuberculosis.

The both infections were successfully treated and the patient restarted anti-TNF-α agent later in disease course with no further complications. We would like to emphasizes the need for maintaining a high level of suspicion for opportunistic infections in patients receiving anti-TNFα treatment. As illustrated abowe, a low threshold for aggressive pulmology workup is needed in patients with CD on biologic therapy presenting with respiratory tract symptoms in order to

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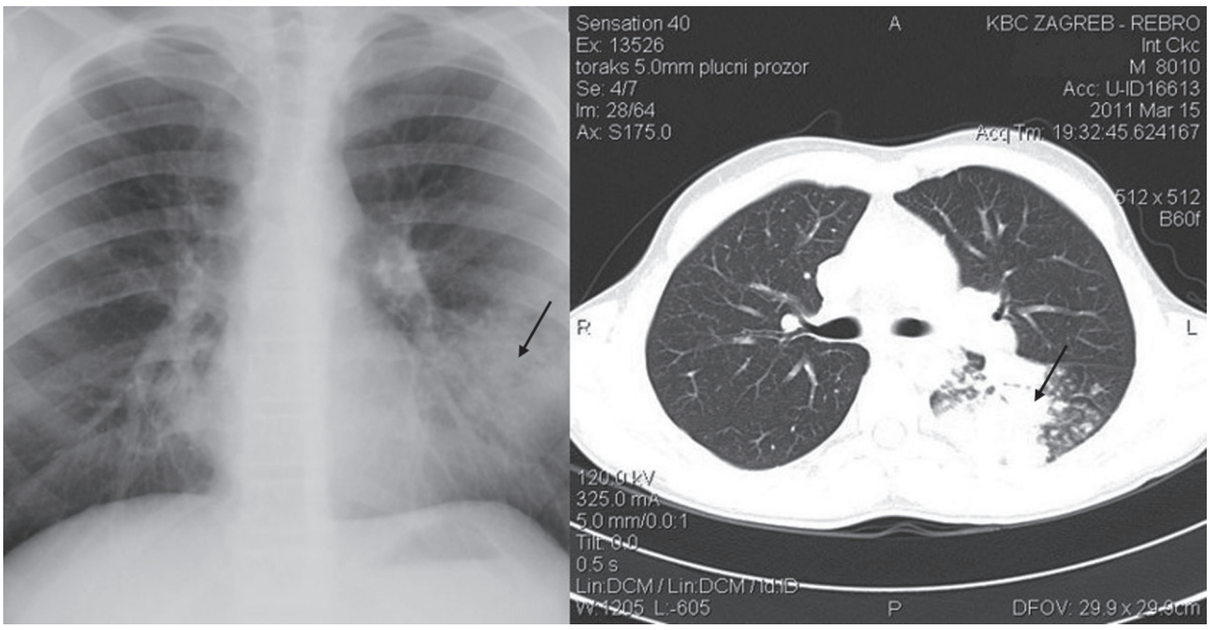

Fig. 1. — Radiological evaluation. A) The signs of left lower lobe consolidation and air bronchogram are consistent with pneumonia. B) Computed tomography scan confirmed an inflammatory infiltrate in the apical segment of the left lower lobe of the lung without signs of tissue destruction.

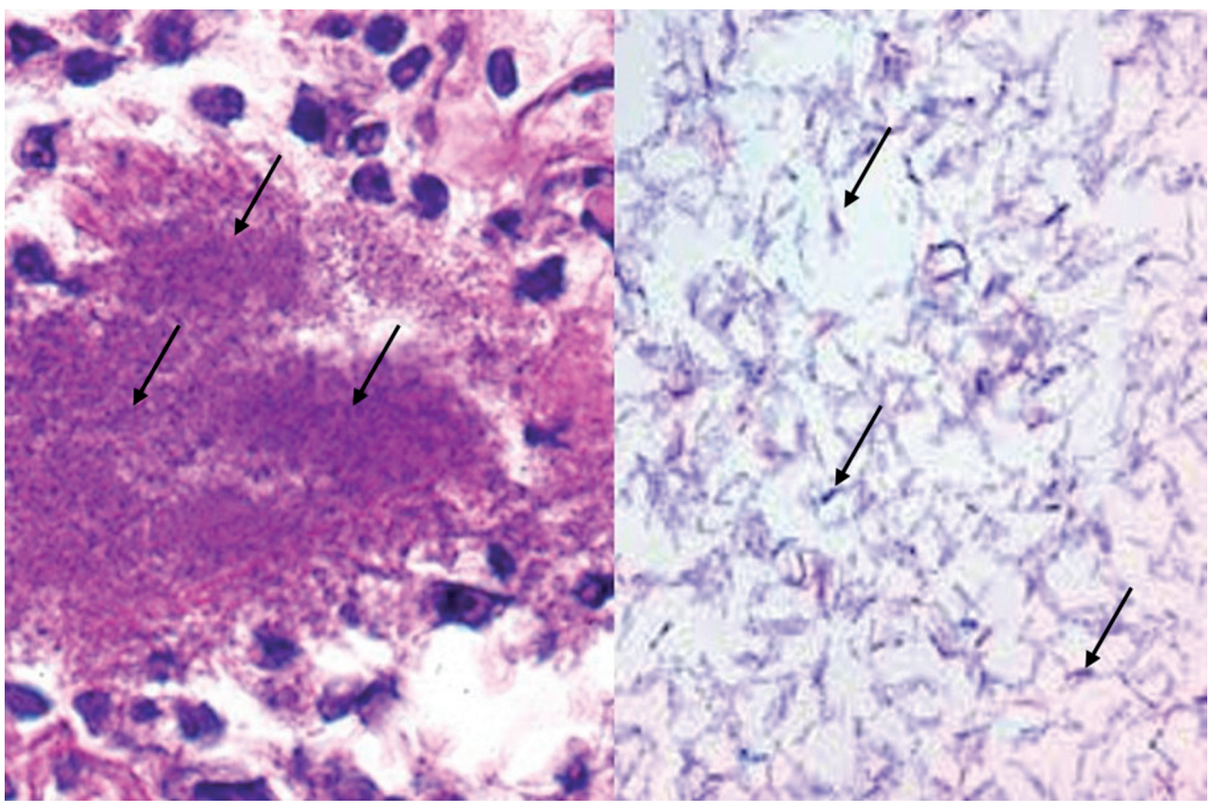

Fig. 2. — Cytological evaluation. Microscopic examination of the bronchoalveolar specimen demonstrated a filamentous microorganism with sulphur granules indicating Actinomyces meyeri (Fig. 2A, Giemsa staining, original magnification 400x). The stool cultures were positive for Mycobacterium tuberculosis (Fig. 2B, Ziehl-Neelsen staining, original magnification 200x).

diagnose the condition in time and prevent potentially hazardous complications.

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