LETTERS TO THE EDITOR

Pulmonary Infiltrates After Initiation of Treatment with Infliximab for Adult Still’s Disease

To the editor:

The first line of treatment for adult Still’s disease is methotrexate, administered orally both as monotherapy and in combination with second-line drugs (sulfasalazine or hydroxychloroquine) or, finally, with agents that block the action of tumor necrosis factor (TNF) such as infliximab or etanercept and more recently adalimumab. TNF-α is a proinflammatory cytokine that is believed to be a mediator in the pathophysiology of pulmonary fibrosis. Therefore drugs in the last group have been trialed as possible treatments for patients with pulmonary fibrosis associated with rheumatoid arthritis.1 Paradoxically, and exceptionally, some patients with rheumatoid arthritis who are in treatment with methotrexate develop a clinical picture of pneumonitis after infliximab therapy is started.2 We report such a case that resolved after treatment with corticosteroids and withdrawal of infliximab.

The patient was a 60-year-old woman with a medical history of overweight, noninsulin-dependent diabetes mellitus, herniorthery, kidney stones, cholecystectomy, and nonfunctioning adrenal nodule. Diagnosed with adult Still’s disease 15 years earlier,3 she had been taking methotrexate at doses ranging from 15 to 7.5 mg/week for 2 years. Due to worsening clinical indicators for joint disease, with increased pain and positivation of rheumatoid factor, infliximab treatment was started at a dosage of 3 mg/kg. Seven days after the first infusion, the patient was admitted with fever and severe pleuritic pain mainly on the left side. Exanthema was not found. Noteworthy laboratory results were an elevated white blood cell count with left shift and elevated erythrocyte sedimentation rate and C-reactive protein level. The sputum culture and smear test were negative. Resting arterial blood gas analysis revealed a PaO2 of 63 mm Hg, a PaCO2 of 31 mm Hg, and a pH of 7.47. A simple x-ray revealed an azygos lobe, bibasal atelectasis, and a small pleural effusion on the left side (Figure 1). A computed tomography (CT) scan of the thorax showed bilateral lung thickening of interlobar septae that suggested interstitial involvement (Figure 2). Lung function tests indicated slight loss of forced vital capacity and normal forced expiratory volume in the first second and carbon monoxide diffusing capacity. Treatment with parenteral methylprednisolone (60 mg/day) led to gradual improvement in symptoms and arterial blood gas. The follow-up chest CT scan 15 days later was completely normal, as were all lung function parameters 3 months later.

The anti-inflammatory effects of TNF blockers have led to their use in a variety of inflammatory diseases (chronic juvenile arthritis, adult Still’s disease, psoriatic arthritis, Crohn’s disease) although the original indication was rheumatoid arthritis. TNF-α plays a central role in inflammation and is considered one of the most potent proinflammatory cytokines. Blocking it rapidly neutralizes inflammatory signs and symptoms (fever, elevated C-reactive protein levels, anemia, and more) and TNF-α blockers are therefore used as an additional treatment in these processes so that the usual immunosuppressant therapy can be reduced.4 Currently, there are 3 biological agents that neutralize the biological action of TNF-α: a chimeric monoclonal antibody (infliximab), a soluble receptor (etanercept), and a humanized monoclonal antibody (adalimumab). All of them reduce T-helper 1-type immunity by blocking interleukins 12 and 18. Because of the resulting immunosuppression, their clinical use has been associated with a wide range of infectious diseases (tuberculosis, histoplasmosis, cryptococcosis) as the most common complication. Other adverse effects described occasionally have been fulminating hepatitis, pulmonary granulomatosis, and induction pneumonitis in patients treated with methotrexate.2

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