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Case report

Adalimumab induced interstitial lung disease

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A B S T R A C T

Tumor necrosis factor inhibitors have been implicated in many pulmonary complications. Before starting these class of drugs latent infection as tuberculosis and preexisting lung disease should be excluded. These agents have been linked to pulmonary nodules, pneumonitis, fibrosis, autoimmune reactions and infection. We report a case of adalimumab induced organizing pneumonia in an old gentleman who was started on the drug for his uncontrolled Psoriasis.

1. Introduction

Tumor necrosis factor inhibitors are used for a number of inflammatory conditions. They have been implicated, however, in serious pulmonary complications. These include granulomatous disease, pneumonitis, fibrosis, autoimmune reactions, and infections. We report a case of adalimumab-induced organizing pneumonia in a gentleman who was started on the drug for uncontrolled psoriasis.

2. Case report

A 71-year-old male presented to pulmonary clinic for a 3-week history of dyspnea on exertion. Review of systems was positive for subjective fever, chills, and night sweats. He reported no recent travel, sick contacts, weight loss, occupational exposure, or smoking history. He had a medical history of uncontrolled psoriasis for several years. Five weeks before presentation, he was started on tumor necrosis factor inhibitor, Adalimumab, by his dermatologist, for uncontrolled psoriasis. One week ago, he was prescribed a course of Levofloxacin by his primary care doctor without any improvement of his symptoms.

On his physical examination, the patient appeared in no distress. His vitals were stable with a pulse oximetry reading of 94% on room air. He had bilateral rhonchi on chest auscultation. He had no positive JVD, no pedal edema, and no palpable neck or axillary lymphadenopathy. He had healed rashes of psoriasis on the extensor surface of both arms.

Pulmonary function tests were notable for a restrictive defect with decreased DLCO. High resolution CT chest (Fig. 1) revealed bilateral opacities predominantly on the periphery. Bronchoscopy for BAL reveled increased cellularity. A transbronchial biopsy of the left lower lobe was positive for subpleural well-formed Masson bodies plugging the airway suggesting organizing pneumonia.

Adalimumab was discontinued and the patient was started on 40 mg of oral prednisone once daily. His symptoms improved dramatically. Repeat CT chest (Fig. 2) in a month showed significant resolution of opacities.

3. Discussion

Cytokines are proteins secreted by T cells and macrophages that help regulate immune responses along with cellular proliferation and differentiation. Tumor necrosis factor-alpha (TNF-a) is a pro inflammatory cytokine, also known as Cachectin. Its inhibitors are used as immunosuppressant modulating drugs. After their discovery in 1991, as effective drugs for rheumatoid arthritis, use of TNF inhibitors has been on the rise. They are now being increasingly used in many inflammatory and autoimmune disorder like rheumatoid arthritis, spondylarthritis, systemic sclerosis, inflammatory bowel disease, systemic lupus erythematosus (SLE) with encouraging outcomes. However, high vigilance is required during administration of anti-TNF drugs as they have been linked to both infectious and noninfectious side effects. Many anti-TNF-induced pulmonary complications have been identified. These include exacerbations of underlying lung disease, development of accelerated lung nodules, interstitial lung disease (ILD), unmasking of latent infections, granulomatous lung disease, SLE-like reactions and vasculitis [1,2].

The exact mechanism of pulmonary toxicity, however, remains unclear. Inhibition of inflammatory cells by anti-TNF drugs leads to unopposed activity of inflammatory cells resulting in characteristic changes of interstitial pneumonitis. Old age, delayed onset of symptoms, co-administration of other immunosuppressant, and, especially, prior diagnosis of ILD are associated with poor prognosis.

Anti-TNF-induced diffuse interstitial lung disease (ILD) is an

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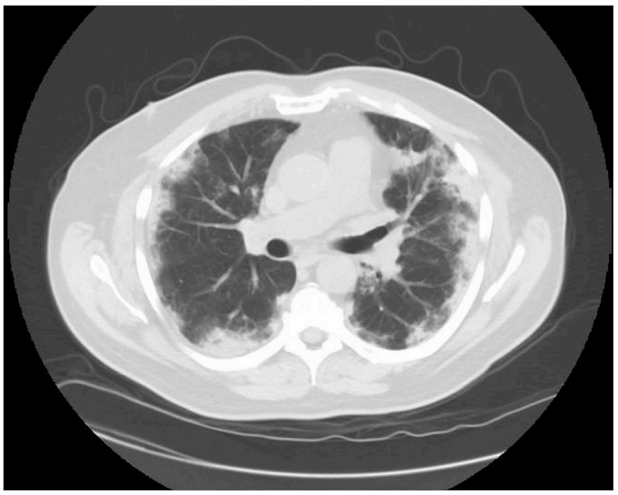

Fig. 1. HRCT scan chest showing extensive peripheral opacities.

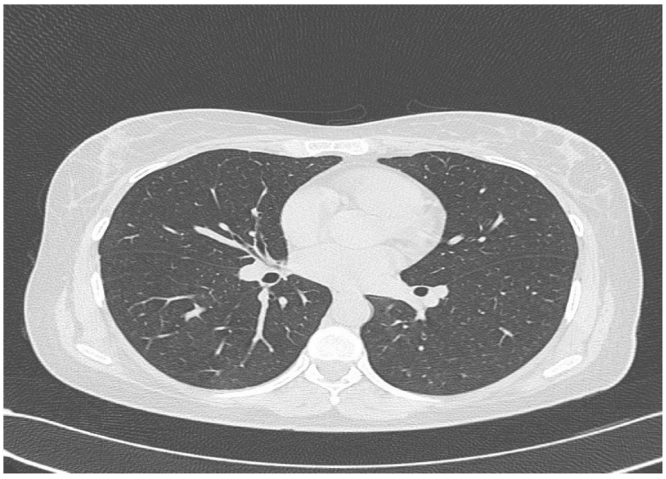

Fig. 2. CT scan chest showing resolution of opacities following Adalimumab discontinuation and 4 weeks course of steroid therapy.

emerging entity with a prevalence of 0.5–3% [3]. A spectrum of ILDs has been associated with this class of drugs. Perez-Alvarez et al. review article mentioned 122 cases of anti-TNF induced lung injury; three of which were secondary to adalimumab [4]. Adalimumab, a monoclonal antibody, is the least tied to lung toxicity, among anti-TNF drugs. Bibliography review showed ten case reports of adalimumab-induced ILD. Of these ten cases, two involved patients with psoriasis [5–11].

Patients with adalimumab-induced ILD mostly present with difficulty breathing, dry cough, fever, malaise, and shortness of breath, as seen in the presented case. Symptoms are dose-dependent and worsen with cumulative doses. Mean time to symptom onset after drug initiation is about 26 weeks. Imaging modalities like high resolution computed tomography (HRCT) disclose ground glass opacities (83%), honeycomb appearance (22%), and reticulonodular opacities (38%) [4]. Pulmonary function tests reveal restrictive ventilatory pattern and reduced diffusion capacity of lungs. Bronchoscopy with bronchoalveolar lavage and lung biopsy are mostly reserved to rule out other possible causes. Conditions including heart failure, infections, idiopathic interstitial pneumonia, and exacerbation of pre-existing ILD must be ruled out.

Drug-disease association is usually made on the basis of prior reports of similar complications with anti-TNF agents, former absence of symptoms, rapid onset and progressive nature of disease after drug initiation, negative infectious disease workup, pathological confirmation, exclusion of other possible causes and improvement of symptoms after drug discontinuation. The disease course varies from either complete resolution, in about 65% of cases, to failed treatment with rapid progression to death.

The mainstay of treatment is discontinuation of adalimumab. Adjunctive measures also include treatment with steroids and addition of immunosuppressants in steroid-unresponsive cases or patients with fulminant disease. Symptom improvement along with radiological improvement is seen within one to two weeks of adalimumab cessation. Despite the side effects, preexisting lung diseases is not an absolute contraindication to the use of TNF inhibitors. However, patients must be forewarned of the side effects of the drug as it can significantly affect their quality of life. Higher degree of clinical suspicion is required to make the diagnosis of adalimumab-induced ILD as it reversible.

Declaration of competing interest

We know of no conflicts of interest associated with this publication.

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