Case report

Adalimumab induced interstitial lung disease

Anum Aqsa*, Dikshya Sharma, Michel Chalhoub

Staten Island University Hospital, 522A seaview avenue, Staten Island, United States

ABSTRACT

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 revealed 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 disorders 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 unsupported 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
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 is reversible.

**Declaration of competing interest**

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

**References**

[1] K. Thavarajah, P. Wu, E.J. Rhew, A.K. Yeldandi, D.W. Kamp, Pulmonary complications of tumor necrosis factor-targeted therapy, Respir. Med. 103 (5) (2009) 661–669.
[2] M. Ramos-Casals, P. Brito-Zeron, S. Munoz, N. Soria, D. Galan, L. Bertolaccini, et al., Autoimmune diseases induced by TNF-targeted therapies: analysis of 233 cases, Medicine (Baltim.) 86 (4) (2007) 242–251.
[3] W.G. Dixon, K.L. Hyrich, K.D. Watson, M. Lunt, D.P. Symmons, Influence of anti-TNF therapy on mortality in patients with rheumatoid arthritis-associated interstitial lung disease: results from the British Society for Rheumatology Biologics Register, Ann. Rheum. Dis. 69 (6) (2010) 1086–1091.
[4] R. Perez-Alvarez, M. Perez-de-Lis, C. Diaz-Lagares, J.M. Pego-Reigosa, S. Retamozo, A. Bove, et al., Interstitial lung disease induced or exacerbated by TNF-targeted therapies: analysis of 122 cases, Semin. Arthritis Rheum. 41 (2) (2011) 256–264.
[5] K. Komiyama, H. Ishii, N. Fujita, H. Oka, A. Iwata, H. Sonoda, et al., Adalimumab-induced interstitial pneumonia with an improvement of pre-existing rheumatoid arthritis-associated lung involvement, Intern. Med. 50 (7) (2011) 749–751.
[6] O.M. Dias, D.A. Pereira, B.G. Baldi, A.N. Costa, R.A. Alhazzazy, R.A. Kairalla, et al., Adalimumab-induced acute interstitial lung disease in a patient with rheumatoid arthritis, J. Bras. Pneumol. 40 (1) (2014) 77–81.
[7] S. Alase, Q. Jones, Case of drug-induced interstitial lung disease secondary to adalimumab, BMJ Case Rep. 2018 (2018).
[8] M.J. Casanova, M. Chaparro, C. Valenzuela, C. Cisneros, J.P. Gisbert, Adalimumab-induced interstitial pneumonia in a patient with Crohn’s disease, World J. Gastroenterol. 21 (7) (2015) 2250–2252.
[9] H. Yamazaki, S. Iseki, T. Sakurai, K. Nagasaka, A case of adalimumab-associated interstitial pneumonia with rheumatoid arthritis, Mod. Rheumatol. 20 (5) (2010) 518–521.
[10] J.D. Reid, B. Bressler, J. English, A case of adalimumab-induced pneumonitis in a 45-year-old man with Crohn’s disease, Canc. Res. J. 18 (5) (2011) 262–264.
[11] K.P. Phang, G.G. Teng, L.L.S. Teo, J.E. Seet, C.M. Teoh, F.S.W. Teo, A 67-year-old man with psoriatic arthritis and new-onset dyspnea, Chest 154 (5) (2018) e127–e134.