

Received: 2013.03.25
Accepted: 2013.05.09
Published: 2013.05.27

Adalimumab (Humira) induced acute lung injury

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: **Male, 78**
Final Diagnosis: **Acute lung injury due to Adalimumab**
Symptoms: —
Medication: **Adalimumab**
Clinical Procedure: **Intubated and put on mechanical ventilation**
Specialty: **Pulmonology**

Objective: **Unusual or unexpected effect of treatment**





Background: Adalimumab is a recombinant human monoclonal antibody that blocks the effects of tumor necrosis factor- α . Adalimumab related acute lung injury is a rare form of acute respiratory distress syndrome of possible immune etiology that develops immediately after an infusion.

Case Report: We describe a 78 year old, male with no previous cardiac comorbidities, who developed acute lung injury (ALI) within one hour of administration of adalimumab. He was successfully treated with mechanical ventilatory support and adjuvant therapy.

Conclusions: TNF α antagonists are a part of a new and revolutionary treatment for severe and difficult-to-treat autoimmune and inflammatory diseases. This report emphasizes that this fatal complication may occur with use of this drug. Clinicians need to be aware of this condition as prompt recognition and supportive management can prevent unwanted morbidity and mortality.

Key words: **respiratory distress • Adalimumab • acute lung injury (ALI)**

Full-text PDF: <http://www.amjcaserep.com/download/index/idArt/889200>

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Background

Adalimumab is a recombinant human monoclonal antibody directed against tumor necrosis factor alpha (TNF α) which has been increasingly used presently in the management of a variety of inflammatory and auto immune diseases. Recently there is a growing evidence of use of these agents in refractory Hidradenitis suppurativa(HS), which is a common inflammatory skin disease [1]. The known secondary effects related with adalimumab,include skin reactions, reactivation of tuberculosis, congestive heart failure, lupus like syndromes, and demyelinating neurologic diseases Acute lung Injury as a side effect to adalimumab infusion is rare.

Case Report

This is a pleasant 78-year-oldgentleman with a past medical history significant for hypertension, colon cancer status post sigmoid colectomy, diabetes and gout, admitted to the hospital for treatment of hidradenitis suppurativa(HS) involving the groin, which appeared refractory to antibiotics and had multiple previous recurrence despite incision and drainage, wound care and antibiotic use. He was started on Adalimumab infusion which is the new proposed treatment modality for refractory HS [2,3].The patient developed acute respiratory distress, tachypnea, and oxygen desaturation within one hour after the infusion of adalimumab. As he had progressive, severe hypoxia he was intubated and put on mechanical ventilation (MV). The patient did not had any clinical features of congestive cardiac failure at that time. Left ventricular size and function were normal on transthoracic echocardiogram.

Chest radiograph performed at the onset of symptoms showed bilateral new diffuse alveolar and interstitial infiltrates with no cardiomegaly. Chest high resolution computed tomography (HRCT) scan done 12 hours later showed diffuse symmetrical ground glass opacities in both lungs, mainly bibasilar consistent with diffuse alveolar damage or multilobar pneumonia. Empirical antibiotics started initially were stopped after 3days as the patient had remained afebrile and the blood cultures were sterile. Arterial blood gas values and chest radiography improved with continous ventilatory and other supportive measures and he was extubated on the third day of the MV. The chest radiograph was remarkably better before discharge (Figure 1).

Discussion

ALI is characterized by simultaneous presence of severe hypoxemia, bilateral alveolar infiltrates on chest radiograph and

no evidence of left atrial hypertension/congestive heart failure/fluid overload.

The differential diagnosis of sudden onset respiratory distress in such a setting includes, infections, pulmonary embolism, pneumothorax, congestive cardiac failure, fluid overload, pulmonary hemorrhage, and anaphylactic reactions. ALI in our case is a diagnosis of exclusion. Cardiogenic pulmonary edema and fluid overload were ruled out by the absence of pre-existing heart disease, good left ventricular systolic function and negative clinical findings for heart failure. The only possibility seems to be adalimumab infusion. Although rechallenging can definitely establish the causal link, we did not believe it safe for purely diagnostic purposes.

Little is known about the mechanism of adalimumab induced lung injury. Tumor necrosis factor is produced as a type 2 transmembrane protein which activate TNF receptors (TNFR). TNFR activation is associated with cytotoxicity, stimulation of cytokine and chemokine production. While TNF plays an important role in T cell activation, it can also down-regulate T cell receptor signaling. The absence of this latter role may explain autoantibody development in patients receiving TNF-targeted therapy [4,5]. Whether this autoantibody formation leads to interaction with inflammatory cytokines and contribute to capillary leakage and respiratory distress is a hypotheses which is still to be validated.

The literature on adverse effects of anti-TNF α antibody therapy typically divides complications into infectious and noninfectious categories. Descriptions of lung disease attributed to anti-TNF α vary considerably, ranging from interstitial pneumonitis to malignancy [6–8]. There is limited literature about acute diffuse lung injury due to TNF inhibitors. Few case reports have associated adalimumab with interstitial pneumonia, but the onset of these changes was over a period of two to 6 months, unlike our case where ALI manifestations were abrupt. [9]

Diagnosing drug-induced ALI is actually an exercise of exclusion as there is no diagnostic test available. Attributing lung disease to adalimumab in the present case was based on the temporal association between inception of therapy, onset of respiratory symptoms, a negative infectious workup, and the clinical improvement following discontinuation of the adalimumab. Although rare, anti-TNF α -induced lung disease is a potentially harmful side effect of this medication. Our purpose of reporting this case is to alert physicians of this acute complication related to adalimumab infusion so that they are prepared to treat it promptly. Further investigation to determine the exact mechanism of injury and predisposing patient characteristics is needed.

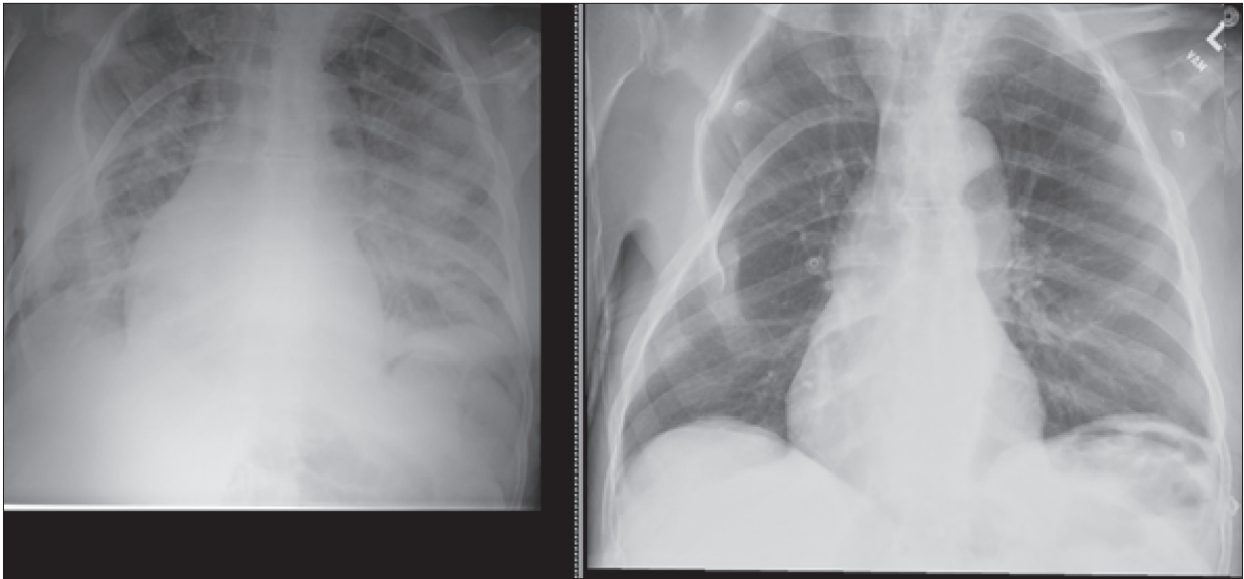


Figure 1. CXR before and after the stoppage of Humira.

Conclusions

TNF α antagonists are a part of a new and revolutionary treatment for severe and difficult-to-treat autoimmune and inflammatory diseases. The indication and the use of anti-TNF

therapy with various new agents like adalimumab will spread rapidly and widely; therefore, such unexpected adverse effects could be encountered more frequently. Therefore, great care must be practiced by patients undergoing anti-TNF therapy.

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