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CASE REPORT

TB or Not TB, That is the Question?

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Abstract

A 26-year-old female presented with a 3-month history of dry cough, unintentional weight loss, night sweats and fatigue. Her background history was significant for ulcerative colitis, managed with Adalimumab for almost 2 years. Clinical examination was unremarkable, apart from some mild pallor. Abnormal chest x-ray findings prompted a computerised tomography (CT) thorax which demonstrated multifocal peri-bronchial consolidation. The differential diagnosis was multifocal organising pneumonia and tuberculosis (TB). Extensive investigations, including invasive bronchial imaging and biopsy, ultimately ruled out TB. This paper reports a case of Adalimumab-induced organising pneumonia and discusses its clinical implications.

Key words: organising pneumonia; tuberculosis; immunosuppression; Adalimumab

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Introduction

A 26-year-old female presented to the Acute Medical Unit with respiratory and constitutional symptoms, on a background of inflammatory bowel disease (IBD), managed with biologic therapy. Tuberculosis (TB) was initially suspected on the basis of her clinical presentation and abnormal chest x-ray, and her sputum direct film microscopy was initially positive for acid-fast bacilli (AFB), although subsequent AFB gene expert and mycobacterial culture were negative for TB. Given the diagnostic uncertainty, a lung biopsy was ultimately performed, which did not reveal granulomatous changes consistent with TB. Following multidisciplinary team involvement, the final diagnosis was Adalimumab-induced organising pneumonia. Adalimumab was discontinued, and the patient was commenced on systemic corticosteroid therapy, which resulted in a full clinical and radiological resolution of the organising pneumonia.

Anti-tumour necrosis factor (TNF)-induced diffuse interstitial lung disease is an emerging entity with a prevalence of 0.5–3% (Perez-Alvarez et al, 2011). Organising pneumonia has been reported in several case reports to be linked with Adalimumab. This has a significant impact on patients who are on this medication for the treatment of their autoimmune condition, particularly for a patient like the one in this case report, as she already had an adverse reaction to a previous agent (Infliximab).

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Case Report

A 26-year-old female presented with a 3-month history of dry cough, unintentional weight loss of 4–5 kg, night sweats, and fatigue. Her past medical history was significant for ulcerative colitis, which she had been treated with Adalimumab for almost two years. She was commenced on a starting dose of 80 mg of Adalimumab, with a maintenance dose of 40 mg fortnightly thereafter. She was also on Pentasa (Meclizine) 2 g twice daily. She previously had a drug reaction to Infliximab, which resulted in facial flushing, shortness of breath and vomiting, which was ultimately discontinued. She had no significant family history of note. She was studying veterinary science in Poland, was a non-smoker and consumed roughly 3 units of alcohol per week. System review was non-contributory. The patient appeared relatively well, apart from some mild conjunctival pallor; her baseline observations were within normal limits; her clinical examination was otherwise unremarkable.

Laboratory investigations revealed the following: a new microcytic anaemia, haemoglobin 10.6 g/dL (normal range 12–15 g/dL), mean corpuscular volume (MCV) 78.3 fL (84–96 fL); serum ferritin 243 ng/mL (normal range 13–200 ng/mL); transferrin saturation 5% (normal range 19–43%); mildly elevated white cell count at 12.6×10^9 ($4–10 \times 10^9$); platelets 631×10^9 ($150–400 \times 10^9$); elevated C-reactive protein at 63 mg/L (0–5 mg/L); albumin 34 g/L (39–51 g/L). Her chest x-ray (Fig. 1) revealed right and left upper lung zone consolidations, patchy consolidation in the left lower lung zone and bilateral hilar lymphadenopathy. Differential diagnosis reported on the chest x-ray was broad, including: infectious (including TB), sarcoidosis, and malignancy.

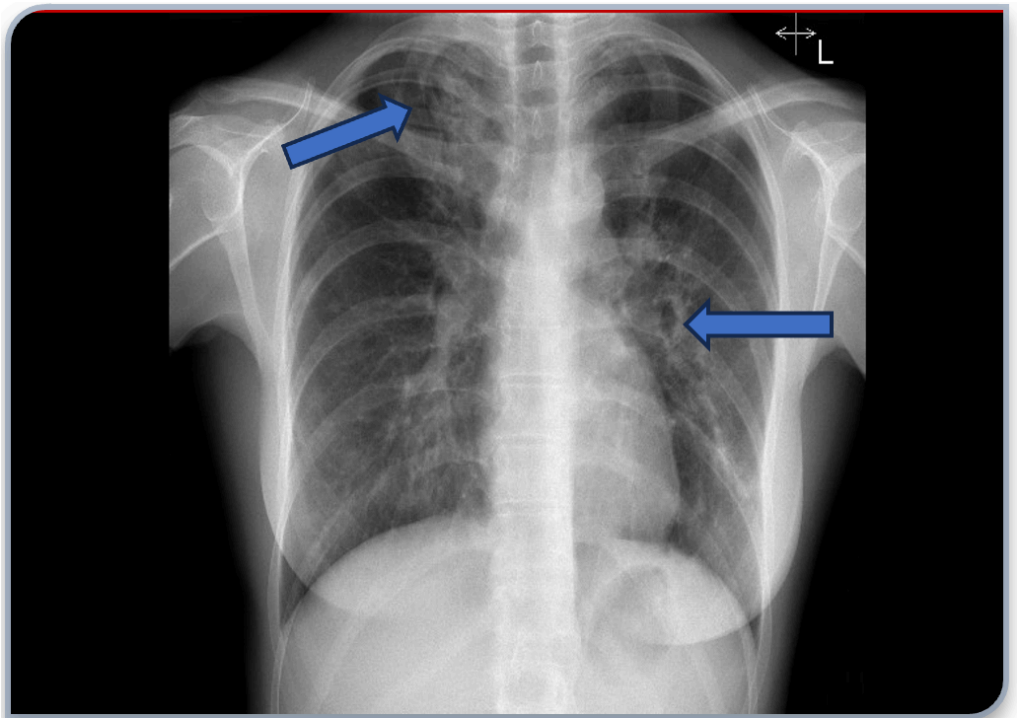

Fig. 1. Chest x-ray illustrating multifocal patchy consolidation (arrows) and bilateral hilar lymphadenopathy. L indicates the patient's left side.

The patient subsequently underwent a computerised tomography (CT) thorax which showed multifocal peri-bronchial consolidation, most likely representing multifocal organising pneumonia (Fig. 2). However, given the history, abnormal radiology, and immunosuppression, the working diagnosis at this point was tuberculosis (TB).

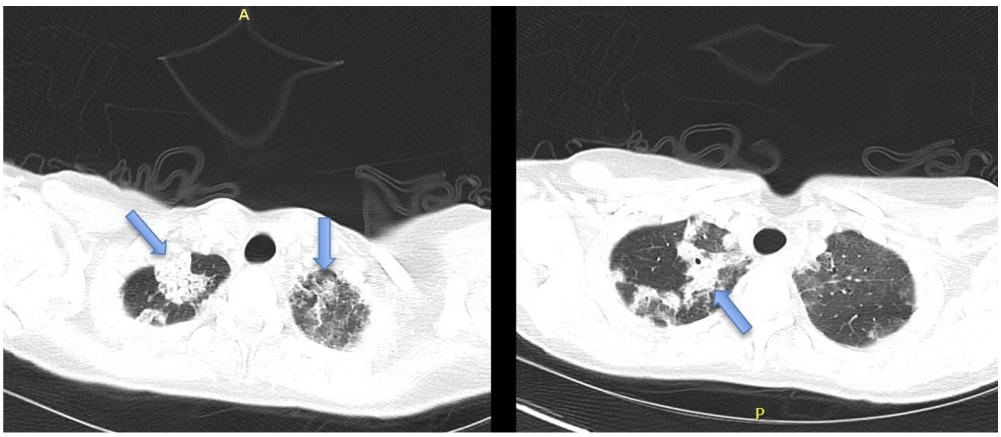

Fig. 2. Computerised tomography (CT) thorax demonstrating multifocal peri-bronchial consolidation (arrows), consistent with an organising pneumonia. A, anterior; P, posterior.

Initial sputum direct film microscopy was positive for acid-fast bacilli (AFB) but subsequent AFB gene expert and mycobacterial culture were negative for TB. Mycobacterium culture failed to isolate mycobacterium species after prolonged incubation. Subsequent 'cepheid GeneXpert system' testing was performed, and failed to detect mycobacterium tuberculosis complex DNA (**Supplementary Fig. 1**). Following consultation with our Microbiology colleagues, it was felt that the initial sputum culture result was most consistent with the presence of a mycobacterium other than tuberculosis (MOTT). Furthermore, AFB could not be detected on direct film microscopy using repeat cultures (**Supplementary Fig. 2**).

Bronchoscopy was performed by the Respiratory Medicine team, and endobronchial ultrasound showed no evidence of malignancy or granulomatous disease, and AFB was not detected on bronchoalveolar lavage (BAL) (**Supplementary Fig. 2**).

Following the above investigations, the case was discussed at the Respiratory & Joint Thoracic Clinic Multi-Disciplinary Meeting. It was decided to proceed with mediastinoscopy and lung biopsy to definitively exclude TB. The histology (**Supplementary Fig. 3**) derived from this showed acute and chronic inflammation, with no evidence of granulomata.

The final diagnosis was Adalimumab-induced organising pneumonia. The patient's Adalimumab treatment was discontinued and she was commenced on oral steroids. This regimen consisted of prednisolone 60 mg daily, tapered by 5 mg to complete cessation within one month. This led to a full clinical and radiological recovery within just a week of commencement of the steroids (Fig. 3). Of note, her C-reactive protein (CRP) returned to within normal ranges and her anaemia resolved.

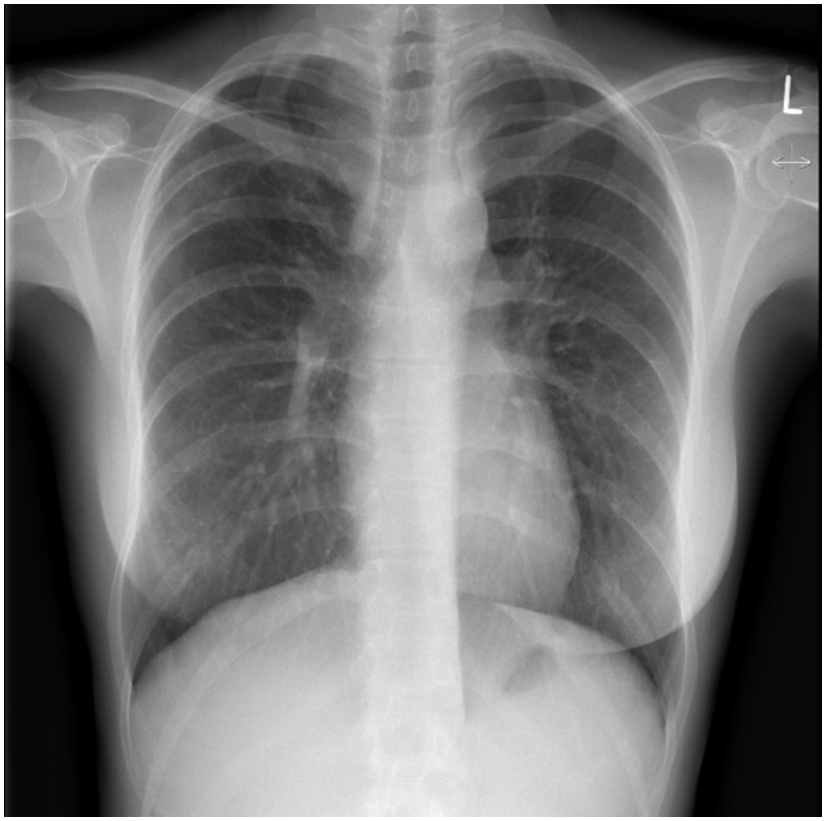

Fig. 3. Chest x-ray demonstrating a full radiological resolution following discontinuation of Adalimumab and commencement of oral steroids (9 weeks from initial presentation). L indicates the patient's left side.

Outpatient follow-up with the gastroenterology team was planned to discuss treatment options going forward for the management of the patient's inflammatory bowel disease. Currently, her ulcerative colitis remains well controlled on Mesalazine 2 g twice daily. A repeat surveillance colonoscopy is planned in due course. Careful consideration ought to be given to any future attempts to initiate biologic treatment, owing to the patient also experiencing an adverse reaction to Infliximab in the past.

Discussion

Organising pneumonia typically presents in an acute or subacute manner. The symptoms vary and can include fever, dyspnoea, cough, and chest pain. Radiological findings can range from patchy focal consolidation to diffuse opacities (Camus et al, 1993).

Infliximab and Adalimumab are two common pharmacological agents used to treat IBD and have been reported to cause multiple pulmonary complications, including organising pneumonia, usual interstitial pneumonia, and non-specific interstitial pneumonia (Perez-Alvarez et al, 2011; Ramos-Casals et al, 2007). They have also been associated with infectious complications, including TB (Keane et al, 2001).

The above points are relevant to this case, and upon initial presentation, the working diagnosis of TB was therefore justified owing to the patient's symptoms on a background of immunosuppression. Distinguishing between these two clinical entities is challenging, but an important undertaking, as management of them varies significantly.

An important factor to be aware of is that patients with IBD can have a number of associated pulmonary complications. Thus, a careful history is essential to help narrow down the list of differential diagnoses in these patients when they present with respiratory symptoms. Blood tests (to assess for peripheral blood eosinophilia and anti-nuclear antibodies), pulmonary function tests (PFTs), and high-resolution CT thorax to assess for ground glass opacities, are some of the relevant investigations which can help confirm or rule out suspected diagnoses (Pipavath and Godwin, 2004).

The diagnosis is usually established following a thorough assessment of the clinical presentation and exclusion of other potential causes, coupled with the known likelihood of the drug in question causing toxicity. A trial of discontinuation of the drug can help to confirm the diagnosis. BAL, as well as lung biopsy, may be performed in selected cases when the diagnosis still remains unclear.

Treatment of this condition centres upon discontinuation of the drug in question (Storch et al, 2003), and some patients may also require systemic corticosteroids. Recommended initial therapy is systemic glucocorticoids, which usually result in rapid symptomatic and radiological improvement. The typical dosing regimen is prednisolone of 0.5 to 1 mg/kg per day, based on ideal body weight, up to a maximum of 60 mg/day (Bradley et al, 2008; Epler et al, 1985; Lazor et al, 2000). In most cases, patients begin to have a positive clinical response to steroid treatment within a number of days, and significant responses are then usually seen after multiple weeks of treatment. The decision to initiate treatment and the type of treatment depends on symptom severity, pulmonary function, radiographic findings and the rate of disease progression (Bradley et al, 2008; Zaman et al, 2017).

Conclusion

In summary, we present a case of a young female diagnosed with Adalimumab-induced organising pneumonia, which was successfully treated with medication discontinuation and commencement of a tapering dose oral steroids. This clinical diagnosis was obtained following close attention to the patient's past medical history, as well as performing extensive investigations to rule out important differential diagnoses including, in this case, TB. Multidisciplinary team input was essential in helping to clinch the clinical diagnosis. This case is important in outlining a rare diagnosis but one with important clinical implications as it has ramifications for future treatment options for this patient's principal co-morbidity. Additionally, the growing use of biologic agents in clinical practice warrants clinicians to be more cognisant of their possible side effects.

Learning Points

- Whilst biologic therapy has helped to transform the management of many autoimmune conditions, there are a number of associated side effects, including organising pneumonia.
- Organising pneumonia can be a difficult diagnosis to make, and due regard to the clinical history is important, as is the use of appropriate radiological investigations.
- Tuberculosis is an important differential diagnosis to be excluded in patients presenting with respiratory symptoms on a background of immunosuppression. It is especially pertinent that it is ruled out in cases where commencement of systemic steroid therapy is required, such as in the management of adalimumab-induced organising pneumonia.
- Complex presentations in the acute medical setting are often best managed using a multidisciplinary team approach.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

EM and BR were both responsible for the acquisition and analysis of the clinical data, drafting the initial manuscript and revising the final manuscript. Both authors contributed to the important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Both verbal and written informed consent to write and publish this manuscript was obtained from the patient. The research done and included in this manuscript was conducted in strict accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0180.

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