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Case Report

Steroid Refractory Desquamative Interstitial Pneumonia, Macrolides Beneficial Effect

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Abstract

Desquamative interstitial pneumonia (DIP) is a very rare type of interstitial lung disease that is usually very responsive to corticosteroids treatment. In rare cases it can be refractory to corticotherapy, treatment regimen for these patients doesn't exist. We report a very rare case of steroid refractory DIP that improved clinically and radiologically after the addition of clarithromycin to a low dose of prednisone. The patient remained stable for several months of macrolide therapy.

Keywords: *Desquamative Interstitial Pneumonia; Interstitial Lung Disease; Macrolide*

Abbreviations

DIP: Desquamative Interstitial Pneumonia; PFTs: Pulmonary Function Test PFTs

Introduction

Macrolide is a family of antibiotics that has been used for multiple noninfectious indications due to its well established anti-inflammatory effect. It has been used in a wide range of pulmonary diseases such as cystic fibrosis [1]. Its use in interstitial lung diseases has also been studied in cryptogenic organizing pneumonia and idiopathic pulmonary fibrosis [2]. But its effect in other lung diseases is still not well established. We present a case of DIP refractory to conventional therapy that showed marked improvement, clinically and radiologically after treatment with macrolides.

Case Presentation

We present a case of a 32 year old male with no previous medical issues, current smoker with a 15 pack year history of smoking, obese with a basal metabolic index of 32, presented to the outpatient clinic for several months history of increasing dyspnea until it became at mild exertion and dry cough. He was diagnosed in another clinic with hypersensitivity pneumonia and was started on prednisolone 50 mg/d with salmeterol/fluconazole inhaler with no marked improvement. Pulmonary Function Test (PFTs)was done and revealed a restrictive pattern with both decreased FEV1 and FVC of 60%, normal TLC, and decreased DLCO of 40%. CT chest was done and is presented in figure 1.

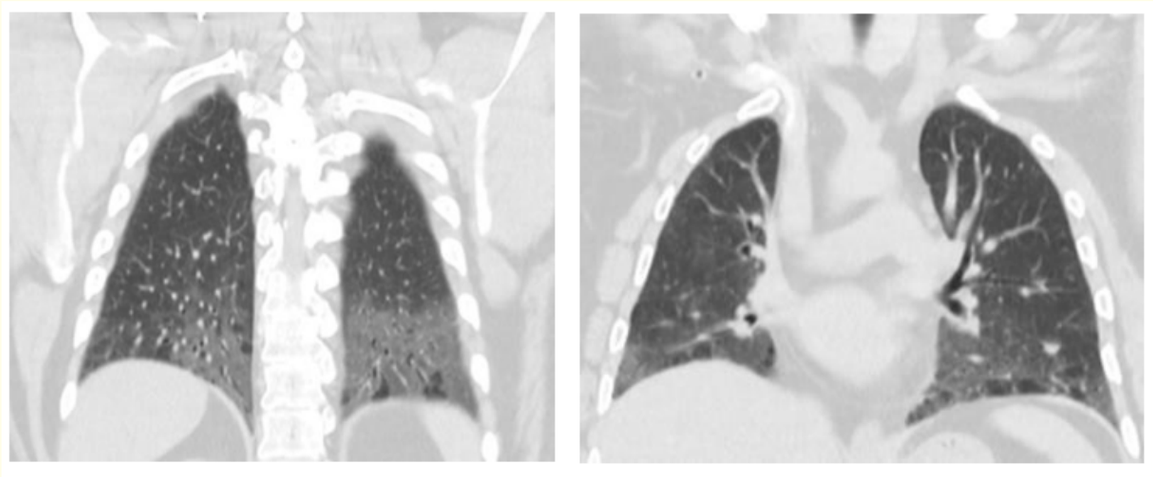

Figure 1: *Diffuse Ground glass opacities predominant in both lower lobes.*

Autoimmune work up came back negative. Steroids were tapered gradually in order for the bronchoscopy to be done without the camouflage of steroids. Bronchoalveolar lavage was cellular and showed 20% lymphocytes. Open lung biopsy was done and pathologic report was in favor of nonspecific interstitial pneumonitis NSIP. Steroids hence were increased to 1 mg/kg with advice to stop smoking. Three months later, follow up CT and PFT were still the same with a DLCO of 40% also.

Patient was admitted for a bolus methylprednisolone of 1g for 3 days and he was discharged on prednisolone 60 mg and azathioprine 50 mg twice per day. Follow up after 3 months showed no clinical deterioration, stable disease with no changes in the CT scan findings or the PFT.

A second opinion was requested on the lung biopsy; the pathologist described a diffuse pattern consisting of alveolar lumens filled with macrophages, some of them pigmented, and thus proposed the diagnosis of DIP (Figure 2a and 2b). As the patient was already on steroids with no improvement, he was diagnosed with steroids refractory DIP and a treatment trial with done by adding clarithromycin 500 mg per day on the patient's regimen. One month after this new protocol, steroids were tapered to 2.5 mg, azathioprine was continued in addition to clarithromycin. After 3 months, follow up PFT showed increase in the FEV1 and FVC by 30% and DLCO by 20%. Also a new CT chest was done and the result is shown in figure 3.

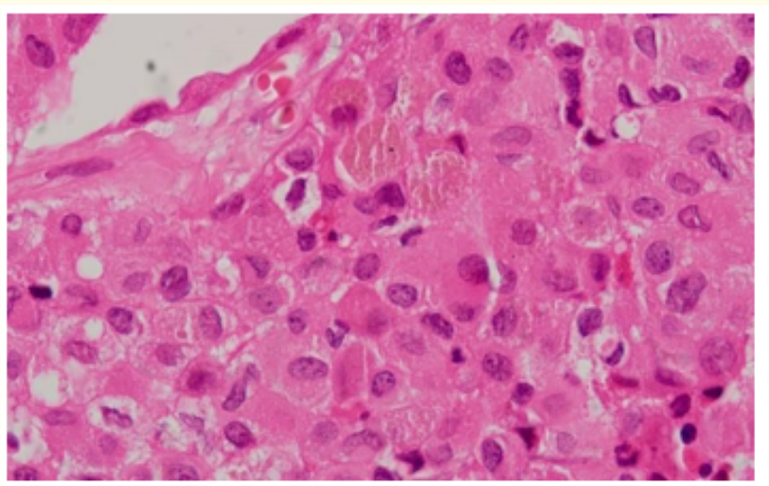

Figure 2a: *Objective x 40 HE, Alveolar macrophages with nicotinic pigment.*

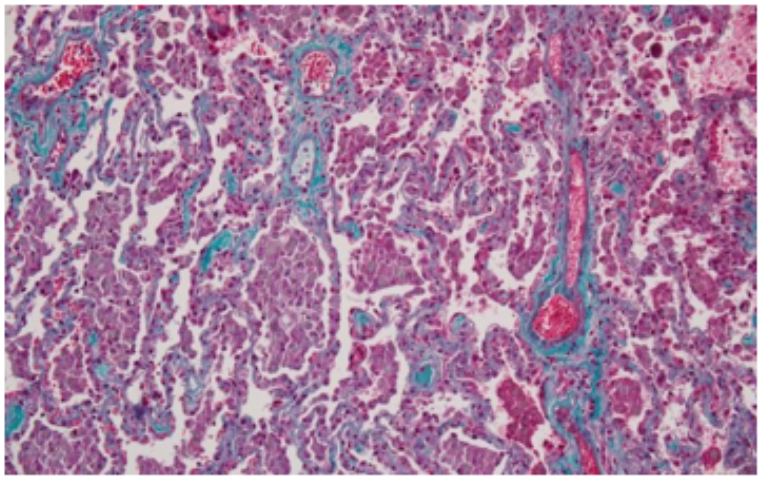

Figure 2b: *Objective x10, Gomori trichrome, Clusters of loaded macrophages filling alveolar spaces in a diffuse pattern.*

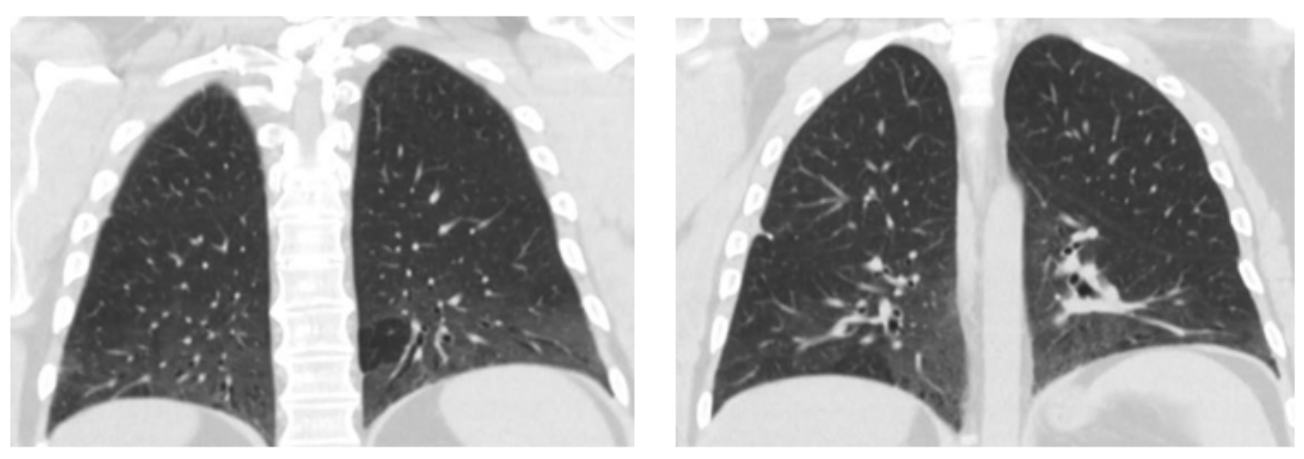

Figure 3: *Marked improvement in the ground glass opacities after starting macrolides.*

Discussion

DIP is a rare form of idiopathic interstitial pneumonia usually associated with exposure to tobacco smoke. A diagnosis of DIP can be established based on clinical and radiological features with a surgical lung biopsy. The histomorphology is characterized by the diffuse accumulation of numerous pigmented macrophages within most of the distal airspace of the lung and, sometimes, an admixture of eosinophils and/or giant cells [3]. The mainstay of treatment of DIP is steroids and smoking cessation, and if there is no major improvement, a

more potent immunosuppressor such as azathioprine or cyclophosphamide can be added [3]. But data about immunosuppressive agents are still limited [4]. Very rarely, DIP doesn't respond to steroids and smoking cessation. There are two cases where macrolides had a beneficial effect on DIP, the first one was published by Knyazhitskiy., *et al.* where the patient was deteriorating on prednisolone 1 mg/kg and improved dramatically on clarithromycin 500 mg twice per day, similar to our patient. Another case was published by Dong Won Park., *et al.* for a patient with DIP complicated by bilateral recurrent tension pneumothorax despite steroid treatment, clinical and radiological findings improved markedly after surgical treatment and the addition of clarithromycin [5]. There are multiple effects of macrolides as an anti-inflammatory agent that might be the cause of its beneficial effect in ILD but it is still unclear which mechanism is exactly responsible for the improvement seen clinically and radiologically in these patients. First macrolides have a regenerative effect on the damaged respiratory epithelium, they also promote autophagy and clearance of intracellular protein aggregates, third they work on the lung microbiota and finally macrolides act on lipid metabolism and surfactant homeostasis.

Conclusion

In conclusion, steroid refractory DIP is a very rare disease and there are very few therapies that have shown benefit. Our case is the third reported case of steroid refractory DIP that showed clinical and radiological improvement after the addition of macrolide on usual therapy. The beneficial effect of macrolides on ILD in general and DIP in particular should be further evaluated. It should also be noted that in ILDs, when the clinical course does not fit with the pathology result, it is widely recommended to ask for a rereading of the lung surgical biopsy.

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