Use of IL-6 receptor inhibitor for the management of cortico-resistant cryptogenic organizing pneumonia

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Background

Cryptogenic organizing pneumonia (COP) is an idiopathic diffuse interstitial lung disease caused by dysregulated alveolar fibroproliferation[1] characterised on CT lung imaging by migrating peripheral and multifocal consolidations or ground glass opacities[2,3]. When treated with corticosteroids, COP generally results in a rapid improvement of symptoms but there have been reports of corticosteroid-resistant and refractory cases of COP[4].

Clinical case:

A 44-year-old woman was referred to the emergency department by her rheumatologist for dyspnea, dry cough and fever lasting for 3 weeks with no improvement after 2 antibiotics. The patient had a personal history of rheumatoid arthritis (RA) and systemic sclerosis treated with rituximab for over 15 years, currently in remission.
Upon admission, high-resolution computed tomography (HRCT) showed no pulmonary embolism but ground glass opacifications in the left lower lobe and the left upper lobe.
Bronchoalveolar lavage was performed and antibiotherapy with ceftriaxone was initiated. Given the patient's immunocompromised status, anti-viral treatment with aciclovir was started but without clinical nor biological improvement. Antibiotics and aciclovir were discontinued 5 days after initiation.
An RA-associated lung disease was hypothesized and corticosteroids (CS) were administered at the initial dose of 80mg IV methylprednisolone. The patient seemed to improve initially but fever persisted and respiratory symptoms worsened after dose tapering with an oral CS regimen.
New HRCT showed migrating ground glass infiltrates in the right upper lobe and in the left upper lobe, suggesting COP.
125mg IV methyprednisolone was administered to the patient. The dose was further increased to 500mg due to lack of clinical improvement. Fever resolved under 500mg methylprednisolone and the patient reported an improvement in her cough. CS were tapered but at the dose of 80mg methyprednisolone, new crackles were heard at the left lung base. Re-evaluation of the HRCT showed new migrating pulmonary infiltrates. Immunosuppressive treatmentseemed therefore necessary, and tocilizumab was considered given the underlying systemic diseases. Administration of 8mg/kg IV tocilizumab was efficacious and clinical improvement was noted 24 hours after the first dose. Cough and dyspnea disappeared, auscultation cleared and serum C-reactive protein level drastically decreased. At 2 months follow-up, no relapse was observed and a second 8mg/kg tocilizumab injection was administered, allowing a quick steroid tapering.

Discussion :

The effect on tocilizumab on interstitial lung disease are conflicting. To the best our knowledge, there are only 2 case reports on the use of anti-IL6 receptors in interstitial lung disease in auto-inflammatory[5] and connective tissue disease[6] allowing a good therapeutic response. However, a few articles describe tocilizumab-induced COP or lung fibrosis exacerbations[7,8,9].
We describe here a positive effect of tocilizumab to improve COP in a patient with RA and systemic sclerosis, leading to a quick respiratory improvement and steroid tapering. This opens the door to new therapeutic possibilities, but more studies are needed before routine use of tocilizumab in this indication.

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