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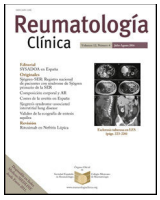

Case Report

Remission of Rheumatoid Arthritis and Primary Biliary Cholangitis After Treatment With Tocilizumab

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ABSTRACT

Rheumatoid arthritis (RA) is characterized by synovitis of multiple joints which if untreated progresses to joint destruction. Primary biliary cholangitis (PBC) is an autoimmune and progressive disease of the liver of unknown origin. About 1.8–5.6% of individuals with PBC have RA and patients with RA are at higher risk of developing PBC compared to the general population.

We report a case of a 76-year-old man, with a history of PBC, and a recent RA diagnosis, in which tocilizumab therapy was effective in the control of RA and PBC, and a literature review was performed.

This case, along with only one case published in literature in which tocilizumab was used in the treatment of RA and PBC, suggests that tocilizumab may be effective and safe in the treatment of RA in patients with PBC. Inhibition of IL-6 may also be effective in PBC treatment.

Remisión de artritis reumatoide y colangitis biliar primaria tras tratamiento con tocilizumab

Palabras clave:
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RESUMEN

La artritis reumatoide (AR) se caracteriza por sinovitis de múltiples articulaciones que, de no tratarse, deriva en destrucción articular. La colangitis biliar primaria (CBP) es una enfermedad hepática autoinmune y progresiva de origen desconocido. Cerca del 1,8-5,6% de los individuos con CBP padecen AR, y los pacientes con AR tienen mayor riesgo de desarrollar CBP, en comparación con la población general.

Reportamos el caso de un varón de 76 años con historia de CBP y diagnóstico reciente de AR, en el que la terapia con tocilizumab fue efectiva para el control de ambas situaciones y realizamos una revisión de la literatura sobre el caso.

Este caso junto con otro publicado en la literatura, en el que se utilizó tocilizumab para tratar CBP y AR, sugieren que este fármaco puede ser efectivo y seguro para el tratamiento de AR en pacientes con CBP. La inhibición de IL-6 puede resultar también eficaz en el tratamiento de la CBP.

Introduction

When liver damage is present in rheumatoid arthritis (RA) patients, it can be an hepatic manifestation of RA, an associated primary liver disease or whether hepatotoxicity of RA treatment.[1,2] Patients with RA are more susceptible to have an associated autoimmune liver disease.[2]

Primary biliary cholangitis (PBC) is an autoimmune disease and it is characterized by inflammation and destruction of intrahepatic bile ducts.[3] Diagnosis is suspected in the presence of increased alkaline phosphatase and/or bilirubin levels and may be established in the presence of anti-mitochondrial antibodies.[4]

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Nowadays, diagnosis confirmation with liver biopsy is restricted to cases with doubtful presentation.[6] About 1.8–5.6% of individuals with PBC have RA.[5] Patients with RA are at higher risk of developing PBC.[2]

Ursodeoxycholic acid (UDCA) is the first line treatment in PBC. However, 30% of patients do not respond.[4] Initial treatment of RA comprises different conventional synthetic disease modifying antirheumatic drugs (csDMARDs). However, these drugs are associated with significant hepatotoxicity, creating difficulties in its use when hepatic function changes already exist.[6]

We report a case in which tocilizumab therapy was effective in the control of RA and PBC.

Clinical observation

A 76-year-old man, diagnosed ten years earlier with PBC treated with UDCA, with initial response but for more than a year he presented an elevation of cholestasis markers. He was observed in our Rheumatology Department with symmetric and additive polyarthritis of metacarpophalangeal and proximal interphalangeal joints with six months of evolution. Blood sample analysis revealed positive anti-cyclic citrullinated peptide antibodies and rheumatoid factor along with increased inflammatory parameters, elevation of gamma glutamyltranspeptidase (5 times the upper limit of normal (ULN)) and alkaline phosphatase (2 times ULN). Plain hand radiographs showed erosions and ultrasound revealed synovitis of several metacarpophalangeal and interphalangeal proximal joints. The diagnosis of RA was established. Due to abnormal cholestasis blood markers it was decided to start only with prednisolone 10 mg/day, with clinical and analytical improvement. However, a relapse was observed with the reduction of corticoid dose. Introduction of csDMARDs was contraindicated due to the hepatic abnormalities. At this point, the rheumatologist and gastroenterologist opinion was to start biological therapy in monotherapy and tocilizumab was chosen. With this treatment, the patient experienced significant improvement, without new episodes of arthritis and with normalization of both inflammatory and hepatic cholestasis markers. Thus, prednisolone was progressively tapered and the patient maintained sustained remission of RA and PBC with tocilizumab and UDCA.

Discussion

There have been great advances in our understanding of the pathophysiology of RA and on the elucidation of many critical cytokine pathways that have been successfully targeted leading to the development of biological DMARDs.[7] Tocilizumab (a humanized IgG1 monoclonal antibody) is one of these agents, in monotherapy was shown to be superior to methotrexate monotherapy. This was not observed with TNF-α inhibitors.[8]

In PBC there is a deregulation of the T lymphocytes, with lymphoid infiltration in the portal ducts. In addition, local inflammation leads to the activation of mononuclear cells. Serum levels of IL-6 significantly increased in PBC patients in comparison with healthy controls.[9] This increase of IL-6 shown in PBC may justify tocilizumab good response in this clinical case.

Saito et al. reported another case of PBC with remission following tocilizumab initiation; in this case, the patient had an overlap syndrome RA/Systemic Sclerosis and had generalized lymphadenopathies.[10]

Conclusions

Thus, this case report, along with published literature data suggests that tocilizumab may be effective and safe in the treatment of RA in patients with PBC. Inhibition of IL-6 seems to lead to normalization of inflammatory activity, what may be effective in PBC treatment, but further studies will be necessary to confirm this hypothesis.

Conflict of interest

The authors declare that they have no conflicts of interest.

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