

CASE AND RESEARCH LETTER

Omalizumab-Associated Steatohepatitis



Esteatohepatitis asociada a omalizumab

To the Editor:

Chronic spontaneous urticaria (CSU) is characterized by the recurrence of itchy hives, angioedema, or both, for a minimum of 6 weeks, without any known external trigger. The EAACI/GA²LEN/EDF/WAO guidelines¹ recommend second-generation H1 antihistamines as the first-line treatment for CSU, with up to fourfold dose increase as required. If disease control is not achieved, add-on therapy with omalizumab is recommended. Other options such as cyclosporine A may also be considered, as well as short-course oral corticosteroids for exacerbations.¹ Omalizumab, a humanized, recombinant, monoclonal anti-IgE antibody, is the only approved add-on therapy for H1-antihistamine refractory CSU patients.² It is generally well tolerated. The most common adverse events include nasopharyngitis, sinusitis, upper respiratory tract infection, headache and cough.²

We report the case of a 40-year-old non-obese man diagnosed with severe CSU (Urticaria Activity Score 7 (UAS7) > 30) with angioedema. He denied previous relevant medical history. Initial investigations including full blood count, liver enzymes, renal and thyroid function, erythrocyte sedimentation rate and total IgE were all within normal ranges, as well as negative viral hepatitis serology. He was previously treated with up-dosed non-sedating H1-antihistamines with poor response. Oral cyclosporine 5 mg/kg/day was added and symptom control was achieved (UAS7 0). However, due to rapid recurrence after dose-tapering and infectious adverse effects with higher doses, it was discontinued. Short courses of systemic corticosteroids were also required to relief the symptoms. Liver enzymes remained unchanged.

Omalizumab 300 mg by subcutaneous injection every four weeks was added to fourfold-H1 antihistamines. Complete remission of symptoms was achieved within two weeks. Three months later, the patient started complaining of post-prandial fullness and abdominal pain. Laboratory workup revealed persistent elevation of liver enzymes (aspartate transaminase 35–61 U/L, alanine transaminase 79–157 U/L,

gamma-GT 115–276 U/L), which were within the normal range at baseline. Lipid profile, viral hepatitis serology and autoimmune blood tests were unremarkable. Abdominal ultrasound and computed tomography showed no significant changes. A liver biopsy was performed and revealed low grade steatohepatitis, which in the absence of another plausible cause (dyslipidaemia, alcohol intake, viral infection, metabolic syndrome), was assumed to be most likely associated with omalizumab. The drug was discontinued and liver enzymes returned to normal ranges. However, the patient experienced worsening of the CSU, without satisfactory control with H1-antihistamines and cyclosporine (4 mg/kg/day). Due to the high impact on patient's quality of life, not only because of the associated pruritus, but also due to the fact that urticaria lesions were located in visible areas, the possibility of reintroducing omalizumab was considered and discussed with his hepatologist.

Given the lack of other available options for the treatment of CSU, the patient's desire to maintain therapy, the low degree of hepatic inflammation on liver biopsy, and the reticuloendothelial clearance of omalizumab making it unlikely to be altered by hepatic impairment,² it was decided to restart omalizumab administration with close analytical monitoring. Such therapeutic strategy has been followed in the last two years, maintaining moderate liver enzymes rise and CSU activity was completely controlled (UAS7 0).

To the best of our knowledge, this is the first case report of steatohepatitis associated with omalizumab. Liver function impairment has not yet been described. Additionally, the effectiveness and safety of omalizumab has been reported in patients with CSU and hepatitis C and B.^{3,4} Considering that fact, as well as the safety data available and the mechanism of omalizumab metabolism, nothing would predict the hepatotoxicity of the drug. Our patient's symptoms triggered the investigation that revealed an unintended adverse effect. However, it has been possible to continue therapy with omalizumab without severe adverse effects. Such approach should always be considered on a case-by-case basis.

Conflicts of interest

Ana Brasileiro participated in educational activities for AbbVie, Janssen-Cilag, Leo-Pharma and Novartis.

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