Drug induced autoimmune hepatitis after turmeric intake

Hepatitis autoinmune inducida por tóxicos tras la toma de turmeric

Autoimmune hepatitis (AIH) is a chronic liver disease of unknown etiology. It can appear after exposure to toxins, being difficult to differentiate it from an immune-mediated DILI (drug-induced liver injury) and a DI-AIH (drug-induced autoimmune hepatitis). In DILI, hypersensitivity symptoms may appear and autoimmune signs may be observed, but the treatment consists in suspending the toxic. In DI-AIH autoimmunity data are observed too but, it is required immunosuppressive treatment, which might be suspended. AIH is characterized by autoimmunity data, a compatible biopsy, and the need to maintain immunosuppressive treatment in the long term. This last point is the main difference with DI-AIH.[1]

We present the case of a 28-year-old male admitted in our Hospital for severe acute hepatitis. On admission laboratory studies showed GPT 3770 U/L, GOT 2276 U/L, FA 200 U/L, GGT 183 U/L, and bilirubin 7.3. Coagulation and a Doppler ultrasound were normal. Hepatopathy screening was performed, everything being normal except for ANA (1/160). IgG levels were 823 but the patient carries HLA DRB1*13, which has been described as a genetic predisposing factor in patients with type I AIH of Caucasoid/North American origin.[2] He also carries HLA-B*35:01 which has recently been associated with liver cell damage in individuals taking turmeric.[7] He denied the usual consumption of any drug. However, 5 days earlier he consumed cocaine and alcohol. In addition, he reported daily consumption of TURMERIC + (Scientific Nutrition brand). 5 months before admission, at the same time he started the supplementation, analytical alterations were already detectable (GOT 99 U/L, GPT 60 U/L).

Upon initial suspicion of DILI, turmeric was discontinued. However, liver function parameters worsened. The study was completed with a CT angiography and a liver biopsy. As the study was normal except for autoimmunity, and until the anatomo-pathological result was available, a course of intravenous corticosteroids at a dose of mg/kg was started with subsequent biochemical improvement.

Liver biopsy showed acute portal and periportal inflammation with limiting involvement and a moderate inflammatory cell infiltrate. Lymphocytes, neutrophils and eosinophils were identified, as well as some plasmatic cells (CD38 positive staining). There was piecemeal necrosis and vascular ectasis with discrete sinusoidal dilatation without fibrosis (Fig. 1).

Azathioprine was associate with analytical improvement. However, a new worsening was observed and forced the increase of the prednisone dose. Nevertheless, it is worth mentioning a doubtful adherence to the treatment. In addition, he suspended treatment and abandoned follow-up for several months. When resumed, transaminase normalization was observed.

Turmeric is a supplement used for antioxidant and anti-inflammatory actions. Its ingredients include turmeric, ginger, Bioperine® black pepper, bulking agent and anti-caking agents among others. Its main component is curcumin. It is often associated with piperine to increase its bioavailability, which could enhance direct toxicity of the turmeric product.[3] Turmeric has been implicated causing liver injury, and several cases of liver injury associated with turmeric and curcumin have been published. All of them were resolved after discontinuation of the supplement without receiving immunosuppressive treatment.[4–6,8] Ten cases of turmeric-related liver injury have recently been published, highlighting it's growing incidence.[7]

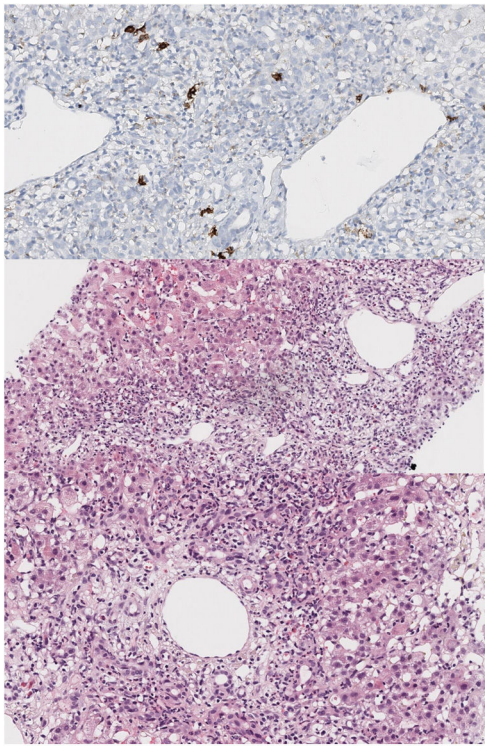

Figure 1 Histological findings. Widening of the portal space with reactive ductular proliferation accompanied by a moderate polymorphous inflammatory infiltrate composed of lymphocytes, neutrophils, eosinophils with presence of some plasma cells (CD38+). The inflammatory infiltrate exceeds the limiting factor, with punch necrosis. Accompanying portal and sinusoidal vascular dilatation.

According to the simplified criteria of the International Autoimmune Hepatitis Group, the patient obtained a score of 6 (probable AIH); according to the classic criteria for the diagnosis of AIH, a diagnosis of probable AIH was also reached with a score of 14; furthermore, after calculating the CIOMS-RUCAM score for DILI, a score of 6 (probable DILI) was obtained.

In our case, the histological findings and the predisposing HLA (DRB*13) support the diagnosis of AIH. However, the normalization of liver biochemistry despite the suspension of immunosuppressive treatment and the HLA B*35:01 positivity supports the diagnosis of DI-AIH induced by turmeric intake. Notice that the patient took cocaine and alcohol prior the admission, which may have been a factor influencing the onset of DI-AIH. However, the analytical alterations were noticed long before its consumption.

There is growing evidence that turmeric can induce severe liver injury. Due to this and the analytical normalization after the suspension of immunosuppressive treatment we conclude that the most probable diagnosis for our patient is DI-AIH. However, the number of cases published so far is small, and more, it is needed to establish a definitive causal relationship.

Funding

There was no funding for this article.

Conflicts of interest

There were no conflicts of interest.

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Effectiveness and safety of high-dose dual therapy PPI-amoxicillin dual therapy for first-line *Helicobacter pylori* in Chile: Experience from the retrospective study

Efectividad y seguridad de la terapia dual IBP-amoxicilina en dosis altas como terapia de primera línea en la erradicación de *Helicobacter pylori* en Chile: experiencia desde un estudio retrospectivo

In Chile, over 70% of adults are infected with *Helicobacter pylori*. This bacterium plays a key role in the development of a number of different diseases, gastric cancer in particular, so effective treatment is essential in clinical practice. It has been suggested that clarithromycin should not be used in any regimen when resistance to this antibiotic is >15%.[1] Recently, a Chilean study showed a resistance rate to clarithromycin of 26%. In this scenario, the effectiveness of triple therapy (proton pump inhibitor [PPI], clarithromycin and amoxicillin) was only 63.8%.[2] Despite that, a study in Chile involving 242 patients showed that 54.9% were treated with this therapy.[3] The Spanish Consensus Conference has suggested a non-bismuth-based quadruple (concomitant) regimen (PPI, clarithromycin, amoxicillin and metronidazole) or a quadruple combination with bismuth (PPI, bismuth, tetracycline and metronidazole) as first-line treatment.[1] Others have also recommended high-dose dual therapy as a first-line treatment for *H. pylori* eradication.[3,4]

We describe here the results on the effectiveness and safety of high-dose dual therapy from a retrospective, observational, descriptive study conducted at our centre from March to September 2022. The research protocol for the study was approved by the scientific ethics committee of the Universidad de los Andes [University of the Andes] with ID CEC2022071. We excluded all patients who had previously received any other *H. pylori* eradication regimen. All patients were treated with esomeprazole 40 mg three times a day (30 min before breakfast, lunch and evening meal) and amoxicillin 750 mg four times a day (with breakfast, lunch, afternoon tea and evening meal) for 14 days. The effectiveness of the dual therapy was evaluated with the *H. pylori* stool antigen test (Pylori-Strip test) which was performed six weeks after the end of eradication treatment and with at