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LETTERS TO THE EDITOR

Toxic hepatitis after concomitant interferon beta and aloe vera treatment in a patient with multiple sclerosis: A case report☆

Hepatitis tóxica tras tratamiento concomitante con interferón beta y aloe vera en un paciente con esclerosis múltiple: a propósito de un caso

Dear Editor:

Interferon beta (IFNβ) is considered a safe treatment for relapsing-remitting multiple sclerosis (RRMS). However, hepatotoxicity due to IFNβ is not uncommon.[1,2]

Aloe vera (AV) has also been associated with liver damage.[3,4] Some patients with RRMS use AV to alleviate constipation.

No cases of hepatitis in patients taking IFNβ and AV have previously been described in the literature. We present the case of a patient with RRMS who developed toxic hepatitis following long-term treatment with IFNβ and AV.

Our patient was a 61-year-old woman with RRMS who had been receiving intramuscular IFNβ-1a dosed at 30 μg per week for 10 years (Avonex®) and LX_Trem® (182 mg AV) for 3 years to prevent constipation. She attended the emergency department complaining of asthenia and abdominal pain. Examination revealed jaundice and pain upon palpation of the right hypochondriac region. A blood analysis revealed AST 1236 U/L, ALT 824 U/L, GGT 169 U/L, ALP 121 U/L, and prothrombin activity 73%. Results from serology tests (hepatitis A, B, and C) and an autoimmune study (ANA, AMA, LKM, and SMA) were negative. A liver ultrasound and a thoracic-abdominal CT scan revealed a fatty liver with no associated hepatomegaly or space-occupying lesions; liver biopsy results (Fig. 1) were compatible with toxic hepatitis. Intramuscular IFNβ-1a and AV were discontinued due to clinical suspicion of hepatotoxicity. An analysis performed 3 weeks later showed improved liver function, which normalised after 6 months.

Our patient scored 7 points (probable causality) on the Roussel Uclaf Causality Assessment Method (RUCAM).[5] Our patient's drug reaction was reported to the Catalan pharmacovigilance authorities.

Asymptomatic transaminase elevation constitutes the most frequent liver alteration associated with IFNβ; this is usually mild and transient and does not normally require drug discontinuation or dose adjustment.[1] In the study published by Francis et al.,[1] IFNβ was discontinued due to toxicity in only 0.4% of the patients taking it, and the rate of severe hepatotoxicity was one case in 2300 patients. Severe, late-onset hepatotoxicity due to IFNβ, as in our case, is exceptional[6,7]; drug-induced liver damage usually occurs during the first year of treatment, and is uncommon after the first 6 months.[1] Regarding type of IFNβ, toxicity increases with higher doses and frequency of administration and rarely occurs in patients receiving weekly doses.[2]

Hepatotoxicity due to AV is common during the first months of treatment. According to our literature search, only one case of late-onset toxic hepatitis (>5 years from treatment onset) has been reported to date.[3]

The pathophysiological mechanisms of IFNβ- and AV-induced liver damage are not known. IFNβ is thought to cause hepatotoxicity by directly damaging hepatocytes or by inducing autoimmunity against the liver[1,8]; the drug's immunomodulatory properties may trigger immunological alterations such as autoimmune hepatitis. AV-induced hepatotoxicity, in turn, may be due to direct toxicity or to hypersensitivity.

Hepatotoxicity is more frequent in men but tends to be more severe in women. The reason for these sex-related differences is unknown; it has been hypothesised that a lower body mass index and a higher level of treatment adherence may predispose to hepatotoxicity.[6]

Our patient developed toxic hepatitis after several years of treatment with IFNβ and AV; hepatotoxicity resolved with treatment discontinuation. In our case, we cannot rule out an association between hepatotoxicity and either of the 2 drugs, given that both IFNβ and AV can cause delayed hepatotoxicity and that symptoms improved after discontinuation of both drugs. As for the pathophysiology of the disease, the autoimmune study yielded negative results, which rules out autoimmune hepatitis and points to drug toxicity as the most likely cause.

In conclusion, the risk of IFNβ-induced hepatotoxicity increases when this drug is combined with other drugs or herbal products.[9] Doctors administering IFNβ to patients with RRMS should monitor use of concomitant treatments. Although the risk of hepatotoxicity is greater during the

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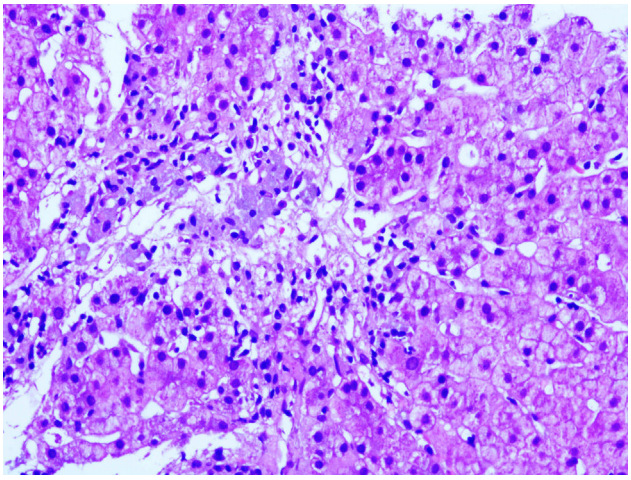

Figure 1 Liver biopsy. Central lobular confluent necrosis with inflammatory infiltration of histiocytes. No signs of fibrosis or chronic hepatocellular disease were seen. These findings were compatible with toxic hepatitis (haematoxylin and eosin ×20).

first months of treatment, liver damage may also occur at later stages.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Combined central and peripheral demyelination: A case description☆,☆☆

Descripción de un caso de *Combined central and peripheral demyelinization*

Dear Editor:

The medical literature includes case reports and series of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) plus central nervous system (CNS) demyelination as well as patients with multiple sclerosis (MS) associated with demyelinating neuropathy.[1—3] Onset of central and peripheral nervous system symptoms is usually acute in paediatric patients.[4] In recent years, the term ''combined central and peripheral demyelinisation'' (CCPD) has been proposed to describe the occurrence of demyelination in both these locations.[5] However, there is still no formal definition for the condition, and its aetiopathogenic mechanisms are yet to be established.

Among the different phenotypes of CIDP, Lewis-Sumner syndrome, also known as multifocal acquired demyelinating

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