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Letter to the Editor – Comments on published articles

ANA, lupus and hepatitis C. Comment to "Infection with hepatitis C virus, interferon α and lupus: An odd association"☆

ANA, lupus y hepatitis C. Comentario a «Infección por virus de la hepatitis C, interferón α y lupus, una curiosa asociación»

To the Editor,

Regarding the published article by Auñón-Rubio et al.[1] on the development of systemic lupus erythematosus (SLE) in patients with hepatitis C treated with alpha-interferon (IFN-α), I would like to add the issue of some patients with hepatitis C being positive for antinuclear antibodies (ANA), and the possible liver damage of these antibodies.[2] I would also like to report the apparently innocuous development of these antibodies after receiving IFN-α,[3] which occurred in one of our patients.

This was a 51-year-old woman with chronic renal failure secondary to interstitial reflux nephropathy, on regular haemodialysis since 1982, testing positive then for genotype 1b HCV. She received a renal transplant in 1988, and re-started haemodialysis due to chronic graft nephropathy in February 2007. In December 2007, after a normal autoimmune study (including ANA), ultrasound, and Fibroscan®, she received pegylated IFN monotherapy, with a sustained virologic response and subsequent relapse. In January 2010, she was successfully treated with IFN plus ribavirin, with ribavirin level monitoring. At present, viral load has remained negative, and hepatic Doppler ultrasound and Fibroscan® are normal (4.8 kPa).

The following complications of antiviral treatment occurred: depressive mood, leukopenia without need for IFN adjustment, graft intolerance syndrome (GIS), and abnormal erythrocyte morphology (dacrocytosis, anisocytosis). These all resolved after finishing treatment, without the need for transplantectomy.

Regarding auto-immunity, at baseline, the patient was negative for the various autoantibodies (ANA, ENA, AMA [anti-mitochondrial], ASMA [anti-smooth muscle], APCA [anti-parietal cell] and LKM1 [liver kidney anti-microsomal type 1]), and complement was normal (C3, C4). From the sixth month post-treatment, she began to test positive for ANA, reaching a titre of up to 1:640 on IFL, and then became negative before the first IFN withdrawal. She again tested positive for ANA, after the second IFN treatment, and has remained positive after withdrawal of the drug until present. Anti-DNA and anti-ENA antibodies and complement have always been within the normal range. She has not had any symptoms suggestive of lupus.

"Native" and post-IFN-therapy positivity for ANA autoantibodies are known to occur in patients with hepatitis C,[2–6] being present in up to one third of cases, although the homogeneous pattern is less common.[2] Other autoantibodies have also been detected in this population (SMA, anti-LKM 1), though less frequently. Therefore, even with a high suspicion of viral liver disease, the protocol is to determine the auto-antibody profile in these patients, due to the co-existence of viral hepatitis and auto-immune hepatitis (AIH), particularly if the patient is to receive antiviral therapy.

The ability of ANA antibodies to cause systemic lupus erythematosus has been studied,[1] as has their possible relationship to the severity and clinical course of liver disease,[2,4,5]

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though the different ways in which one condition causes the other are not known. Some studies have suggested that in patients with chronic HCV+ hepatitis, the whole panel of autoantibodies (AMA, ANA, anti-SMA, anti-LKM) could affect the response to interferon and clinical profile of liver disease.[6] However, when ANA was analysed separately, it did not appear to confirm these assumptions.[5] Fortunately, it seems that the presence of these ANAs in HCV+ patients with or without IFN is not related to IFN efficacy.[3]

Our patient became positive only for ANA, remaining negative for the rest of the antibodies related to both lupus and AIH. She has not developed either of these clinical syndromes or classical viral relapse (occult HCV not analysed). Although she has not had a liver biopsy at any time, currently, we see no justification for monitoring these antibodies unless she shows clinical or biochemical abnormalities of some form.

In patients with hepatitis C, with or without interferon treatment, ANA not only bears the possibility of developing SLE, but could also be related with the hepatic infection itself.

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Reply to the comment "Infection with hepatitis C virus, interferon α and lupus: An odd association"☆

Respuesta al comentario de «Infección por virus de la hepatitis C, interferón α y lupus, una curiosa asociación»

Dear Editor:

We hereby thank Dr Martín-Gómez for her interest in our article "Infection with hepatitis C virus, interferon α and lupus: An odd association"[1] and her comment on it.

As she clearly explains in her remark, the presence of antinuclear antibodies (ANA) among patients with chronic HCV infection has been extensively described in the literature as an immune epiphenomenon lacking clinical significance in most cases.[2]

Additional supporting tests, including extending the autoantibody profile, should only be performed in patients whose clinical or analytical findings are unrelated to hepatitis C. This rules out associated diseases, such as autoimmune hepatitis or drug-induced lupus.

Following treatment, our patient had fever, asthenia, and arthralgia, as well as positive anti-histone antibodies. The temporal relationship between concomitant interferon treatment and negative HCV tests resulted in the diagnosis and subsequent therapy of the patient.

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