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Letter to the Editor

Answer to the Letter to the Editor: The Liver in Rheumatic Diseases☆

Respuesta a la carta al editor: El hígado en enfermedades reumáticas

To the Editor:

I immensely appreciate the interest of Dr. Cortina in reading our editorial,[1] and in the most cordial and respectful manner I allow myself to answer his objections one by one:

1. In the editorial, I specifically referred to the biochemical evaluation of cholestasis by means of liver function tests. Therefore, it was not a review of any of the liver enzymes, including the gamma glutamyl transpeptidase (GGT). Cholestasis is an alteration that may involve the process of bile formation or its flow, and it can occur everywhere, from the basolateral membrane of the hepatocyte (sinusoid) until the ampulla of Vater.[2] The most elemental marker of this alteration is the elevation of alkaline phosphatase (ALP) above 1.5 times the upper limit of normal.[3] However, in addition to the liver, this enzyme is also produced in the bone, the intestine, the kidney, the placenta and the leukocytes.[3,4] Therefore, the elevation of the ALP can be a dilemma for the clinician, and thus, when evaluating an increase of that enzyme, the first step is to determine its origin, and there are 3 basic ways to do it: determining by electrophoresis, the isoenzyme of ALP of hepatic origin, or measuring the 5'-nucleotidase or the GGT in blood (> 3 times the upper limit of normal), which are elevated in hepatobiliary diseases.[4,5] In clinical practice, is used the measurement of these 2 enzymes. In this context, one of the main clinical applications of the measurement of GGT is precisely to identify the source of the elevation of ALP,[3-5] and if it is elevated along with ALP, then it is most likely that the elevation of ALP is originated at the hepatobiliary level, since GGT is a very sensitive marker of liver damage. It is not used in isolation to investigate cholestasis, because in the majority of cases in which it is elevated in isolated form, there is no cholestasis. The next step is to determine the intra or extrahepatic origin of the cholestasis. The importance of GGT in cholestasis lies in its excellent negative predictive value.[4] It is not found in the bone, and therefore it is particularly important in children with elevation of ALP,[3,4,6] since many physicians are often uncertain about whether or not the elevation is due to a hepatobiliary disease.[3,4,6] In addition to the liver, it is also present in the kidney, the pancreas, the spleen, the brain, the seminal vesicles, and the heart, but its serum elevations seem to be originated mainly in the hepatobiliary system.[4,5] As can be seen, the discourse about the GGT in the editorial was only concerning its importance in cholestasis. Therefore, we do not understand the comment of Dr. Cortina, requesting the revision of all the characteristics of GGT, which are many, and in addition to the implications mentioned by him, it is also useful in other hepatobiliary diseases, such as alcohol,[7] etc., and more recently even to determine the fetal prognosis[8] and the severity of periodontitis.[9]
2. Autoimmune hepatitis is an entity that is currently classified as types I and II.[10] The term "lupoid hepatitis" makes reference to some patients studied in the 1960s, with a florid clinical picture of autoimmune hepatitis, who had also positive LE cells.[11] These patients did not have SLE, and therefore, they did not have either specific liver involvement by this disease. For this reason, the experts agree in insisting that this term should be abolished.[12-14] The situation is similar to the "miserere colic" (*Miserere mei*), used as synonym for appendicitis in antiquity, but that probably corresponds to an intestinal obstruction.[15] Regardless of what it intended to mean, the term disappeared when appendicitis and intestinal obstruction were identified. Dr Cortina insists that although "lupoid hepatitis" may not exist, the same thing does not occur with "lupus hepatitis," which he considers that it does exist.

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However, the article with which he supports his asseveration,[16] says just the opposite: "there is evidence that SLE by itself does not cause a specific, severe and progressive hepatic injury" and what some authors consider "lupus hepatitis," is a mild and asymptomatic elevation of transaminases that are normalized when the SLE is controlled with steroids."[16] I personally consider that if it was thought similarly for each alteration of the different organs in systemic diseases, the scientific gibberish would be unsustainable: "pneumonic hepatitis" for the hepatic alteration seen in pneumonia, "septic hepatitis" for that found in sepsis, "arthritic hepatitis," etc.

3. Regarding the request of Dr. Cortina that it would have been preferable to write an editorial for all articles of that issue of the Journal, it is very important to mention a few basic concepts. When an editorial is written, is in order to analyze and comment on an article, usually original, that the editor has chosen, and that is the only article that the guest writer knows. Yet, there are minimum points to be considered by the editorialist when commenting on a publication. Among those are the rigor of the methodology used, which includes the type of design, calculation of the sample size, blinding (single or double bind), randomization, losses to follow-up, measurement of variables, biases, confounding variables, etc., that is, the internal validity of the article that has been entrusted to him. Based on the foregoing and on the expertise of the guest, he will make the respective inferences and the contribution that he could make, or not, to current knowledge. It is never a document to make unfounded praises or criticisms. The article entrusted to us was a review article.
4. Regarding the liver involvement in SLE, although occasional in adults,[17-19] it has been demonstrated for a long time, independently of the "personal conviction" of Dr. Cortina. This association was never denied in the editorial. In this regard, in the document was chosen what we thought it was a challenge in daily practice: to establish whether a specific patient has hepatitis as a systemic involvement of SLE versus an original autoimmune hepatitis with rheumatic manifestations. We commented what we believe it would be useful to focus on the dilemma, including the liver biopsy with the characteristic findings of AIH. Dr. Cortina makes us realize about the liver biopsy, whose importance had already been described in the editorial. By the way, who must interpret a liver biopsy is a hepatopathologist, i.e. a pathologist devoted to the pathology of the liver, not an internist-gastroenterologist-pathologist, which, currently, does not exist!

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