LETTER TO THE EDITOR

Circulating histone H4 values can relate to disease severity in patients with alcoholic hepatitis and cirrhosis

Los valores circulantes de histona H4 pueden relacionarse con la gravedad de la enfermedad en pacientes con hepatitis alcohólica y cirrhosis

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To the Editor,

We read with interest the article by Küçük et al.[1] assessing serum histone H4 (sHH4) levels in patients with alcoholic hepatitis and cirrhosis. This timely study enhances our understanding of extracellular histones as danger-associated molecular patterns that link liver cell injury to systemic inflammatory responses. While standard prognostic models for acute-on-chronic liver failure emphasize bilirubin, international normalized ratio, and creatinine, histone H4 behavior may offer additional insight into disease severity and prognosis.

Two observations stand out:

1. Biological plausibility: Similar to findings in sepsis and trauma – where high histone levels relate to multi-organ dysfunction and worse outcomes – the elevated sHH4 in alcoholic liver disease may reflect immune activation stemming from hepatocellular necrosis and contribute to systemic injury[2].
2. Clinical implications: In our own cohort of 64 cirrhotic patients, sHH4 concentrations rose during episodes of decompensation but did not consistently differentiate between septic deterioration and progression of hepatic failure (unpublished data). This diagnostic ambiguity underscores the need for validation in larger cohorts and standardized measurement protocols.

On the therapeutic front, emerging experimental data suggest that neutralizing circulating histones or modulating Toll-like receptor signaling can attenuate tissue damage in inflammatory conditions[3]. Whether such strategies can be translated to the treatment of severe alcoholic hepatitis is a compelling area for future investigation.

We congratulate Küçük et al.[1] for advancing this promising biomarker field and encourage further studies to determine the prognostic utility and therapeutic target potential of histone H4 in advanced alcohol-related liver disease.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. N/A (Non-experimental research).

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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