Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

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DOI: 10.17235/reed.2023.9972/2023
Link: PubMed (Epub ahead of print)

Please cite this article as:
Fernández-Gordón Sánchez Flor M., Gómez Labrador Celia, Riado Mínguez Daniel, Agudo Fernández Sandra, Castaño Milla Carlos. Persistently elevated alkaline phosphatase without hepatopathy? Literature review. Rev Esp Enferm Dig 2023. doi: 10.17235/reed.2023.9972/2023.

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CC 9972 inglés

Persistently elevated alkaline phosphatase without hepatopathy? Literature review

Flor M. Fernández-Gordón Sánchez, Celia Gómez Labrador, Daniel Riado Mínguez, Sandra Agudo Fernández, Carlos Castaño Milla

Hospital Universitario Rey Juan Carlos. Móstoles, Madrid. Spain

Correspondence: Flor M. Fernández-Gordón Sánchez
e-mail: florfgs@hotmail.com

Conflict of interest: the authors declare no conflict of interest.

Keywords: Alkaline phosphatase. Alkaline phosphatase isoenzymes. Intestinal alkaline phosphatase.

Dear Editor,

Elevated alkaline phosphatase (ALP) levels are found in multiple hepatobiliary diseases, and less frequently in bone diseases.

Case report

We present the case of a 39-year-old male with a history of grade 3 obesity (body mass index [BMI] 40.2 kg/m^2) and prediabetes, who was referred for evaluation due to persistent elevation of ALP levels (300-400 IU/l; normal < 129). The rest of the liver profile was within normal limits. The patient does not consume alcohol or hepatotoxic substances, and is asymptomatic.

Etiological investigations for hepatopathy, including autoimmunity, were negative. Abdominal ultrasound revealed hepatic steatosis as the only notable finding. The patient met the criteria for metabolic associated fatty liver disease (MAFLD), with no indirect signs of liver fibrosis based on validated scores. Since the expected hepatic abnormality would be hypertransaminasemia, the ALP isoenzymes were determined to

complete the study. Electrophoresis revealed bands of hepatic origin (14 %), bone origin (16 %) and intestinal origin (70 %).

Discussion

In healthy individuals, 90 % of serum ALP originates from the liver, bones and kidneys, less than 10 % from the intestines and less than 1 % from the placenta. It is well-established that intestinal ALP (IALP) increases after ingestion and can lead to abnormally high ALP levels (1). For this reason, it is recommended to confirm these findings in fasting conditions. Elevated IALP has been described in cases of intestinal perforation, acute mesenteric ischemia, and less commonly, cirrhosis. Very few cases of persistent elevations of IALP (1-3) or in the context of benign familial intestinal hyperphosphatasemia (BFIH) (4,5) without underlying pathology have been reported in the literature.

IALP is found in intestinal microvilli and enters circulation through the lymphatic system. The majority of it is bound to AB0 antigens, with a minimal portion being free in serum. Persistent elevations of IALP are more prevalent in healthy individuals with blood type B or 0 (1). However, the patient presented here was blood type A.

On the other hand, BFIH is a disorder with a pattern suggestive of an autosomal dominant inheritance. It is not yet well-defined whether there is an involvement of the gene encoding the intestinal isoenzyme or the mechanism of control for its entry into circulation (4,5). This condition has no clinical consequences.

In the evaluation of elevated ALP, most patients will not require a determination of its isoenzymes. However, it is important to be aware of this entity to avoid unnecessary additional studies and to establish the diagnosis of a persistent but benign biochemical abnormality.

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