

Letters to the Editor

Recurrent cholestasis by amoxicillin-clavulanic acid: The importance of a correct diagnosis of hepatotoxicity

Key words: Jaundice. Amoxicillin-potassium clavulanate combination. Drug-induced liver injury.

Dear Editor,

The amoxicillin-clavulanic acid (AC) is one of the most used antibiotics in Spain. Although it is thought to be a relatively secure drug, adverse reactions and liver damage, although not frequent, occurs occasionally.

Case report

We present the case of a 62-years-old male, diabetic, in treatment with metformin, who was hospitalized because of jaundice and itching. He presented symptoms of jaundice the previous year. It was performed a cholangioRNM, a study of autoimmunity and hepatitis serology, but all these studies were normal. However, a hepatic hydatid cyst was detected and surgically operated. The patient had taken AC some days before. The jaundice vanished after 4 months. He was hospitalized for jaundice and itching with two weeks of evolution. He showed neither fever nor abdominal pain. He has been taken AC for the last 20 days. The physical examination revealed jaundice with normal cardiopulmonary and abdominal exploration. The additional tests showed: normal hemogram and coagulation, total bilirubin 12 mg/dl (0-1.1) at the expense of the direct bilirubin, alkaline phosphatase 107 U/L (40-129), gammaglutamyl transpeptidase, 161 U/L (9-48), normal GOT and GPT, as well as tumor markers and proteinogram.

Although the first suspicion was the toxic hepatitis, it was made a wide differential diagnosis. An abdominal ultrasound and a magnetic cholangioRNM were requested and showed: sequelae of the hydatid cyst surgery and abnormalities suggesting the existence of diffuse inflammatory changes in the hepatic parenchyma. The vesicle, bile ducts and pancreas were normal. In addition, it was carried out a wide study to exclude other causes, including immunity study (ANA, anti-KLM, anti smooth muscle antibody, AMA) which was negative. Negatives viral serology (VHA, VHC, VHB, VEB, VIH, CMV). Serum alfa-1 antitrypsin, ferritin and ceruloplasmin were also normal.

During hospitalization, the pruritus persisted and total bilirubin increased up to 25 mg/dl. Considering the negative results and the anxiety of the patient, a hepatic biopsy was performed that was informed as morphologic changes supporting cholestasis.

The patient was discharged home with the following diagnosis: Toxic hepatitis by AC. Two months later, the patient was asymptomatic and serum bilirubin, transaminases and alkaline phosphatase were normal.

Discussion

Since 1988, a large number of cases of cholestatic jaundice associated to AC have been published (1-3).

To establish the causality of toxic hepatitis by AC, other causes must be excluded (4) and it is very useful the identification of positives criteria for the drug toxicity (hypersensitivity manifestations, compatible biopsy, removal effect, re-exposition, etc) (5). In our case, the evolution, the exclusion of other causes, the liver histology, and the previous history of the same symptoms after taking AC the previous year confirmed the diagnosis. The predisposing factors that have been mentioned in some study are age and male gender (6).

The average period of latency in Spanish patients is 3 weeks; however, it may be delayed until the end of treatment in almost a 50%, as was the case of the patient here reported (7). In general, it has a mild evolution after the drug removal, with the normalization of the laboratory tests in 1-4 months. It has been described, notwithstanding, some case of evolution to chronicity (8) and

even death (9). Furthermore, it must be pointed out the singular phenotypic expression of our case in which there was an isolated increase in serum bilirubin levels without enzymatic movement.

The main interest of this case lies in the recurrence of cholestatic features under the unnoticed re-exposition to AC due to a mistaken initial diagnosis. An analysis of the causes of unnoticed re-exposition in cases of hepatotoxicity evidenced that the most frequent mistake was an incorrect diagnosis/lack of information in the discharge report of the patient who made possible the new prescription of the responsible treatment (10).

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