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LETTER TO THE EDITOR

Acalculous cholecystitis during the course of acute Epstein–Barr virus infection and Gilbert's syndrome

We read with great interest the article by Attilakos et al. regarding the development of acute acalculous cholecystitis (AAC) during the course of Epstein–Barr virus (EBV) infection in two children with Gilbert's syndrome (GS).¹

GS is a benign condition characterized by mild unconjugated hyperbilirubinemia in the absence of liver disease or overt hemolysis; it occurs in 11–16% of Caucasians. In Caucasians, all patients with GS appear to be homozygous for an additional TA in the TATAA box of the UGT1A1 gene promoter, which encodes a uridine diphosphate glucuronosyltransferase that catalyzes bilirubin glucuronidation.²

We found very interesting the hypothesis that the co-occurrence of GS may play a role in the pathogenesis of AAC during the acute EBV infection, and so recalled the case of an 18-year-old girl who presented one year ago with AAC during the course of acute EBV infection, which we have previously described,³ to ascertain if she was a carrier of the UGT1A1 gene promoter mutation.

Analysis of the A(TA)_nTAA motif in the promoter region of the UGT1A1 gene was performed by PCR using previously described primers.⁴ The analysis gave a negative result with the presence of a normal (TA)₆ allele.

The exact mechanisms that are implicated in the pathogenesis of AAC during the course of acute EBV infection have not been elucidated, but direct invasion by EBV of gallbladder epithelium and/or irritation of the gallbladder from the bile stasis are considered possible causes. Recently, EBV-induced hepatitis has been recognized as an important cause of cholestasis. To date, ten cases of AAC associated with an EBV infection have been reported and all have occurred in European patients, four of them from Greece.^{1,3,5–11}

The high levels of unconjugated bilirubin and the 30% increase in bilirubin monoglucuronide (less water soluble than the normal diglucuronide) excreted in the bile observed in patients with GS might increase the cholestasis induced by EBV infection. However, this was not the case in our patient.

We think that if the hypothesis of Attilakos et al. were true, many more cases of AAC would have occurred in

patients with GS, and GS would probably already have been considered a risk factor for cholecystitis independently from an EBV infection. On the contrary, a MEDLINE search combining the term 'Gilbert' AND 'cholecystitis' yields only four papers and in none of them is an association between GS and cholecystitis considered.

Conflict of interest: No conflict of interest to declare.

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