Extrahepatic Biliary Atresia, Liver Function Tests, and Hemoglobin Variants

Sir,

We read with interest the article from Rafeey *et al*., in which anti-smooth muscle antibodies (ASMA) and liver enzymes were used in the differentiation of extrahepatic biliary atresia (BA) and idiopathic neonatal hepatitis (INH).[1] The alanine transaminase to alkaline phosphatase ratio (ALT/ALP; ≤2 in cholestatic liver injury; ≥5 in hepatocellular liver injury; 2–5 in mixed type of injury) has been used in the differential diagnosis of jaundice.[2] Judging from the laboratory findings presented by Rafeey *et al*.,[1] ALT/ALP ratio seems to be much higher in INH than in BA cases, but there are no data regarding associations with outcome. In the latter study, higher ALP and gamma-glutamyltransferase (GGT) serum levels were strongly associated with BA. Nevertheless, the presence of hemoglobinopathy may confuse clinicians by altering liver function tests.

We hereby describe a 10-month-old female infant of Nigerian descent with extrahepatic BA and double heterozygosity for sickle-cell disease and alpha-thalassemia. ASMA levels were undetectable. Liver biopsy set the diagnosis and documented prominent fibrosis of portal fields and fibrous septa between adjacent fields. Beyond portal-based inflammation and sinusoidal congestion, multiple sites of extramedullary hematopoiesis were recognized. Kasai hepatoportoenterostomy (HPE) was performed before completing its second month of age (i.e., 1 month after its initial admission) and was uneventful with no complications. Of note, post-HPE fluctuations in the infant's liver function tests (milder than those seen in sickle-cell intrahepatic cholestasis[3]) suggested an interplay between aberrant red blood cells, ischemic damage to bile ducts, cholestasis, and hepatocellular damage. Failure of HPE – although performed timely – is currently taken for granted, and the patient awaits liver transplantation. Interestingly, a recent case report described a 5-month-old female infant with sickle cell anemia, extrahepatic BA, and histological features akin to our case.[4]

In our case, statistical analysis of laboratory results over time was conducted by means of SPSS (version 20.0.0; IBM Corp., NY, USA): (i) hemoglobin levels associated more strongly with direct bilirubin levels (r_p = 0.438; P = 0.005) than with its indirect form (r_p = 0.354; P = 0.027) and also correlated positively with albumin levels (r_p = 0.533; P = 0.001); (ii) Mentzer index – i.e., the mean corpuscular volume/red blood cell ratio – was correlated negatively with ALP levels and positively with ALT levels and therefore with the ALT/ALP ratio (r_p = 0.64; P < 0.001); (iii) platelet count and mass were both associated with various parameters, notably with SGPT, GGT, and direct, but not with indirect, bilirubin levels, while a strong and negative correlation was calculated for ALP levels (stronger correlations with platelet mass: r_S = 0.617 with P < 0.001, r_p = 0.483 with P = 0.005, r_p = 0.398 with P = 0.012, r_p = −0.601 with P = 0.002, respectively). Regression analysis, as well as histological findings, confirmed the previous results, which plead for a crucial role of hematologic indices in these patients' liver function and hence transplantation outcomes.

Even not contributing directly to BA pathogenesis, the presence of hemoglobinopathy is definitely a negative prognostic factor for BA, and it should be investigated and recorded (especially in patients of African descent), as it may alter liver function tests and confuse clinicians. From this aspect, more specific biomarkers for BA are needed.

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Conflicts of interest

There are no conflicts of interest.

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