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Correspondence

Pre-operative screening for biliary atresia in cholestatic infants: A case for percutaneous liver biopsy

Dear Editor:

We read the article by Okazaki, et al. [1] with interest and would like to take issue with some of their conclusions. This article was a review of 132 cases of suspected biliary atresia (BA) from 1998 to 2018. They argue that laparoscopy, in addition to "basic" studies (including blood biochemistries, ultrasound, and PMT hepatobiliary scintigraphy), are sufficient to reach a diagnosis of BA and that the former standard, pre-operative needle liver biopsy is unnecessary by both delaying treatment and being, in their words, "obsolete". We do not agree with classifying the liver biopsy as obsolete with respect to its utility in the evaluation of an infant with cholestasis.

First, no one would argue against operative inspection and cholangiography as a final diagnostic tool for suspected BA and *preliminary* to a Kasai portoenterostomy, but, it is simply not a screening test for BA. It is an expensive, major operative undertaking requiring general anesthesia in a potentially sick infant. Certainly, it has not been argued that open laparotomy in all cholestatic infants with possible BA be adopted in efforts to hasten a firm diagnosis when a pre-operative percutaneous needle biopsy could help identify those infants that have non-BA diagnoses. Is a laparoscopic procedure for this purpose that much more attractive solely because the incisions are potentially smaller?

Second, their own data illustrate the lack of sensitivity and specificity with this approach. As reported in the article, "basic" studies eliminated only 7 of 132 (5.3%) infants, i.e. only 30% of the final non-BA group (23 infants total). This exposed 16 of the remaining 125 (12.8%) infants to a negative laparoscopy, which, in our experience, is an unusually high proportion. Published literature reviewing the utility of needle liver biopsy suggests greater than 90% discrimination in infants with cholestasis, including those performed at age < 60 days [2]. Therefore, a significant proportion of these 16 infants may have avoided surgery and the associated longer exposure to anesthesia to arrive at their alternative diagnoses.

Clearly, we agree that an additional screening test for BA is needed beyond "basic" testing before securing a firm diagnosis. There is some hope that the serum matrix metalloproteinase-7 (MMP-7) level may confirm its potential in this regard [3], but, at the moment, percutaneous liver biopsy using ultrasound guidance continues to be a standard of care in many institutions around the world and can be performed expeditiously with acceptable complication rates while providing results within 24 h [2].

Since the Authors do not include a percutaneous liver biopsy in their algorithm, it is not surprising that they do not provide data regarding the delay they feel is attributed to biopsy. So how does a liver biopsy delay treatment? It doesn't. Will eliminating a liver biopsy really make a clinical difference to warrant their nearly 13% negative laparoscopy rate? On the contrary, we would argue that performing a liver biopsy in their series could have assisted in the diagnosis of the 16 infants that had alternative diagnoses (Alagille syndrome in 8, neonatal hepatitis in 4, and PFIC in 4) without exposing the infants to an invasive surgical procedure.

Finally, in these 16 infants with the alternative diagnoses noted above, the Authors mention that 10 underwent "tube cholangiodrainage". Neither the nature of this procedure nor its indications are ever made clear to support the argument that surgery was absolutely necessary in those patients.

We agree with the authors that a delay in evaluation and treatment for cholestatic infants must be avoided and applaud their effort to complete a work up within 5–7 days after referral but would argue that a liver biopsy would not meaningfully delay that time frame. While omitting a percutaneous liver biopsy may be the quickest pathway to diagnosis at their center, in many centers around the world the Authors' algorithm cannot be directly extrapolated or applied.

We thus conclude that this study confirms the belief that laparoscopic or open surgical inspection of the liver and biliary tree with cholangiography is indeed exceedingly good at confirming the diagnosis of BA but it does not provide a clear strategy for avoiding surgery or general anesthesia in infants who have alternative diagnoses. Furthermore, the study fails to provide data to support its assertions that liver biopsy delays diagnosis and is obsolete during the evaluation of an infant with cholestasis and possible BA.

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