Editor/Reviewer comment: Many hepatologists use 60 days as the standard time by which Biliary Atresia should be diagnosed (see references below). This is still debated in the literature and not a black and white issue (see references), but is a generally accepted standard. However, this detail needs to be more directly addressed in the discussion of the case report especially since there was not a HIDA scan until after day 75 and liver biopsy until day 81. This timeframe is one of the most important discussion pieces when evaluating these complex NICU patients. It should also be discussed why this patient wasn't evaluated until after 60 days (there may be very valid reasons, but unless they are discussed the reader won't know about them), did prematurity play a role? What does the literature say about prematurity and the timing of Kasai?

Author response: We appreciate this observation as this was the impetus for writing this case report. We have attempted to clarify the reasons that this patient’s evaluation may seem delayed. In particular we have attempted to highlight that given the patient’s initial intestinal failure and prolonged TPN exposure his clinical picture was most consistent with TPN cholestasis. We have added text about this clinical judgement both in the case description and the discussion. We have also described the uncertainty regarding use of chronologic age vs. corrected age for premature infants.

Manuscript changes: “Throughout his NICU course he maintained a conjugated hyperbilirubinemia (Figure 1). On DOL 75 he had acholic stools and his conjugated bilirubin rose to 3.1 from 1.1 mg/dL (normal ≤ 0.3 mg/dL). Evaluation at the time included an abdominal ultrasound that did not visualize the gallbladder, and a non-excreting hepatobiliary iminodiacetic acid (HIDA) scan (after 22 hours). He underwent liver biopsy on DOL 81 which showed minimal periportal fibrosis, mild bile ductular reaction, mild portal inflammation, as well as microvesicular steatosis and intrahepatic and canalicular cholestasis, findings which were
consistent with effects of TPN but were not distinguishable from extrahepatic biliary atresia (Figure 2A,B). His history of prolonged TPN exposure, absence of bile duct plugging and improving bilirubin (2.6 mg/dL from 3.1 mg/dL) suggested PNAC was the most likely etiology. In addition, screening for other causes of cholestasis (e.g. hypothyroidism, alpha-1-antitrypsin deficiency, galactosemia, cystic fibrosis, tyrosinemia, urinary tract infection, TORCH infections, etc.) was negative.

Editor/Reviewer comment: Can the cholangiogram be included as an image?

Author response: Thank you for this suggestion. Although we would have liked to include the cholangiogram, when the procedure was attempted there were no biliary structures that would even allow for performance of a cholangiogram. We have included a description of this fact in the case discussion.

Manuscript changes: “During the procedure he was noted to have a small gallbladder remnant with no lumen large enough for a cholangiogram catheter, and a fibrotic extrahepatic biliary tree. He underwent HPE and was discharged on post-op day 6.”

Editor/Reviewer comment: Was there any other work up such as alpha-1-antitrypsin phenotype, etc?

Author response: Thank you for pointing this out. We have added text to describe the additional work-up performed.

Manuscript changes: Case

“In addition, screening for other causes of cholestasis (e.g. hypothyroidism, alpha-1-antitrypsin deficiency, galactosemia, cystic fibrosis, tyrosinemia, urinary tract infection, TORCH infections, etc.) was negative.”

Discussion

“This patient’s conjugated hyperbilirubinemia was initially felt to be related to TPN initially, especially since work-up for additional causes of cholestasis was negative.”

Editor/Reviewer comment: Line 82, page 6: case presentation> bilirubin at 2 months indicated success. I would include data on three months since that it is similar to your reference

Author response: Thank you for this observation. We have updated the text to include the fact that the conjugated bilirubin at 3 months post HPE was also < 2 mg/dL.
Manuscript changes: “After HPE, total bilirubin normalized and was <2 mg/dL at 3 months post-HPE indicating success of Kasai procedure[5]”

Editor/Reviewer comment: -Is it your usual practice to obtain HIDA scans on all cholestatic infants, and if not what made you obtain it on this child.

Author response: It is the general practice at this institution to obtain HIDA scans in patients who have a low likelihood of BA as the HIDA’s high sensitivity gives it excellent negative predictive value.

Manuscript changes: Not applicable

Editor/Reviewer comment: -Is your usual practice a biopsy or intraop cholangiogram after a non-excreting HIDA

Author response: It is the general practice at this institution to follow non-excreting HIDA scans either with a liver biopsy or an intraoperative cholangiogram based on clinical judgement

Manuscript changes: Not Applicable

Editor/Reviewer comment: Please list additional lab work performed to evaluate the cholestatic child. Such as alpha one ati trypsin, thyroids etc.

Author response: See Author response above

Manuscript changes: As above

Editor/Reviewer comment: Figure 2. Would appreciate adding GGT to the figure as well if possible.

Author response: Thank you for this suggestion, we have added data about the GGT values of the patient into what was Figure 2 but is now Figure 1

Manuscript changes: Figure 1