Biliary atresia treated with Kasai procedure in a 2.5-month-old

Tatum Eddy, OMS-IV, Meriah Parker, OMS-IV, Dr. Amie Hinshaw, MD

A. T. Still University School of Osteopathic Medicine in Arizona, Mesa, AZ

Corewell Health Grand Rapids Hospital, Grand Rapids, MI

Background

- Biliary atresia (BA) is a neonatal cholestatic disease that occurs due to inflammation and fibrosis of the intra- and extrahepatic biliary tract, thus leading to partial or complete obliteration of the bile ducts [1]. This destruction leads to severe cholestasis and biliary cirrhosis with the potential for death if left untreated [1].
- Prevalence in the United States: 1 in 12,000 live births [2].
- Prenatal diagnosis:
  - ultrasound findings consistent with a cystic structure in the porta hepatis increases suspicion [3].
- Post-natal diagnosis:
  - Classical triad: persistent jaundice beyond 2 weeks of life (i.e. conjugated bilirubin), acholic stools and dark urine, and hepatomegaly [3].
  - Further workup:
    - Liver function tests with elevated total and conjugated bilirubin, increased gamma-glutamyl transpeptidase and alkaline phosphatase, and normal to elevated transaminases [3].
    - Imaging studies include abdominal ultrasound, hepatobiliary iminodiacetic acid (HIDA) scan, and magnetic resonance cholangiopancreatography (MRCP) [3].
- Treatment: Kasai hepatoportoenterostomy (HPE),
  - Typically performed after an intraoperative cholangiogram proves absent bile flow, in the neonatal period to restore bile flow with eventual anticipation of liver transplantation either if the Kasai fails or when biliary cirrhosis complications appear [3].
  - Studies show the earlier the Kasai procedure is done, the more successful the outcomes are.
    - Target age: within the first 45 days of life [4].

Objective: Present a case of a 2.5-month-old with progressive jaundice who was found to have biliary atresia and was treated with a Kasai procedure despite concern for benefit given age and suggest possible universal screening tools to increase early diagnosis of BA.

Case Report Information

- 76-day-old female, born at term, with a past medical history notable for jaundice and small for gestational size. She was jaundiced at birth but did not require phototherapy. The patient did not take any medication or have any previous surgeries. There were no pertinent family medical conditions, including no history of genetic disorders or biliary atresia.
- During the first few weeks of life, the patient was found to have mild scleral icterus with intermittent jaundice. Prior to her two-month-old well child exam, the patient was noted to have increasingly jaundiced skin and associated pale colored stools, but no notable dark urine. She remained feeding well on a full breast milk diet.
- Two-month-old well child exam
  - + weight loss (z-score from -2.03 to -2.68)
  - + jaundice.
  - Labs revealed direct hyperbilirubinemia (total bilirubin was 8.0mg/dL, direct bilirubin was 5.7mg/dL).

    This discovery prompted a conversation with pediatric gastroenterology and immediate admission for further workup for biliary atresia.
- Admission workup revealed:
  - Direct hyperbilirubinemia
  - Chest x-ray was negative for butterfly vertebrae (Alagille syndrome)
  - Ophthalmic exam was negative posterior embryotoxon (Alagille syndrome)
  - HIDA scan detailed nonvisualization of the gallbladder or bowel at 21 hours.

    These findings which were clinically suspicious for biliary atresia but could not definitively rule out other biliary disorders, including Alagille syndrome or hepatitis causing cholestasis.

Intervention/Treatment/Result

- Intraoperative cholangiogram, wedge liver biopsy, and subsequent Kasai HPE.
  - Wedge biopsy showed cholestasis, ductular reaction, and fibrosis consistent with an obstructive pattern causing liver damage as seen in biliary atresia.
- No significant postoperative complications. Patient was discharged on postoperative day 11.
- Patient continued to follow outpatient pediatric gastroenterology. Repeat labs detailed improved but persistently elevated liver enzymes and bilirubin levels. Clinically, her jaundice and scleral icterus remained.

Discussion

- Receiving a Kasai HPE between the age of 30 and 45 days improves outcomes of both the native liver function and decreases the need for liver transplantation [5].
  - In a cohort study looking at the long term native liver survival rate, it showed an advantage to receiving an early Kasai procedure, marked at less than or equal to 30 days of age, which showed about a 15 to 20% higher native liver survival rate at age 15 to 20 years old. Additionally, it is shown that even if a late diagnosis of BA is provided, clinicians should continue to refer for a Kasai procedure due to its significance in reducing liver transplantation mortality rates [6].
- Challenges in the early diagnosis of BA:
  - Relatively low incidence
  - Persistent neonatal jaundice can be mistaken for physiologic jaundice [7].
    - In our patient's case, there were signs of jaundice, however, other concerning findings such as failure to thrive or acholic stools were not appreciated until her two-month-old well child exam.
- Additional differential diagnoses: inborn errors of bile acid synthesis, Alagille syndrome, idiopathic neonatal hepatitis, cholestasis, choledochal cysts, and galactosemia.
- The current gold standard diagnostic tools are invasive and include liver biopsy and intraoperative cholangiogram [7].
- Lack of *non-invasive* diagnostic test for BA strongly warrants a universal screening tool. Current tools include:
  - Stool color card (SCC)
    - Using a stool color chart to help alert caregivers to report pale colored stools prior to the 1 month newborn visit.
      - A study in Taiwan showed an improved age of diagnosis of BA around 48 days of life, compared to 60 days, with the implementation of the SCC. Additionally, the study showed an improved three year jaundice free survival rate in native liver with the use of SCC. Countries including Switzerland, Germany, Canada, Brazil, and Japan have adopted the SCC, which have shown a benefit to diagnosing BA earlier [5].
  - Fractionated bilirubin measurements
    - In the United States specifically, there have been studies concluding high sensitivity and specificity in using direct bilirubin to diagnose BA [8,9]. These studies have highlighted the important consideration of laboratory cut-off values. A recent study aimed at determining the sensitivity and specificity of elevated direct bilirubin and the direct-to-total bilirubin ratio demonstrated that direct bilirubin ≥1.0 mg/dL was better for BA detection than the ratio in infants aged 3 to 60 days [10].
    - Limitations in the healthcare infrastructure for such programs, including:
      - Varying reference ranges considered to be normal for newborn bilirubin, thus prompting the need for further studies to replicate the findings such as the study's mentioned above [5].
      - Individual healthcare laboratories with their own reference ranges, leading to discrepancies between normal and abnormal lab values across hospital systems [5].
      - Race-based lab differences (e.g. Black infants ages 24 to 48 hours old have higher, albeit normal, levels of bilirubin) [5].

Discussion (Continued)

- If an infant has elevated bilirubin, there must also be precise coordination between outpatient pediatricians and nurses to retest bilirubin level at two weeks [5].
- Cost-effectiveness of obtaining a fractionated bilirubin is currently unknown [5].
- Bile acid testing
  - A recent study has shown that measuring taurocholate acid levels from dried blood spot samples collected between 3 and 4 days of life were significantly higher in patients subsequently diagnosed with BA compared to those patients who were jaundiced (non-cholestatic) and those who were healthy [5].
  - The measurement of taurocholate levels showed a sensitivity of 79.1% and a specificity of 62.5% for BA when using the threshold of 0.63 µmol/L [5].
- OMM considerations: The condition's impact on the liver and gallbladder, Chapman points found at the right fifth through seventh intercostal space could be palpated [11].
- In our patient's case, there were no screening tests performed to detect this serious condition due to a lack of infrastructure and consensus on best methods. This ultimately led to delayed diagnosis and treatment after the timeframe that is known to offer the best survival outcomes.
- We suggest that standardizing SCC, testing fractionated bilirubin level, or using dry blood from newborn screening to obtain bile acid levels would be beneficial in diagnosing BA within the early stages of the disease. As mentioned above, establishing a more standardized approach to screening for BA has limitations within the healthcare infrastructure but could show impressive cost-effectiveness in receiving a diagnosis within the earlier stages of this condition.

Conclusions

Biliary atresia is a complicated heterogeneous neonatal disease that has long been treated with the Kasai procedure followed by liver transplantation, if needed. With the overwhelming knowledge that early diagnosis, and thus the potential to perform the Kasai procedure early in life, leads to greater survival, it is clear that a universal screening tool for BA is necessary. There has been support for using SCC, fractionated bilirubin, and bile acid testing, although there is no clear current infrastructure to support their implementation. This suggests that further research is needed to determine the most appropriate universal newborn screening tool for BA that can be implemented into our current healthcare systems. This case report involved a 2.5-month-old patient who received a Kasai operation after the current recommended age for improved survival outcomes.

References

SCAN ME

Acknowledgments

Thank you Dr. Roy, PhD and ATSU-SOMA library staff