Biliary atresia

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Neonatal jaundice is a very common condition. Although most neonatal jaundice is benign, it is important for family physicians to be aware of the potentially fatal diseases that present with jaundice. The pathogenesis is traditionally classified as either unconjugated or conjugated hyperbilirubinemia. *Conjugated hyperbilirubinemia*, which indicates cholestasia, is usually defined as having a proportion of conjugated bilirubin exceeding 20% of the total serum bilirubin or a conjugated bilirubin level greater than 20 µmol/L. It always warrants further investigation. In newborns, the main causes are infections (eg, urinary tract infection, TORCH [toxoplasmosis, other infections known to attack the fetus, rubella, cytomegalovirus infection, and herpes simplex] infection, sepsis), genetic or metabolic diseases (eg, cystic fibrosis, Alagille syndrome), and extrahepatic obstruction.

Included in the differential diagnosis is biliary atresia, a rare obstructive condition for which early diagnosis is crucial. Identification can be challenging, as most family physicians will not encounter this condition during their careers. We report a case of a newborn with biliary atresia for which diagnosis was delayed despite follow-up in a family medicine unit.

Biliary atresia is a fibrosing cholangiopathy affecting the extrahepatic biliary tree. It causes neonatal cholestasia, obstruction of the biliary tree, and—eventually—liver damage. The pathogenesis remains unknown. This condition usually presents with neonatal jaundice, but babies initially grow well and appear to thrive. Acholic (pale) stools and dark urine are other early symptoms, followed by coagulopathy. Failure to thrive, ascites, and splenomegaly are typical late findings (>3 months) caused by cirrhosis and progressive hepatic fibrosis.[1]

Left untreated, this condition usually leads to progressive cirrhosis and death by the age of 2 years. Fortunately, treatment options include portoenterostomy (the Kasai procedure), which can return biliary flow and thereby prevent early cirrhosis. Previously, portoenterostomy was believed to be merely palliative, as most affected children eventually developed progressive hepatic failure necessitating liver transplantation within a few years of diagnosis. More recent studies have suggested that early surgical intervention leads to better outcomes and might postpone the need for eventual liver transplantation. Survival rates with native liver improve if early clearance of jaundice is achieved. A large Canadian study found that 49% of infants who underwent surgery before 30 days of life still had their own livers 4 years later, compared with 25% of those who underwent surgery between 31 and 90 days of life and 15% of those treated after 90 days of life.[2]

Case

Table 1 summarizes the case described here. A 31-year-old woman with 3 pregnancies, 1 live birth, and 1 abortion, and no past medical history, was followed for prenatal care at a family medicine unit. Routine follow-up and screening tests were provided, including a second-trimester ultrasound scan. All prenatal test results were normal and the pregnancy was uncomplicated.

Routine vaginal delivery occurred at 39 weeks and 2 days. The infant had Apgar scores of 9 at 1 and 5 minutes and a birth weight of 3.770 kg. At

EDITOR'S KEY POINTS

- Early recognition of biliary atresia improves treatment outcomes.
- Stool colour charts are simple screening tools and should be given to all parents as part of normal newborn discharge instructions.
- All newborns with elevated conjugated bilirubin levels should have a follow-up serum bilirubin test and an appropriate follow-up visit within 1 to 2 weeks of discharge. All newborns with persistent jaundice at 2 weeks of life should be sent for a serum bilirubin test that also measures the conjugated fraction.

POINTS DE REPÈRE DU RÉDACTEUR

- La détection précoce de l'atrésie des voies biliaires améliore les issues thérapeutiques.
- Les palettes de couleurs des selles sont des outils de dépistage simples qui devraient être remis à tous les parents dans le contexte des instructions habituelles lors du congé de l'hôpital du nouveau-né.
- Il faudrait faire effectuer une autre analyse de la bilirubine sérique et donner un rendez-vous de suivi dans un délai de 1 à 2 semaines après le congé à tous les nouveau-nés qui ont des taux élevés de bilirubine conjuguée. Tous les nouveau-nés dont l'ictère persiste après la deuxième semaine de vie devraient passer un test de la bilirubine sérique qui mesure aussi la fraction conjuguée.

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Table 1. Summary of events

TIME	EVENTS	INVESTIGATIONS
Pregnancy	• Unremarkable pregnancy • Mother receives routine follow-up	Normal screening test results and normal second-trimester ultrasound results
Birth	• Spontaneous vaginal delivery at 39 wk, 2 d • Apgar scores of 9 at 1 and 5 min; BW of 3.770 kg • No complications	None
2 d	• Weight loss of 4.8% of BW • Child is mildly jaundiced • Child is discharged	TSB level of 195 µmol/L Conj level of 9 µmol/L
3 d	• Routine visit by nurse (nurse 1) from local community services centre	None
20 d	• First physician visit (physician 1) • No jaundice noted	Normal examination findings
41 d	• Call from mother who is concerned about jaundice. Nurse 1 notes yellow and soft stools; child is well • Mother is reassured	None
45 d	• Nursing visit. Jaundice of sclera and skin. Child is thriving. Nurse 2 discusses jaundice with physician 2. Diagnosis of breast milk jaundice	None
60 d	• Vaccination visit (nurse 3)	None
69 d	• Mother calls about persistent jaundice • An appointment is offered for the next d but the mother is not available • Follow-up remains as planned	None
76 d	• Second physician visit (physician 3) • Normal development but substantial jaundice with pale yellow stools, dark urine, and hepatomegaly	Urgent ultrasound and bloodwork ordered
78 d	• Laboratory results received • Child is sent to emergency department for urgent workup	TSB level of 169 µmol/L Conj level of 105 µmol/L ALT level of 149 IU/L AST level of 209 IU/L
83 d	• Portoenterostomy is performed • Workup confirms diagnosis of biliary atresia	None

ALT—alanine aminotransferase, AST—aspartate aminotransferase, BW—birth weight, Conj—serum conjugated bilirubin, TSB—total serum bilirubin.

36 hours of life, the baby was found to be mildly jaundiced, with a total serum bilirubin level of 195 µmol/L, below the threshold for intervention. Of note, the conjugated serum bilirubin level was 9 µmol/L, slightly above the normal range of 0 to 5 µmol/L used by the local laboratory. No follow-up was requested for this minimally elevated conjugated bilirubin level. Weight loss of 4.8% was noted 2 days after birth, but was believed to be within the normal range. The baby was discharged from the hospital and routine follow-up was scheduled.

The first home visit by the nurse from the local community service centre during the first week of life revealed no concerns.

At 20 days of life, the baby was seen by the delivery physician for a routine visit. Findings of the physical examination were unremarkable and no jaundice was noted.

At 41 days of life, the mother called the clinic because she was concerned about jaundice. A telephone assessment by a nurse revealed that breastfeeding was adequate and the baby was doing well and had soft yellow stools. The mother was reassured and advised to follow up in the clinic for a planned visit in 4 days.

On the nursing visit at 45 days of life, jaundice of the sclera and skin was noted. The nurse consulted the physician on call, who assessed the baby. As the baby was gaining weight appropriately and looked clinically well, a diagnosis of breast milk jaundice was made and a follow-up appointment was scheduled for 1 month later.

When the baby was 2 months old, he was brought to a different clinic for vaccinations. The nurse noted jaundice and wondered whether this was a contraindication to vaccination. However, she could not reach a physician and the baby was vaccinated and returned to routine care.

At 69 days of life, the mother called to mention persistent jaundice. The clinic offered her an

appointment for the next day but the mother was not available. She decided to wait for a planned follow-up visit with a physician that had been scheduled for when the baby would be 10 weeks of age.

At 76 days of life, the infant showed normal development and weight gain. However, substantial jaundice was noted, along with pale yellow stools, dark urine, and hepatomegaly. An outpatient abdominal ultrasound scan and bloodwork were ordered urgently.

The blood test results were received 48 hours later. The total serum bilirubin level was 169 µmol/L, the conjugated serum bilirubin level was 105 µmol/L, the alanine aminotransferase level was 149 IU/L, and the aspartate aminotransferase level was 209 IU/L. After discussion with the pediatric gastroenterologist on call, the family physician referred the baby to the emergency department for urgent workup. The baby was admitted for investigations, which confirmed the diagnosis of biliary atresia. Portoenterostomy was done at 83 days of life. During surgery, remnants of the biliary tree were seen but with substantial fibrosis. Jaundice resolved during the next 3 to 4 weeks; however, the baby had 3 episodes of cholangitis in the following months, requiring readmission to hospital. The baby continues to be followed by the specialists at a liver clinic in a tertiary care hospital.

Discussion

We present a recent case of biliary atresia seen in a university-based family medicine setting, where there was a delay to diagnosis. To understand this delay, we reviewed the best practices regarding neonatal jaundice and available screening tools for biliary atresia, and determined how these were being applied in a family medicine setting. We observed a gap in the application of this information in the clinical setting. Given the importance of early recognition of this condition, universal screening for biliary atresia is being actively studied. The most widely studied method is the use of stool colour charts or cards; an example of a stool colour card is available at **CFPlus**.[3]* This tool helps parents and health care providers to recognize pale stools, an early sign of biliary atresia, and has been shown to accelerate time to diagnosis. In Taiwan, a national screening program using stool cards was initiated in 2004. The sensitivity of this screening test in identifying biliary

*A **stool colour card** is available at **www.cfp.ca**. The BC Infant Stool Colour Card is reproduced from Schneider et al[3] with permission from R.A. Schneider and Perinatal Services BC. Go to the full text of the article online and click on **CFPlus** in the menu at the top right-hand side of the page.

atresia is 97.3%.[4] Screening programs are now being studied in Argentina, Japan, and Switzerland. In Canada, British Columbia recently started a provincewide screening program.

Quebec has no formal system of screening for biliary atresia, and stool cards were not routinely used at our institution. These simple tools could have assisted both the health care professionals and the parents in earlier identification of acholic stools. The fact that many of the health care professionals who saw the baby documented "yellow" stools in the chart is of particular note. Use of the stool cards could have helped both the health care professionals and the parents identify the stools as "pale yellow" and therefore abnormal.

Different national organizations, including the Canadian Paediatric Society, have proposed guidelines regarding management of neonatal jaundice. Recommendations include identification and management of hyperbilirubinemia in the first days of life using bilirubin nomograms.[5] Adequate follow-up should be ensured for all infants who are jaundiced. In infants for whom the jaundice persists for longer than 2 weeks or is associated with hepatosplenomegaly, measurement of the conjugated bilirubin fraction is recommended.

Guidelines for the detection and management of neonatal jaundice are well established in our hospital nursery, including test ordering for bilirubin levels and the use of nomograms. However, these guidelines do not take into account conjugated bilirubin levels. As such, no follow-up was recommended to the mother at the time of discharge, even though the baby had a mildly elevated conjugated bilirubin level. Moreover, during later visits to the clinic, health care professionals were reassured by the fact that the baby was thriving. No laboratory tests were ordered for this reason, despite the jaundice persisting for longer than 2 weeks. The early measurement of conjugated bilirubin levels could have differentiated pathologic biliary atresia from common but benign breast milk jaundice.

The lack of an integrated computer system also played a role in our case. Indeed, the initial laboratory results with an elevated conjugated bilirubin level were not communicated to the mother, nor were they sent to the community physician. Thus, health care professionals were reassured by the mother's report that the bilirubin levels were normal. Better communication of abnormal results might have led to a follow-up bilirubin test sooner after birth.

Finally, fragmented follow-up contributed to the delay in diagnosis. During the first 3 months, the baby was seen by 3 different nurses and 3 different physicians before the diagnosis was made.

Conclusion

In our case, a baby presented with classical features of biliary atresia—a mildly elevated conjugated bilirubin level, prolonged jaundice, and acholic stools—yet the baby thrived, with normal weight gain and developmental milestones. Despite treatment from medical and nursing staff experienced in newborn care, the diagnosis of biliary atresia was delayed. We believe this is owing to several factors including the uncommon nature of the disease, the lack of screening for this condition using stool colour charts, the lack of an institutional policy regarding follow-up of neonatal jaundice, and the lack of provincial or national strategies to implement well established guidelines and screening tools. Absence of an electronic medical record and fragmented and difficult access to community care also contributed to late diagnosis.

Following this case, we have increased awareness of this condition among all professionals at our centre. We provided training to reinforce the use of stool colour charts in our family medicine unit, reviewed the Canadian Paediatric Society guidelines regarding follow-up of neonatal jaundice, and provided continuing medical education on this topic. We would encourage policy makers to consider implementing screening for this condition with stool colour charts and to encourage health care providers to use this tool as a part of routine newborn care. Both health care provider awareness and parental engagement in screening are likely to have positive effects on reducing delay to diagnosis and optimizing early intervention. The simple strategy of a stool colour chart has the potential to improve outcomes and decrease the health care costs associated with biliary atresia.

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Competing interests

None declared

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