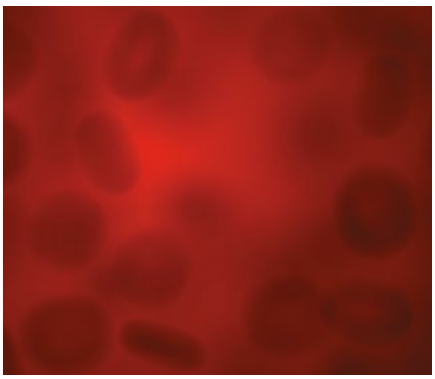
A case of prolonged hyperbilirubinaemia in a neonate



CPD

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CASE

A girl aged one week presented to the general practitioner (GP) for a routine baby check. She was born at term following an uncomplicated vaginal delivery. The antenatal period was uneventful, the morphology scan was normal, and maternal serology was negative. Clinical examination prior to hospital discharge was unremarkable.

Her birth weight was 3650 g (80th percentile) with adequate weight gain to date. She had been fully breastfed with no feeding concerns. On examination, she was jaundiced with an otherwise unremarkable physical examination. Her urine output had been adequate, with normal-coloured urine and stool.

QUESTION 1

What are the different causes of neonatal hyperbilirubinaemia?

QUESTION 2

What background information is relevant in a neonate with hyperbilirubinaemia?

ANSWER 1

The different causes of neonatal hyperbilirubinaemia are listed in Table 1.

Causes that must be urgently ruled out include infections and biliary obstruction. Breastmilk and physiological jaundice are diagnoses of exclusion, only to be diagnosed after initial investigations are normal (blood group, direct antiglobulin test, thyroid function test and glucose-6-phosphate dehydrogenase screen). Neonates with hyperbilirubinaemia should be reviewed at least every 48 hours to ensure improvement in the bilirubin levels and adequate weight gain.

ANSWER 2

A thorough history can help identify risk factors and the cause of hyperbilirubinaemia. Important questions on history are outlined in Table 2.

CASE CONTINUED

At six weeks of age, the patient was referred to the GP by the child health nurse for persistent jaundice. Her weight was noted to have dropped (4800 g, 40th percentile). On examination, her liver was firm and enlarged at 4 cm below the right costal margin. Her urine was dark, and her stools were acholic (pale grey/white coloured). The total bilirubin was 179 μmol/L with conjugated bilirubin of 129 μmol/L (72% of total bilirubin), and the patient was therefore referred for an urgent paediatric review.

QUESTION 3

When is hyperbilirubinaemia considered prolonged?

QUESTION 4

What are the differential diagnoses for prolonged neonatal hyperbilirubinaemia?

QUESTION 5

What is the definition of conjugated hyperbilirubinaemia?

ANSWER 3

Hyperbilirubinaemia is prolonged if it persists for more than 14 days of life in a term neonate and more than 21 days of life in a preterm neonate.[1]

ANSWER 4

There are numerous causes of prolonged neonatal hyperbilirubinaemia (Table 1). The initial step is to differentiate between unconjugated and conjugated hyperbilirubinemia.

ANSWER 5

While unconjugated hyperbilirubinaemia can be benign or pathological, conjugated hyperbilirubinaemia is always pathological and requires urgent investigation and management.[2] Conjugated hyperbilirubinemia is defined as conjugated bilirubin >35 μmol/L or if the conjugated bilirubin fraction is >20% of the total bilirubin.[1,3]

Table 1. The differential diagnosis for neonatal hyperbilirubinaemia[1,2]

Early (within 24 hours of life): Pathological	Intermediate (2–14 days of life): Common and mostly benign	Prolonged (beyond day 14 of life)
• Haemolysis – Rhesus/ABO incompatibility – G6PD deficiency – Hereditary spherocytosis – Alpha thalassaemia • Intrauterine infection • Sepsis	• Physiological jaundice that may be exacerbated by/associated with: – prematurity – bruising – cephalohaematoma – polycythaemia – delayed passage of meconium – exclusive breastfeeding – dehydration – Asian ethnicity – infant of mother with diabetes • Haemolytic causes	• Breastmilk jaundice • Sepsis • Hypothyroidism • Inherited deficiencies of glucuronyl transferase enzymes (very rare) • Conjugated jaundice: biliary atresia, neonatal hepatitis

G6PD, glucose-6-phosphate dehydrogenase

Table 2. Pertinent questions on the history of a neonate with hyperbilirubinaemia[1]

History	Risk factors for jaundice
Day of onset of jaundice	• Always pathological if <24 hours of life
Antenatal factors	• TORCH infections (toxoplasmosis, other [syphilis, hepatitis B], rubella, cytomegalovirus, herpes simplex) • Maternal diabetes
Maternal blood group	• Blood group O and baby group A or B (ABO incompatibility) • RhD negative for rhesus-related haemolytic jaundice
Birth history	• Prematurity • Traumatic delivery: cephalohematoma, bruising
Neonatal feeding	• Exclusive breastfeeding • Dehydration • Poor weight gain
Family history	• Siblings with neonatal jaundice • Gastrointestinal disorders • Haemolysis
Stool and urine colour	• Acholic stool and dark urine are concerning features of conjugated jaundice

RhD, rhesus factor

CASE CONTINUED

The patient's liver enzymes were abnormal, with gamma-glutamyl transferase 285 U/L (reference range 15–132 U/L), alanine aminotransferase 539 IU/L (reference range <30 IU/L), aspartate aminotransferase 448 IU/L (reference range <79 IU/L). An abdominal ultrasound showed no biliary dilation or choledochal cyst, but biliary atresia could not be excluded. An urgent transfer to a tertiary liver centre was organised on the basis of the clinical presentation. The patient underwent an intraoperative cholangiogram, which confirmed the absence of biliary flow.

QUESTION 6

What is biliary atresia?

QUESTION 7

What are the long-term complications of biliary atresia, and is surveillance required?

ANSWER 6

Biliary atresia is a disorder of progressive obliterative cholangiopathy of the intra- and extrahepatic bile ducts that presents during infancy.[4] Early diagnosis is vital, as urgent intervention improves outcomes. The mainstay of treatment is the Kasai portoenterostomy, which involves excising the atretic extrahepatic ducts and creating an anastomosis between the liver and the jejunum to re-establish biliary flow.[5,6] Ideally it should be performed before 60 days of life and is avoided if the child is aged >100 days because of poor likelihood of jaundice clearance; older children would be considered for early liver transplantation.[7]

ANSWER 7

The Kasai procedure is considered a palliative procedure, and children

with this condition remain at risk of progressive liver fibrosis even after successful procedures.[5,7] Monitoring for progressive portal hypertension, worsening malnourishment and ascending cholangitis is required. Children who remain jaundiced after the Kasai procedure are at risk of fat malabsorption and malnutrition and typically require vitamin supplementation.

CASE CONTINUED

The patient underwent the Kasai procedure. Initially she required partial parenteral nutrition because of malnutrition, but she transitioned to full enteral feeds once reaching an adequate weight and was discharged with frequent gastroenterology and GP reviews. On follow-up review, her jaundice had resolved, and her weight gain improved.

Key points

- A thorough history and physical examination are vital in assessing a neonate with hyperbilirubinaemia.
- Regular clinical reviews, including growth assessments, are recommended until bilirubin levels are reassuring are within normal ranges.
- Paediatric referral is indicated for early-onset jaundice (within 24 hours of life), prolonged jaundice and conjugated hyperbilirubinaemia.

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