Prolonged neonatal hyperbilirubinaemia in a case of congenital hypopituitarism

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Accepted 22 January 2019

DESCRIPTION

A 2-month-old girl presented with prolonged neonatal jaundice along with progressive abdominal distension and intermittent passage of hard stools. There was no history of high coloured urine, clay coloured stool, poor feeding, lethargy or high-pitched cry. There was no history of thyroid or liver disease in the family.

On examination, baby had icterus with carotenaemia tinge, along with hypertelorism, depressed nasal bridge, narrow palpebral fissures, macroglossia and short neck (*figure 1A*). She had stunting (length at $-5.15z$ score for age), with preserved weight and head circumference. Systemic examination was unremarkable except for abdominal distension with everted umbilicus. Investigations revealed macrocytic red blood cells (RBC) (Mean Cell Volume 105.7 fl) along with unconjugated hyperbilirubinemia (T Bil: 19.06 mg/dL, C Bil: 1.32 mg/dL) along with mild elevation of transaminases (aspartate transaminase: 157 IU/L, alanine transaminase: 89 IU/L). Coagulogram was normal (Prothrombin Time: 14 s, International Normalised Ratio: 1.00, activated partial thromboplastin time : 33 s) and urine culture was sterile.

Haemolytic workup was unremarkable (normal glucose-6-phosphate-dehydrogenase, reticulocyte – 2.39%, and negative Coombs test, urine and plasma haemoglobin).

Ultrasonography of the abdomen revealed dilated bowel loops and USG neck revealed hypoechoic thyroid gland, with normal structure.

X-ray bilateral knee joint revealed absent tibial epiphysis (*figure 1B*).

Endocrinological investigations revealed secondary hypothyroidism (thyroid stimulating hormone (TSH): 0.026 μ IU/L (0.27–4.2), T3: 0.397 nmol/L (0.8–2) and T4: 0.587 μ g/dL (4.8–12.7)). 08:00 hours cortisol (343 nmol/L) and adrenocorticotrophic hormone (42 pg/mL) were normal; prolactin (0.144 ng/mL) and luteinising hormone (LH) (0.980 mIU/mL) were low with normal follicle stimulating hormone (FSH) (19.99 mIU/mL). Growth hormone (GH) was low (0.030 ng/mL) in response to hypoglycaemia, while parathormone was normal (10.23 pg/mL). Insulin like growth factor 1 was also found to be low (17.6 ng/mL).

In view of panhypopituitarism, MRI pituitary gland was done which revealed reduced bulk and mildly decreased height of adenohypophysis (1.5 mm) (*figure 1C*).

A diagnosis of congenital hypopituitarism, with secondary hypothyroidism was considered, and she was started on oral thyroxine supplementation, following which there was resolution of jaundice and transaminase levels became normal, along with improvement of growth.

Congenital hypothyroidism is a well-known cause of prolonged neonatal jaundice, and presents with other features like constipation, macroglossia, delayed closure of fontanelles, umbilical hernia, coarse facial features and macrocytic RBC.

However, central congenital hypothyroidism is a rare entity (1:20 000–1:50 000) and is often missed on neonatal screening, where only TSH is measured.

The index child had deficiencies of GH along with TSH, prolactin and LH, thereby qualifying as hypopituitarism, with probable mutation of PIT-1, a nuclear protein necessary for maturation and functioning of lactotrophs, somatotrophs and thyrotrophs.¹

Cholestatic jaundice with hypopituitarism is well reported in literature.² However, unconjugated hyperbilirubinaemia has been rarely reported to be associated with congenital hypopituitarism. There is one publication by Copeland *et al* in 1981, that congenital hyperbilirubinaemia, if associated with hypoglycaemia may warrant investigation for congenital hypopituitarism.³ However, our index child did not have any hypoglycaemic records. Hyperbilirubinaemia in the

Figure 1 (A) Dysmorphic facies with carotenaemia tinge and distended abdomen with umbilical hernia. (B) Anteroposterior skiagram of bilateral knee joints showing absent tibial epiphyses. (C) MRI brain—T2 sagittal section showing reduced height (1.5 mm) and bulk of adenohypophysis, with normal stalk and posterior pituitary.

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To cite: Bhattacharya D, Kumar R, Dayal D. *BMJ Case Rep* 2019;**12**:e228793. doi:10.1136/bcr-2018-228793

Learning points

- ▶ Unconjugated hyperbilirubinaemia may occur in hypopituitarism due to deficiency of thyroxine if cortisol is normal.
- ▶ Prolonged jaundice with stunting and facial dysmorphism mandates workup for central hypothyroidism.
- ▶ Panhypopituitarism must be ruled out in central congenital hypothyroidism.

index child is attributed to decreased conjugation of bilirubin, due to hypothyroidism.

Contributors DB: Patient management, literature review and preparation of the initial draft of the manuscript. RK: Patient management, literature review and

preparation of the initial draft of the manuscript. DD: Clinician-in-charge, critical review of the manuscript for important intellectual content and final approval of the version to be published.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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