ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

"PANHYPOPITUITARISM PRESENTING AS INFANTILE CHOLESTASIS AND HYPOGLYCEMIC SEIZURES IN INFANT BORN TO MOTHER SUFFERING FROM HYPOTHYROIDISM IN PREGNANCYA RARE CASE REPORT"

KEY WORDS: Congenital hypopituitarism, Infantile cholestasis, Non-ketotichypoglycemia, Multiple pituitary hormone deficiency, Hormone replacement therapy, MRI brain anomalies

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ABSTRACT

Background: Congenital hypopituitarism (CHP) is a rare endocrine disorder with an estimated incidence of 1 in 4,000 to 10,000 live births. It may present subtly in neonates with nonspecific signs such as cholestasis, hypoglycemia, and seizures, often leading to delayed diagnosis. **Case Presentation:** A 3-month-old male infant presented with a 7-day history of jaundice and pale stools, along with multiple seizures. He had failure to thrive, subtle facial dysmorphism, and hepatosplenomegaly. Laboratory investigations revealed non-ketotic hypoglycemia, low cortisol, low TSH, elevated direct bilirubin, and high serum bile salts. MRI brain showed an ectopic posterior pituitary, corpus callosum atrophy, tonsillar herniation, and a possible duplicated posterior pituitary bright spot. Workup for infectious, metabolic, and genetic causes of cholestasis was negative. The diagnosis of multiple pituitary hormone deficiency was made. The child improved rapidly following intravenous glucose, hydrocortisone, and levothyroxine therapy, with resolution of hypoglycemia and cholestasis. **Conclusion:** CHP should be considered in infants with prolonged cholestasis and hypoglycemia, particularly when accompanied by neurologic symptoms or dysmorphism. Early diagnosis and hormone replacement therapy are crucial to prevent irreversible complications.

BACKGROUND:

Congenital hypopituitarism refers to a rare condition characterized by a deficiency of one or more hormones that are either produced by the anterior pituitary gland or secreted by the posterior pituitary. The estimated incidence of this disorder ranges between 1 in 4,000 and 1 in 10,000 live births.[1] The pituitary gland plays a vital role in regulating numerous physiological processes, including growth, metabolism, and reproductive function. As such, the timely identification and management of congenital hypopituitarism are crucial to avoid serious complications and long-term health consequences, many of which are potentially preventable if addressed early.Despite its significance, diagnosing this condition during the neonatal period poses considerable difficulty. This is primarily because the clinical manifestations of congenital hypopituitarism in newborns are frequently vague, subtle, or nonspecific. These signs often resemble or overlap with symptoms of various other neonatal disorders, further complicating the clinical picture and delaying recognition.[1-3]Consequently, a high index of suspicion, along with a thorough evaluation, is required to detect the disorder early and initiate appropriate hormonal therapy to mitigate adverse outcomes.

Case Presentation

A 3-month-old male infant, born to a non-consanguineous couple, presented with complaints of yellowish discoloration of the eyes and body for 7 days, pale-colour stools for the same duration, and multiple episodes of abnormal body movements over the preceding week. The first seizure episode occurred after the child had refused feeds for nearly 6–7 hours. It was characterized by generalized hypertonia and jerky movements of the upper limbs lasting for 15–20 seconds, followed by post-ictal lethargy for approximately 20 minutes. Two similar self-aborting episodes occurred in the subsequent days. There was no history of fever, vomiting, loose stools, melena, bruising, itching, or abdominal distension.The infant was born at 37 weeks of gestation via cesarean section, with a birth weight of 1965 grams.The mother was having hypothyroidism in antenatal period and was put on levothyroxine 150 microgam. The neonatal period was notable for physiological jaundice on day of life 3, for which phototherapy was administered. The child also had an episode of neonatal seizures managed with phenobarbitone and antibiotics for suspected late-onset neonatal sepsis. Immunization was up to 6 weeks of age, and the child belonged to a lower socioeconomic background. On developmental assessment, gross motor, fine motor, social, and language milestones corresponded to a developmental age of 3–4 months. On examination, the child had subtle facial dysmorphism with triangular facies, hypertelorism, and thin upper lip. Pallor and icterus were noted. Anthropometry revealed failure to thrive (weight: 3.8 kg, 3.72 Z score; length: 56 cm, 3.32 Z score; head circumference: 36 cm, 5.8 Z score). Liver was palpable 2 cm below the costal margin and spleen tip was also palpable. Neurological and systemic examination was otherwise unremarkable, with no signs of meningitis or raised intracranial pressure .Investigations revealed hypoglycemia with low ketone levels, suggestive of non-ketotic hypoglycemia. Hormonal profile showed low serum cortisol and thyroid stimulating hormone, raising suspicion of multiple pituitary hormone deficiencies. MRI brain demonstrated small posterior fossa with 6 mm tonsillar herniation below the Chamberlain line, diffuse corpus callosum atrophy, pachymeningeal thickening and enhancement along bilateral anterior temporal lobes, and possible duplicated posterior pituitary bright spot—findings consistent with congenital hypopituitarism and CNS malformation.Further workup included tandem mass spectrometry (TMS) and gas chromatography-mass spectrometry (GCMS) to rule out inborn errors of metabolism such as medium-chain acyl-CoA dehydrogenase (MCAD) deficiency. High serum bile salts (297 μmol/L) and transient coagulopathy were noted, suggestive of infantile cholestasis. Other differentials such as galactosemia, progressive familial intrahepatic cholestasis (PFIC), Alagille syndrome, and mitochondrial hepatopathy were considered and ruled out based on clinical findings and laboratory parameters. TORCH serology revealed negative rubella; other reports were awaited.The child was managed with intravenous glucose (GIR 8 mg/kg/min), calcium gluconate, and levetiracetam. Upon confirmation of hormone deficiencies, intravenous hydrocortisone was initiated, followed by oral hydrocortisone (8 mg/m²/day in three divided doses) and levothyroxine (25 mcg/day). Following corticosteroid therapy, hypoglycaemia and cholestasis resolved. The child remained euglycemic and clinically stable throughout the remainder of the hospital stay. Discharge planning included endocrine follow-up for thyroid function reassessment and consideration of growth hormone stimulation testing.

DISCUSSION:

This case highlights the importance of considering congenital hypopituitarism (CHP) as a rare but reversible cause of infantile cholestasis, especially when presenting with recurrent hypoglycemia, seizures, and failure to thrive. The 3-month-old infant described here had features consistent with multiple pituitary hormone deficiencies

(MPHD). MRI findings showed ectopic posterior pituitary, corpus callosum atrophy, and possible duplicated posterior pituitary, confirming CHP with CNS malformations. Rapid clinical improvement after initiating hydrocortisone and levothyroxine affirmed the diagnosis and demonstrated the reversibility of endocrine-related cholestasis.This presentation closely resembles reports by DeSalvo et al[4] and Lim et al[5] where infants with hypopituitarism showed cholestasis and hypoglycemia resolving with hormone therapy. Similarly, Chan et al[6] described cholestasis in the setting of septo-optic dysplasia, where endocrine evaluation and MRI were crucial for diagnosis. Our case was TORCH-negative.In contrast, Dato et al[7] reported a case of isolated glucocorticoid deficiency, without CNS anomalies or dysmorphism. While their patient improved with glucocorticoids alone, ours required thyroid and cortisol replacement, supporting central, rather than primary, adrenal insufficiency. The non-ketotic hypoglycemia in our case reflects impaired counter-regulatory hormonal responses typical of cortisol and GH deficiency. Khang-Choo et al[8] described an infant who, despite normal newborn thyroid screening, developed worsening cholestasis and ultimately suffered respiratory arrest during a fasted state. Their case lacked pituitary imaging, but the clinical course, including refractory hypoglycemia and progressive liver dysfunction, strongly suggests undiagnosed adrenal insufficiency or MPHD. In contrast, our case benefited from timely endocrine evaluation and brain imaging, which revealed an ectopic posterior pituitary, corpus callosum atrophy, and tonsillar herniation—common MRI markers of CHP.The unique finding of a duplicated posterior pituitary bright spot in our case is rarely reported and may reflect a developmental variant of uncertain clinical significance. Poor anthropometry (Z scores < 3) and dysmorphic features point to possible syndromic hypopituitarism; however, genetic testing was not available.This case emphasizes the importance of an endocrine workup in infants with unexplained cholestasis, especially when accompanied by hypoglycemia or neurologic symptoms. The prompt resolution of symptoms after hormone therapy supports previous findings that endocrine cholestasis is reversible with early recognition and appropriate treatment.

CONCLUSION:

Congenital hypopituitarism, though rare, should be considered in any neonate or young infant presenting with prolonged cholestasis, non-ketotic hypoglycemia, recurrent seizures, and failure to thrive, especially in the absence of common hepatobiliary, infectious, or metabolic causes. Subtle dysmorphic features, midline brain anomalies, and pituitary abnormalities on MRI serve as vital diagnostic clues.

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