CASE REPORT

Addisonian-Like Crisis in Congenital Hypopituitarism and Cholestatic Jaundice

W S Lee, MRCP, L C S Lum, MRCP, F Harun, MRCP

Department of Paediatrics, University of Malaya Medical Centre, 50603, Kuala Lumpur

Summary

A six-week-old male infant was admitted for investigation of cholestasis and pale stools. He became lethargic and apnoeic with prolonged seizures after a percutaneous liver biopsy. Subsequent investigations showed conjugated hyperbilirubinaemia, elevated liver enzymes, and hypoglycaemia. The radionuclide hepatobiliary scintigraphy was non-excretory. After an operative cholangiogram, the infant developed Addisonian-like crisis with bradycardia, hypotension, respiratory distress, metabolic acidosis, hypoglycaemia, hyponatraemia, and hyperkalaemia. Blood investigations confirmed congenital hypopituitarism. Hormone replacement therapy with L-thyroxine and cortisone acetate resulted in dissolution of jaundice and the reduction of the liver size.

Key Words: Congenital hypopituitarism, Cholestatic jaundice, Addisonian-like crisis

Introduction

Congenital hypopituitarism is a recognized cause of cholestatic jaundice and may be associated with micropenis and septo-optic dysplasia[1]. Hypoglycaemia may be a feature and could be severe and persistent[1]. Early recognition and prompt treatment of hypoglycaemia is important to prevent permanent neurological sequelae[1]. Severe hyponatraemia and hyperkalaemia are, however, uncommon in central adrenal insufficiency secondary to hypopituitarism as the renin-angiotensin-aldosterone system is not predominantly under pituitary control[2]. We describe a case of congenital hypopituitarism presenting with cholestatic jaundice, hepatomegaly, and non-excreting radionuclide hepatobiliary scintigraphy; clinically indistinguishable from biliary atresia. An Addisonian-like crisis with profound hypoglycaemia, severe hyponatraemia and hyperkalaemia was noted after operative cholangiogram. Subsequent pituitary hormonal assay confirmed hypopituitarism.

Case report

A six-week-old male infant was admitted to the paediatric intensive care unit for intractable hypoglycaemia and seizures. He was delivered to healthy unrelated parents, after a term and uneventful pregnancy. He had been thriving normally.

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Corresponding Author: W S Lee, Department of Paediatrics, University of Malaya Medical Centre, 50603, Kuala Lumpur

He was investigated for cholestasis and persistent pale stools. A radionuclide hepatobiliary scintigraphic examination was non-excretory. A percutaneous liver biopsy was reported as showing infiltration of the portal tracts with neutrophils, eosinophils, lymphocytes and multinucleated giant cells. There was reduction of bile ducts with minimal ductular proliferation. A day after the liver biopsy the infant was febrile, lethargic, and apnoeic with prolonged seizures. He was subsequently admitted to the paediatric intensive care unit.

Physical examination revealed a 4.5kg male infant with jaundice, a 4cm palpable liver and splenomegaly. A diagnosis of sepsis with neonatal hepatitis was suspected. He was commenced on intravenous glucose infusions and antibiotics. The white cell count was 19.6 x 10^9/L; platelet count 52 x 10^9/L, and the blood glucose was 0.6 mmol/L. Serum sodium was 139 mmol/L, potassium 4.2 mmol/L, creatinine 21 µmol/L and blood urea 6.2 mmol/L. Total bilirubin was 232 (mol/L with the conjugated fraction of 141 µmol/L, alanine aminotransferase 122 IU/L, aspartate aminotransferase 425 IU/L, alkaline phosphatase 862 IU/L. Serology for congenital syphilis and IgM for toxoplasmosis, rubella and cytomegalovirus were all negative. α-1 antitrypsin was 163 mg/dL (81 - 178 mg/dL). *Staphylococcus aureus* was isolated from peripheral blood culture. Antibiotics were started and glucose infusion commenced. His condition improved over the following few days.

An ultrasound examination of the abdomen showed an enlarged liver with normal echo texture. The gall bladder was not visualised. Because of persistent pale stools an operative cholangiogram was performed. Intra-operatively the liver was enlarged, congested and firm. The common bile duct was narrowed (measuring 0.5 mm), intrahepatic ducts were visualised but narrowed. There was contrast in the duodenum.

The patient had a stormy post-operative recovery. He had a bradycardia (80 beats per minute) and a blood pressures of 45/30 mmHg, respiratory distress, metabolic acidosis and hypoglycaemia. Serum sodium was 117 mmol/L, potassium 6.4 mmol/L, chloride 94 mmol/L, urea 6.8 mmol/L, and blood glucose 2.5 mmol/L while receiving glucose infusions. Blood pH was 7.083, pO_2 5.2 kPa, pCO_2 7.4 kPa, bicarbonate 16.6 mmol/L, base excess -13.3. Urine sodium was 104 mmol/L and urine potassium 7.2 mmol/L. An Addisonian-like crisis precipitated by surgery was suspected. At this juncture, the infant was noted to have a micropenis (2.5 cm in length, 0.5 cm in diameter) with minimal erectile tissues. Both testes were palpable in the scrotal sacs. A diagnosis of congenital hypopituitarism was made. He received mechanical ventilation and was given intravenous hydrocortisone acetate and dopamine infusion for stabilisation. The blood glucose became stable after the administration of hydrocortisone.

Blood investigations confirmed congenital hypopituitarism: thyroid stimulating hormone level 0.4 µIU/L (0.3 - 5.0 (IU/L), thyroid hormone level 8.9 pmol/L (9.1 - 23.8 pmol/L), and serum cortisol level 33 nmol/L (138 - 690 nmol/L). A glucagon stimulation test showed a baseline growth hormone level of < 0.5 mIU/L, and 30, 60, 90, and 120 minutes post-stimulation of < 0.5 mIU/L, 0.9 mIU/L, 0.8 mIU/L, and 0.7 mIU/L respectively. Hormone replacement therapy with L-thyroxine and cortisone acetate resulted in dissolution of jaundice and the reduction of the liver size.

Ophthalmological review at three months of age showed no optic nerve hypoplasia. The child was able to perceive moving objects. At four months of age, the liver enzymes were within normal ranges. The parents did not agree to magnetic resonance imaging (MRI) study of the brain and the patient was lost to subsequent follow-up.

Discussion

Hypoglycaemia and cholestatic jaundice are manifestations of congenital hypopituitarism[1]. The hypoglycaemia may be asymptomatic initially and manifest later with respiratory arrest during a period of stress, such as fasting for diagnostic procedure[3]. Seizures and general collapse may complicate the clinical picture[2,3].

Addisonian-like crisis with hyponatraemia and hyperkalaemia in infants with congenital hypopituitarism and neonatal cholestasis has not previously been reported[3]. Although hyponatraemia, hyperkalaemia, and hyperchloraemic metabolic acidosis are common in Addison's disease, they are uncommon in central adrenal insufficiency, as the renin-angiotensin-aldosterone system is not predominantly under pituitary control[2]. In this infant, an Addisonian-like crisis, with cardio-respiratory instability, hypoglycaemia, hyponatraemia, hyperkalaemia, and metabolic acidosis, developed after operative cholangiogram. The Addisonisan crisis was most likely precipitated by a combination of stress during anaesthesia for operative cholangiogram, fasting and staphylococcal sepsis. The clue to the underlying diagnosis of congenital hypopituitarism was the presence of micropenis, and the condition was confirmed by the demonstration of low thyroid stimulating hormone, cortisol and growth hormone.

Congenital hypopituitarism may be due to isolated pituitary hypoplasia or associated with pituitary stalk interruption. It may also be associated with abnormalities such as septo-optic dysplasia, in which case unilateral or bilateral optic nerve hypoplasia may be a feature. The underlying cause of congenital hypopituitarism in this infant is uncertain, as the child did not have an MRI study of the brain, although ophthalmological review did not show any optic nerve hypoplasia. Adrenal agenesis or hypoplasia may rarely coexist with congenital hypopituitarism, and in this case, severe electrolytes imbalance may be observed. However, in central adrenal insufficiency secondary to congenital hypopituitarism, severe hyponatraemia and hyperkalaemia rarely occurs[2].

Cholestasis in neonatal hypopituitarism may occasionally be severe enough to result in a non-excretory radionuclide hepatobiliary scintigraphy[1]. Liver biopsy, which usually shows giant cell hepatitis, cholestasis and periportal inflammatory infiltrates by lymphocytes and eosinophils, may be necessary to exclude underlying biliary atresia[1]. Bile ductular hypoplasia may be observed, as in this infant[1].

In conclusion, hypoglycaemia and seizure are not uncommon complications in infants with congenital hypopituitarism presenting with cholestatic jaundice[2]. However, an Addisonian-like crisis rarely complicates the clinical course and severe hyponatraemia and hyperkalaemia are even rarer.

References

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