Hyperinsulinaemic hypoglycaemia in an infant with mosaic trisomy 13

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SUMMARY An infant with mosaic trisomy 13, who was small for gestational age, became severely hypoglycaemic. For the first 19 days of life, glucose requirements to maintain normoglycaemia were high (up to 21.7 mg/kg/min) and at the same time the infant had high plasma insulin levels and low glucose insulin ratios. Treatment with hydrocortisone and susprhine was of questionable benefit. Hyperinsulinism abated by the third week of life. This case illustrates early remission of hyperinsulinaemic hypoglycaemia and raises the possibility of an association with trisomy 13.

Hypoglycaemia, although common in the premature or small for gestational age neonate, is rarely caused by hyperinsulinaemia in the neonatal period. Causes of neonatal hyperinsulinaemic hypoglycaemia are nesidioblastosis, adenomatoid dysplasia, islet cell adenoma, ectopic pancreatic tissue, and Beckwith-Wiedemann syndrome.1

This paper describes a mosaic trisomy 13 infant, small for gestational age, who developed hyperinsulinaemic hypoglycaemia. This association has not hitherto been reported.

Case report

The patient was a 2400 g, 37 week female, small for gestational age, delivered to a 25 year old non-diabetic mother. The pregnancy was complicated by mild hypertension. The family history was negative for congenital malformations or mental handicaps. The infant was born by vaginal delivery and required endotracheal intubation and suction because of the presence of meconium beyond the vocal cords. The Apgar scores were 7 and 8 at one and five minutes, respectively. Because of meconium aspiration syndrome, the infant required mechanical ventilation for 12 hours followed by oxygen therapy for an additional three days.

The physical examination showed the following findings: malformed low set ears with small pinna, hypertelorism, elongated philtrum, micrognathia, elongated retroflexible thumbs held in a cortical position with clenched fists, and a two vessel cord.
Ultrasound of the abdomen revealed normal organ structure, position, and size. The infant had a cardiac dextroposition but echocardiography revealed normal cardiac structures. A patent ductus arteriosus responded to conservative medical management. The infant had congenital dislocated hips for which corrective surgery was necessary.

On admission, magnesium, calcium, and electrolytes were normal and the blood glucose was 50 mg/dl. At 12 hours of age, the infant became extremely jittery. A stat blood sugar was reported as unmeasurable. An injection of 10 cc of 15% dextrose resulted in a blood glucose of 9 mg/dl. The rate of dextrose infusion to maintain normoglycaemia was 14.8 mg/kg/min at 36 hours and progressively rose to 21.7 mg/kg/min on the sixth day. Blood insulin concentrations on the third and fourth days of life were 41 and 31 μU/ml (normal <12) with a concomitant blood glucose concentration of 32 and 26 mg/dl respectively (glucose/insulin ratios 0.8; normal >3).

Intravenous hydrocortisone (15 mg/kg/day) was started on the third day of life and tapered down from the tenth day onwards. It was discontinued on the 15th day of life. Suspirine (0.01 ml/kg sc) was given twice on the seventh day to treat severe hypoglycaemia, but was discontinued because of systemic reaction to the drug.

The intravenous glucose requirements remained high (20 mg/kg/min) up to the tenth day, but decreased the following week to 11 to 13 mg/kg/min. In the third week, frequent oral feedings were begun while the intravenous dextrose was slowly tapered off. The infant was totally on oral feedings at the age of 19 days.

Despite normoglycaemia, the infant remained jittery. An EEG on the twelfth day revealed paroxysmal epileptiform complexes. Phenobarbital therapy was initiated with success and has been discontinued during the first year of life. Both head sonogram and computerised tomography were normal. Chromosomal analysis of skin and blood revealed a mosaic trisomy 13. Developmental follow-up during the first year revealed a Bailey Developmental Quotient ranging between 99 and 110. The infant’s blood glucose has remained normal and at 11 months of age, the fasting blood insulin concentration was 9.2 μU/ml and <5 μU/ml two hours post-prandially.

Discussion

Secondary hypoglycaemia in the neonate has been known to complicate multiple congenital anomalies. Neonatal hypoglycaemia has been described in an infant with trisomy 18 and attributed to intrauterine malnutrition. Although our patient with mosaic trisomy 13 suffered from intrauterine growth retardation, her severe hypoglycaemia was secondary to hyperinsulinism. The diagnosis of hyperinsulinism in our case is confirmed by the demonstration of raised plasma insulin levels during documented hypoglycaemia and a high parenteral glucose infusion rate (over 15 mg/kg/min) to attain normoglycaemia.

Neonatal hypoglycaemia secondary to hyperinsulinism can be transient or persistent. Transient hyperinsulinism has been described in infants of diabetic mothers, erythroblastosis fetalis, Beckwith syndrome, and malposition of an umbilical artery catheter. A 'reactive' hypoglycaemia in response to glucose infusion can be demonstrated in most cases of transient hyperinsulinaemia.

Intractable hypoglycaemia results from persistently excessive secretion of insulin produced by a group of pathological pancreatic conditions which have been termed 'islet cell dysmaturity syndrome'. This syndrome includes the following islet pancreatic lesions: hypoplasia, hypertrophy, nesidioblastosis, nesidioblastoma, and islet cell adenoma. In addition, Beckwith syndrome can also be a cause of protracted hyperinsulinism.

The cause of the hyperinsulinism in our case remains unknown. None of the conditions associated with transient hyperinsulinaemia were present in our patient. To date, only two neonates with persistent hyperinsulinaemia had a spontaneous remission, at 3 weeks and 4 months of age respectively.

Pancreatic heterotopic tissue has been described in association with trisomy 13. Hypoglycaemia and hyperinsulinism can rarely complicate this condition. The short term hyperinsulinism in our patient militates against this possibility.

It has been suggested that persistent hyperinsulinaemic hypoglycaemia of infants is due to a failure in the normal functional maturation of the endocrine portion of the fetal pancreas. Infants with trisomy 13 have been found to have a delayed maturation in the synthesis of haemoglobin A2. It is tempting to speculate that the short lived insulin secretion dysfunction in our patient may represent another expression of delayed maturation in trisomy 13. This speculation, however, needs to be substantiated by concrete data.

In summary, we report a case of hyperinsulinaemic hypoglycaemia which illustrates the possibility of early spontaneous remission. The relationship in our case between trisomy 13 and hyperinsulinism, if any, remains undetermined.
Complex cardiac malformation in a case of trisomy 9

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SUMMARY A case of trisomy 9 showing a complex cardiac malformation is presented with a review of other published cases. A distinct trisomy 9 syndrome can be recognised with intrauterine growth retardation, short survival, consistent facial dysmorphism, congenital heart disease, and abnormalities of the skeletal, genital, and renal systems. There is no evidence for a maternal age effect.

Trisomy 9 has been described only rarely, most commonly in mosaic form. This report describes a baby who died shortly after birth, in whom chromosome studies were consistent with complete trisomy 9. The cardiac abnormalities were particularly severe and of a nature not previously documented in this disorder.

Case report

The patient, a female, was the product of the first pregnancy of healthy unrelated parents, the mother and father being 31 and 30 years of age respectively at the time of birth. A subsequent pregnancy resulted in a normal infant. There is no other relevant family history.

She was delivered at 35 weeks following spontaneous onset of labour and a pregnancy marked by intermittent vaginal bleeding between the tenth and twelfth weeks. Growth parameters at birth were weight 1.65 kg, length 41 cm, and head circumference 31 cm. The baby was cyanosed at birth with irregular respirations and died at the age of 11/2 hours.

Craniofacial abnormalities included large fontanelles with a widely split sagittal suture, bilateral microphthalmia with left corneal clouding, a bony nasal tip, micrognathia with a central posterior cleft of the soft palate, and very low malformed ears (fig 1). Other findings included a loud harsh systolic murmur audible all over the praecordium, single

References


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FIG 1 Post mortem view of the baby showing globular tip of the nose, posterior central cleft of the soft palate, and low set malformed ears.