Transit Neonatal Hyperglycaemia, Hyperlipidaemia, and Hypermethioninaemia

In 1969 Gentz and Cornblath reviewed the literature regarding neonatal hyperglycaemia. In the 30 cases of transient diabetes of the newborn no abnormality in amino acid metabolism has been reported. A case is described here in which an abnormality in amino acid metabolism was found.

Case Report

The pregnancy was the mother's first and had been uneventful apart from a urinary tract infection. The patient was born at 40 weeks' gestation after an assisted breech delivery, birthweight 1.84 kg, head circumference 32 cm. Striking physical features included minimal subcutaneous tissue, a 'wizened' face, a flat abdomen, and thin 'matchstick' extremities.

The baby's weight gain was inadequate and on the 22nd day of life glucosuria (12-6 g/24 hr) was detected. The 24-hour urine collection contained 6-6 mg homocystine and 1 mg cystine, but no ketones. Venous blood withdrawn 4 hours after a feed was noted to be milky and turbid in character. The concentrations of the various blood constituents are shown in the Table. In arterialized capillary blood the pH was 7-35, the PCO2 36 mm Hg, and the standard bicarbonate 20 mEq/l.

A few hours after the blood samples were taken the baby had 5 generalized convulsions. He was treated with chloralhydrate orally and with insulin and 5% dextrose in 0-45% saline intravenously.

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REFERENCE


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infection, cerebral damage, or abnormalities. The effect of insulin treatment on the baby's general condition and weight was striking.

The disturbances in fat and amino acid metabolism are new features previously not recorded in this syndrome. These disturbances are probably related to the hyperglycaemia as such, and not to the newborn state. The rapid disappearance of the hyperlipidaemia with insulin therapy (after 2 days the serum looked clear) suggests that the hyperlipidaemia was of the same nature as that seen in true diabetes mellitus. In contrast to true diabetes mellitus the plasma NEFA level in our patient was normal and there was also no ketoacidosis. Possibly enough nicotinic acid was present in the proprietary formula (3-4 mg/day), to suppress the plasma NEFA and ketacid levels (Bagdade, Porte, and Bierman, 1967). Sufficient insulin might have been present to prevent ketonuria, as has been suggested to occur in hyperosmolar nonketotic diabetes.

In diabetic children aged 1 month to 15 years, Umbarger, Berry, and Guest (1963) found no differences in amino acid excretion levels and patterns as compared to normal children. Mütting (1966) has found increased free and peptide-bound amino nitrogen excretion in diabetes. According to Mütting (1958), methionine metabolism is abnormal in diabetes due to a decreased ability to oxidize methionine in the liver.

The speed with which the plasma methionine level returned to normal and homocystine disappeared from the urine after insulin therapy was begun, suggests that a relative lack of insulin rather than the age of our patient was causing the abnormal plasma and urine amino acid patterns.

### Discussion

Our patient fits the diagnostic criteria of transient diabetes of the newborn (Gentz and Cornblath, 1969). The diagnosis was made at 3 weeks of age, more than 12 hours before the onset of convulsions, and there was no conclusive clinical evidence of water solvent pair (Smith, 1960). Quantitative results were obtained by the same method as used for plasma. Excess disulphides in urine were detected by the cyanide/nitroprusside test (Smith, 1960). Ketones (2-oxoacids or acetone or acetoacetic acid) were tested for by reaction of urine with acetest tablets and 2:4-dinitro-phenylhydrazine.

Methionine and homocystine were identified by quantitative oxidation with performic acid to methionine sulphone and homocysteic acid, respectively.

### TABLE

**Blood Chemistry**

<table>
<thead>
<tr>
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<th>Day of Life</th>
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<tbody>
<tr>
<td></td>
<td>22</td>
</tr>
<tr>
<td>Blood glucose (mg/100 ml)</td>
<td>468</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td></td>
</tr>
<tr>
<td>Urea (mg/100 ml)</td>
<td>386</td>
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<tr>
<td>Sodium (mEq/l.)</td>
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<tr>
<td>Potassium (mEq/l.)</td>
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<td>Chloride (mEq/l.)</td>
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<td>GOT (Karmen Units/ml)</td>
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<tr>
<td>GPT (Karmen Units/ml)</td>
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<tr>
<td>Cholesterol (mg/100 ml)</td>
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<tr>
<td>Phospholipids (mg/100 ml)</td>
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<tr>
<td>TEFA (mg/100 ml)</td>
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<tr>
<td>NEFA (mEq/l.)</td>
<td>1,120</td>
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<tr>
<td>Insulin (µU/ml)</td>
<td>0·61</td>
</tr>
<tr>
<td>Plasma methionine (mg/100 ml)</td>
<td>3</td>
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</tbody>
</table>
Short Reports

Before having received any insulin, the serum insulin level was abnormally low in relation to the blood glucose level (Table). At the time of diagnosis some degree of insensitivity to insulin was suggested since injection of 2 units crystalline insulin intravenously (1·0 unit/kg) caused a less than 50% decrease in blood sugar concentration after 30 minutes. The necessity for insulin treatment for only 21 days, and the improvement of the glucose tolerance test with time, could be interpreted as a maturation of insulin production by the β-cells.

Our patient appeared to have a transient inadequate secretion of insulin, and in addition perhaps some degree of insulin insensitivity.

Summary

A dysmature infant at the age of 3 weeks had a transient nonketotic hyperosmolar hyperglycaemia with glycosuria, hypermethylioninaemia with homocystinuria, hyperlipidaemia, and relative hypo-insulininaemia. Methionine metabolism became normal after 5 days of insulin treatment.

At 9 months of age he responded normally to an oral glucose load.

A transient, inadequate secretion of insulin is suggested as causing the metabolic defects in the infant.

We thank Dr. M. F. G. Buchanan of the Department of Child Health and Paediatrics, University of Leeds, for allowing us to study the patient, and Mr. J. Williams, Institute of Child Health, University of Birmingham for the insulin assay.

REFERENCES


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Congenital Absence of Pituitary Gland and Adrenal Hypoplasia

Congenital absence of the pituitary gland and hypoplasia of the adrenal glands in an infant without anencephaly is rare, and we have been able to find reports of only 3 such cases (Blizzard and Alberts, 1956; Brewer, 1957; Reid, 1960). 3 further cases with similar, but not identical, congenital abnormalities of both the pituitary and adrenal glands have been described (Mosier, 1956; Dunn, 1966). Details of these 6 cases together with the case described in this paper are summarized in the Table. 2 of these 6 infants were boys, and the one described by Blizzard and Alberts (1956) had an extremely small penis.

In this paper we describe a further example of this syndrome in a boy who also had a very small penis. This finding may prove to be a useful external marker of a lethal congenital abnormality.

Case Report

This boy was born by normal vertex delivery at 41 weeks’ gestation to a healthy 17-year-old primigravida, and weighed 3·22 kg. The mother had taken iron and folic acid during pregnancy.

Although the baby breathed spontaneously 30 seconds after birth, he remained cyanosed. He had no detectable abnormalities in his heart or lungs, and a chest x-ray was normal. He was noted to have a very small penis, but the testes were palpable in the inguinal canals. He was nursed in 30% oxygen and became pink but was unable to suck and was fed through a nasogastric tube. On the 5th day of life he had a number of generalized convulsions and became apnoeic. Investigations at this time gave the following results: blood sugar 30 mg/100 ml, serum calcium 7·8 mg/100 ml, blood urea 128 mg/100 ml, serum sodium 155 mEq/l., potassium 6·1 mEq/l., and bicarbonate 27 mEq/l., arterial pH 7·33, Pco2 38 mmHg. There were no cells in the CSF which was sterile on culture, and blood culture was also sterile. He was treated with intravenous dextrose and intermittent positive pressure ventilation, but died a few hours later.

The main findings at necropsy were bilateral broncho-pneumonia, absence of the pituitary gland, and hypoplasia of the adrenal glands. Sections of the pituitary fossa revealed cartilage only, but unfortunately no attempt was made to exclude an ectopic pituitary in the track of Rathke’s pouch. The adrenals measured 1·5 × 0·6 × 0·2 cm and weighed less than 1 g each (normal 4 g). The kidneys were of normal size, and the relative sizes of the adrenals and kidneys were like those seen in the adult or anencephalic fetus. Histological examination of the adrenals showed absence of the fetal cortex, but the definitive adult cortex was twice as wide as normal in the newborn and in places was wider and had an irregular nodular appearance. The