and increased frequency dependency of total pulmonary resistance measured by forced oscillation.⁴ There is only one reference to a younger child with α -1 antitrypsin deficiency and respiratory disease.⁵ This child first presented at 8 years of age with a six and a half year history of chronic pulmonary disease, emphysema was diagnosed by lung biopsy at 13 years of age. In the present study three children, all with α -1 antitrypsin deficiency, one as young as 3 years of age, had significantly raised lung volumes when related to both age and height. In two of these children this was unresponsive to bronchodilator treatment so these findings are highly suggestive of emphysematous changes. Neither child had severe liver disease, nor respiratory symptoms or signs.

In all children with severe liver disease, irrespective of diagnosis, low lung volumes were shown. This association was particularly noticeable when lung volumes were related to age. The children with severe liver disease, however, were not significantly smaller than the other children studied, indeed one was on the 90th centile for height. The most likely explanation, therefore, for the association of severe hepatic disease and reduced lung volume is compression due to hepatosplenomegaly and ascites.

In conclusion, these results suggest that α -1 antitrypsin deficiency even in early childhood may

be associated with emphysema, and that in severe liver disease lung volume is reduced. We now intend to follow all such children prospectively in an attempt to determine the exact incidence of respiratory abnormalities and their evolution with time.

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Melatonin state in Mendenhall's syndrome

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SUMMARY We report a case of Mendenhall's syndrome that presented as hypoglycaemia. The clinical and biochemical features of the case are described including, for the first time, studies of melatonin state showing raised melatonin metabolite excretion in the urine as might be expected with disordered pineal function.

A syndrome of dysmorphism, dental precocity, hirsutism, acanthosis nigricans, abdominal protuberance, phallic enlargement, and insulin resistant diabetes mellitus was first described by Mendenhall in 1950.¹ Since then a number of similar cases have been recognised,² and in each of these diabetes mellitus has developed in mid childhood and the child has died of ketoacidosis, with the exception of

one child in whom hypophysectomy was performed.² Pineal hyperplasia has been found at necropsy of all patients dying.¹⁻³ We describe a further case in which the presenting symptom was hypoglycaemia in the neonatal period.

Case report

A boy, weighing 2520 g, was born after an uneventful pregnancy at 44 weeks' gestation. It was the second pregnancy of healthy non-consanguineous parents. Abdominal distention and facial dysmorphism were noted at birth. The features included a coarse facies with a prominent jaw, large eyes and ears, fine downy hair over the body, and short stubby fingers. He was also noted to have a long penis with normal sized testes. At 10 hours of age the baby started to have seizures secondary to

hypoglycaemia (blood glucose concentration <0.1 mmol/l) and intravenous dextrose was started. The intravenous infusion was required for 48 hours because of recurrent hypoglycaemia but after its withdrawal his blood glucose remained normal. Plasma insulin concentrations were measured by radioimmunoassay and found to be very high (1680 mU/l). These were remeasured at 2 months of age and were again high at 2460 mU/l (with a blood glucose concentration of 6.6 mmol/l).

At 7 months of age a glucose tolerance test gave a normal result but he had persistently raised insulin concentrations. Chromatographic analysis of his serum showed peaks coeluting with proinsulin and insulin. High concentrations of insulin were further confirmed by bioassay. Glucose tolerance tests were performed and insulin concentrations were measured on both parents and gave normal results. The boy's glucagon and testosterone concentrations (taken randomly) at this time were modestly raised: glucagon 53 pmol/l (normal range <50 pmol/l) and testosterone 0.7 nmol/l (normal range 0.07–0.67 nmol/l for prepubertal boys).⁴

The child developed acanthosis nigricans of the neck and axilla at 1 year of age. Primary dentition started at 3 months and secondary dentition at 3 years. His intelligence quotient was assessed as normal (112 by the Stanford-Binet test at 3 years). Other problems included tonsillar/adenoidal hypertrophy leading to middle ear disease. At the age of 7 he developed the first signs of diabetes mellitus with mild ketonuria, and a glucose tolerance test gave a glucose concentration of 3.8 mmol/l fasting and 17.1 mmol/l two hours after the load. Hyperinsulinaemia persisted with concentrations varying from 439 mU/l (blood glucose 3.8 mmol/l) to 4255 mU/l (blood glucose 14.3 mmol/l). A computed tomogram performed at this time showed no evidence of pineal enlargement. Combined pituitary function testing was performed. A total of 0.3 unit/kg of soluble insulin was given intravenously but hypoglycaemia was not induced. Normal concentrations of growth hormone, prolactin, cortisol, luteinising hormone, follicle stimulating hormone, and thyroid stimulating hormone were obtained. Random testosterone concentrations were measured on two further occasions and were 0.3 nmol/l and 0.8 nmol/l, respectively.

At 11 years of age he developed more pronounced glycosuria and symptoms of lethargy. A blood glucose profile over 24 hours showed his blood glucose varying between 5.4 mmol/l (fasting) and 12.5 mmol/l. This latter glucose concentration corresponded with a plasma insulin of 3300 mU/l and C peptide of 19.6 nmol/l showing grossly enhanced endogenous insulin secretion. (His glycosylated

haemoglobin was 11.7%.) Carbohydrate spacing, guar gum, a high fibre diet, and tolbutamide were used in an attempt to control his diabetes but with only minor benefit, which was not sustained. He was therefore started on insulin but despite soluble insulin 50 units in the morning and 44 units in the evening there was no improvement.

Assays for serum melatonin and metabolites have recently been developed⁵ and in view of the evidence for pineal hyperplasia it was clearly of interest to examine the patient's pineal hormone state. Urinary 6-sulphatoxymelatonin (aMT6s) measured over 24 hours was raised at 19.8 μ g (8 am–2 pm, 3.51 μ g; 2 pm–8 pm, 2.31 μ g; 8 pm–2 am, 0.85 μ g; and 2 am–8 am, 13.13 μ g). The mean (SD) normal range obtained from analysing urine from 11 children of this age was 7.58 (2.65) μ g/24 hours (C Bojkowski, unpublished data). Plasma melatonin concentrations were 26.1 pg/ml at 12 noon and 239.6 pg/ml at 12 midnight. Normal data for plasma melatonin concentrations are limited in children but a report by Waldhauser and Dietzel suggests that the night value for our patient is, at least, high normal.⁶

Discussion

The progression to diabetes mellitus in Mendenhall's syndrome has been well documented.^{1–3} Various reasons for the insulin resistance have been advanced but there has never been any evidence for appreciable insulin antibody formation, hormonal antagonists to insulin, nor for secretion of abnormal insulin. Reduced numbers of insulin receptors have been shown in erythrocytes (Perez Corral F, de la Vina S, Carbo ME, *et al.* Rabson syndrome: models of insulin resistance due to decreased number and affinity of insulin receptors in erythrocytes [Abstract]. *Diabetologia* 1980;19:36.), monocytes, and fibroblasts of patients with Mendenhall's syndrome.²

Our patient is the only child yet described to present with hypoglycaemia. He appears to have had a normal response to high insulin concentrations in the neonatal period with progressive resistance to insulin activity developing over the subsequent years. This raises the question whether the underlying abnormality is one of hyperinsulinism with insulin resistance developing as a protective mechanism (at least initially).

Plasma melatonin was at least high normal in the midnight specimen and excretion of melatonin metabolites were clearly raised in our patient. This has not previously been documented but perhaps is not surprising given the evidence for pineal hyperplasia in Mendenhall's syndrome. The features of the syndrome such as hirsutism and phallic enlargement, however, cannot be explained by excessive

melatonin secretion per se as melatonin administration has not been shown to duplicate the functional effects of the pineal. It is possible that other, as yet undefined, pineal hormones or metabolites may be implicated in causing some of the features of the syndrome.

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Collodion babies with Gaucher's disease

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SUMMARY Two neonates with acute infantile cerebral Gaucher's disease had prominent collodion skin. Ichthyosis has been described in some cases of metabolic lipid disorders, however, this is the first report of the association of lamellar desquamation of the newborn (collodion baby) with Gaucher's disease.

Gaucher's disease is characterised by an abnormal accumulation of cerebroside primarily in cells of the reticuloendothelial system. The disease is due to a deficient activity of lysosomal glucocerebrosidase and is transmitted as an autosomal recessive trait. It is a clinically heterogeneous disorder, however, with at least three recognised types. In the acute infantile cerebral form (type II) the baby appears normal at birth but soon exhibits neurological symptoms and hepatosplenomegaly. Death usually occurs in the first year of life. The skin is not pigmented in the acute infantile form. Collodion skin and ichthyosis are not recognised skin manifestations in any of the forms of Gaucher's disease.¹ We report two siblings with generalised ichthyosis associated with infantile Gaucher's disease.

Case reports

A 27 year old Lebanese woman was admitted to this hospital in September 1986 for her second confinement. There was no consanguinity with her Lebanese

husband and there was no family history of Gaucher's disease or ichthyosis. Her first pregnancy in 1984 resulted in the delivery of a boy (case 1) in another hospital in Sydney.

Case 1. A 3500 g boy was delivered by caesarean section at 39 weeks' gestation. Generalised thick collodion like skin, gross hepatosplenomegaly, and apathy were noted at birth. The ichthyotic skin peeled over the next five days and there were no subsequent skin lesions. Soon after birth he had recurrent laryngospasms, generalised convulsions, and a persistent thrombocytopenia. Diagnosis of Gaucher's disease was established by leukocyte enzyme assays. He died at the age of 3 months after a respiratory arrest in hospital. The parents did not consent to a postmortem examination.

Case 2. The mother presented at 20 weeks' amenorrhoea but declined the offer of prenatal diagnosis. Polyhydramnios occurred in late gestation and a boy weighing 3400 g was delivered by caesarean section at 40 weeks' gestation. He was apnoeic at birth and remained dependent on assisted ventilation until death at 11 days of age. Generalised tight collodion like skin (figure), gross hepatosplenomegaly, and generalised joint contractures were noted. He was apathetic from birth and had frequent refractory convulsions and opisthotonos. The tight collodion like skin started to shed from the first day of life. At the time of death the hands, feet, and back were scaling in large sheets.