The only satisfactory clinical approach to this disease at present is heterozygote detection with genetic counselling and antenatal diagnosis.

Summary

Treatment with a diet low in vitamin A failed to halt the neurological deterioration in a 9-year-old girl with juvenile onset metachromatic leucodystrophy.

Thanks are due to Drs. A. P. Norman and R. Stephens for allowing me to publish details of their case; to Dr. Patrick (Enzyme Department, Institute of Child Health) and Mr. Goodwin (Neurochemistry Department, National Hospital, Queen Square) for enzyme and sulphatide estimations; and to Miss C. Vincent for secretarial help.

References


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Lipodystrophy of limbs associated with insulin resistance

In 1974 Dunnigan et al. described a new form of partial lipodystrophy occurring in several women from 2 families from the north of Scotland. They had loss of subcutaneous fat from the limbs and trunk, but with normal or increased facial fat. Other features were acanthosis nigricans, hypertrophy of the labia minora, insulin resistant diabetes mellitus, and hypertriglyceridaemia.

We report a girl in whom the evolution of the disease has been observed over a 3-year period.

Case report

The patient was first seen here at the age of 11 years. She was born at term to healthy unrelated parents; birthweight was 3.5 kg. There were no neonatal problems. At the age of 8 the parents noticed that her legs and arms had become thin. This had developed over a few months, but then remained static. There was no family history of lipodystrophy, nor of diabetes, and there was no family link with the north of Scotland.

Examination showed that she was on the 50th centile for both height and weight. There was marked loss of subcutaneous fat of the lower limbs up to and including the buttocks, and loss of fat of the arms most marked in the forearms and hands (Fig. 1). Facial appearance was normal. Skinfold measurements over triceps, biceps, thigh, and calf were all below the 3rd centile, whereas measurements of abdominal, subscapular and suprailliac skin folds were all on the 50th centile. There was no hepatomegaly. At that time there was no abnormal pigmentation nor any genital hypertrophy. Physical examination was otherwise normal.

The patient has been seen on two further occasions. Examination at the age of 12 was essentially unchanged, but at the age of 14 she was pubertal and had developed
hypertrophy of her labia minora and acanthosis nigricans of the axillae and buttocks. There was no progression of lipodystrophy during the period of observation.

When first seen at the age of 11 fasting serum triglyceride concentration was 107 mg/100 ml (normal range 34–87 mg/100 ml, mean 46); though virtually unchanged a year later, at the age of 14 it was 170 mg/100 ml, and lipoprotein electrophoresis showed an increase in pre-β-lipoprotein: serum cholesterol concentrations have been normal (180 mg/100 ml, mean of 3). Glucose tolerance tests (using oral glucose 1·75 g/kg bodyweight to a maximum of 50 g) were performed at the ages of 11, 12, and 14. Results are shown in Fig. 2. Fasting levels of serum insulin have been persistently high while fasting plasma glucose concentrations have been normal, indicating a degree of insulin resistance. After the glucose load in the first test, plasma glucose remained normal but serum insulin values were high; the two subsequent tests showed increasing hyperglycaemia and hyperinsulinaemia.

Normal results have been obtained for urine analysis, serum thyroxine, serum bilirubin and transaminases, and urinary keto- and hydroxycorticosteroids. There was a normal diurnal variation of plasma cortisol, and growth hormone levels were normal. Bone age was compatible with chronological age and an intravenous pyelogram was normal.

The parents were investigated because of the possible familial nature of this syndrome. Father had a fasting plasma glucose of 86 mg/100 ml and serum insulin 17 μU/ml; serum triglyceride was 81 mg/100 ml, cholesterol 223 mg/100 ml, and lipoprotein electrophoresis was also normal.

**Comment**

Dunnigan *et al.* (1974) have described a new form of lipodystrophy which is associated with hypertriglyceridaemia and diabetes mellitus with some insulin resistance. Additional features in this syndrome are acanthosis nigricans and labial hypertrophy. Lipodystrophy occurred in 2 families from nearby towns in the north of Scotland and although all the patients were female, an autosomal dominant transmission with variable expressivity was suggested. The close geographical origins of both families suggested that this syndrome might have common genetic source.

Our patient fulfils the clinical criteria of this syndrome, having lipodystrophy, acanthosis nigricans, and labial hypertrophy. She has also shown increasing insulin resistance and hyperglycaemia over the past 3 years, and fasting serum triglyceride has become high. There is, however, no family history nor any link with the north of Scotland; if the condition is familial, the mode of inheritance in our patient is unclear.

There are two other well recognized lipodystrophy syndromes occurring in childhood. They are (1) partial lipodystrophy, defined by Senior and Gellis (1964) as symmetrical absence of facial fat, with or without disappearance of fat from arms, chest, abdomen, and hips, but with retention of distal subcutaneous fat, and (2) congenital total lipodystrophy (Seip, 1959) with complete absence of subcutaneous fat and hepatomegaly, excessive growth in early childhood, and diabetes mellitus developing in later childhood. The syndrome described in this patient is distinct from either of these syndromes. It appears to predispose to diabetes mellitus and hypertriglyceridaemia. Further studies are required to elucidate the underlying disease process.

**Summary**

A syndrome comprising lipodystrophy of the limbs, acanthosis nigricans, hypertrophy of the labia minora, and hypertriglyceridaemia and insulin resistance is described. This has not been documented before in childhood.

We are grateful to Dr. J. D. Roscoe for referring this girl to Professor O. H. Wolff.
Short reports

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Perinatal infections caused by
Haemophilus influenzae

Haemophilus influenzae is occasionally isolated from the female genital tract (Hurley, 1970), and a few cases of perinatal infections involving either the mother or the baby have been reported. Ellner and Shahid (1969) described 2 cases of puerperal bacteremia caused by H. influenzae, one due to a capsulated type f strain, the other to a rough untyped strain isolated in mixed culture. Though both patients had evidence of endometritis, their babies appeared to be uninfected. The rarity of neonatal infections has been attributed to the passive transfer of protective antibody to the baby, since most adults possess serum bactericidal activity against H. influenzae type b (Fothergill and Wright, 1933). Graber et al. (1971), however, found a much lower incidence of antibody to a strain of H. influenzae type b in both maternal and cord bloods, and considered that this indicated increasing susceptibility of neonates to this organism. These findings were criticized on experimental grounds by Mpairwe (1972), whose own findings accorded with those of Fothergill and Wright (1933). Neonatal infections were reported by Mathies, Hodgman, and Ivler (1965), Collier, Conner, and Nyhan (1967), and Graber et al. (1971), and were all attributed to absence of protective antibody in the maternal sera at the time of delivery. Ingman (1970) described 2 cases of neonatal septicemia caused by H. influenzae; one strain was capsulated type b, the other strain was not typed. Both mothers had clinical evidence of endometritis, though in neither case was the organism isolated from the maternal genital tract. Berczy, Fernlund, and Kamme (1973) isolated a noncapsulated strain of H. influenzae from the brain of a 22-week-old fetus and subsequently isolated a similar organism from vaginal discharge present in the mother.

Zinner et al. (1972) reported a case of puerperal bacteremia and neonatal sepsis due to Haemophilus parainfluenzae, supported by immunological studies which indicated that the baby was infected during labour.

In this paper we report 2 further cases of perinatal infection, in which noncapsulated H. influenzae was recovered from both mother and baby.

Case reports

Case 1. A 31-year-old mother of 2 healthy children was admitted to hospital at term after an uncomplicated third pregnancy. For 2 days before labour she noticed a white odourless vaginal discharge, which was not investigated further. Onset of labour occurred some 18 hours after spontaneous rupture of membranes. During labour, the patient developed a temperature of 39.6° C, accompanied by rigors, but antibiotics were withheld until after delivery. A female infant weighing 3400 g was delivered by forceps extraction under epidural anaesthesia. The baby gasped after one minute, but regular respirations were not established until 6 minutes, and intubation and intermittent positive pressure ventilation were required initially. At 10 minutes the baby was pink with good tone, but showed tachypnoeas. The heart and lungs were clinically normal, the liver and spleen were not enlarged, but the kidneys were easily palpable. Chest x-ray showed patchy consolidation in the right mid- and upper zones. The maternal liquor was noticed to be slightly offensive. A clinical diagnosis of neonatal septicemia was made, and the baby was immediately treated with intravenous penicillin and intramuscular kanamycin. A blood sample taken from the baby soon after delivery proved sterile on culture. Gastric aspirate showed numerous leucocytes in the Gram-stained deposit, but no organisms were seen and cultures were sterile. The urine was sterile. H. influenzae was isolated in pure culture from swabs of umbilicus, ear, nose, and throat, and from the tip of the endotracheal tube. The organism was noncapsulated. The cord blood IgM level was 40 mg/dl.

Subsequent progress was satisfactory. The tachypnoea settled within 24 hours, and chest x-ray became normal. Jaundice was noticed within the first 24 hours, serum bilirubin rising to 15 mg/dl on the fifth day. Penicillin was replaced on the fourth day by a 10-day course of ampicillin in view of the bacteriological reports, and the infant appeared normal when examined at 4 weeks.

H. influenzae was isolated from the fetal surface of the placenta and from a high vaginal swab taken from the mother soon after delivery. A maternal blood sample taken during labour was sterile on culture. The mother received penicillin and kanamycin after delivery, but H. influenzae was still isolated from the vagina several weeks later before treatment was changed to oral ampicillin combined with povidone-iodine pessaries. There was no personal or family history of infections likely to be associated with H. influenzae.