Hypomelanosis of Itô: a neurocutaneous syndrome

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SUMMARY A 2½-year-old girl with hypomelanosis of Itô is described. There is a bizarre distribution of congenital depigmentation stopping abruptly at the midline anteriorly, with whorl-like and zig-zag patterning. As can happen in this syndrome, there is severe retardation and intractable epilepsy, with computerised tomography showing gross cerebral atrophy.

Hypomelanosis of Itô, a neurocutaneous syndrome which has hypopigmented areas of skin in whorls, streaks, and patches, was first described by Itô.¹ The cutaneous manifestations may be unilateral or bilateral. Often other systems are affected, especially the central nervous system.² The distribution of the hypopigmented skin lesions resembles that of the hyperpigmented lesions in incontinentia pigmenti, and for this reason hypomelanosis of Itô has also been called incontinentia pigmenti achromians.¹ However the two conditions are probably unrelated.

Case report

The patient, a 2½-year-old girl, is the fourth child of healthy Pakistani parents who are 1st cousins. There is no family history of retardation, fits, or skin depigmentation.

No medicines were taken in the first trimester. At 22 weeks' gestation hypertension was noted, and the mother was admitted twice for 5 days' bed rest. Normal delivery took place after spontaneous onset of labour at term, birthweight 2.41 kg, Apgar score 7 at one minute.

From the age of a few hours she began to have intractable epileptic fits, initially in the form of apnoeic and cyanotic attacks, and later obvious major seizures, at first affecting predominantly the left side. Very frequent generalised seizures have continued unabated despite various anticonvulsants.

Depigmentation was noted at birth, and the striking pattern (Figs 1 and 2) has not changed. There is also a large area of 'mongolian blue spot' on the right side of the back (not clearly visible on photographs). A loud pansystolic murmur with a systolic thrill was noted in early infancy, thought to be due to a ventricular septal defect. Digoxin was given, but one episode of cardiac failure occurred

during a respiratory infection. The murmur disappeared by age 2 years, and it is thought that the septal defect has closed.

The patient has remained severely mentally retarded, with no head control or speech, and little response to visual or auditory stimuli. In addition, there is a right hemiplegia.

Investigations for a metabolic defect or an intra-uterine infection have been negative, and the chromosomes are normal (with banding). Electroencephalograms were abnormal. A record at 4 weeks

Fig. 1 Patient at age 2½ years. Depigmented areas can be clearly seen on the chest (stopping near the midline), as well as on both arms and the right leg. The depigmented areas are particularly well shown because of the surrounding normal dark skin.

Fig. 2 Patient at age 2½ years. Depigmented areas can be seen on the back in a zig-zag pattern, as well as on the right arm and leg, and left shoulder.

showed high voltage waves 2 to 3 Hz, sometimes associated with spikes and sharp waves in irregular complexes. These abnormalities were symmetrical but a week later the slow wave activity was very prominent in the left temporal area, with flattening of the corresponding runs on the right side. Seven months later the asymmetries were much more evident and widespread, little electrical activity being recorded on the right side. On the left side there were frequent outbursts of spikes of low voltage and there were also repetitive suppression bursts. Computerised tomography shows gross cerebral atrophy, appreciably worse on the left, and there is porencephalic dilatation of the right lateral ventricle.

Dermatoglyphs were normal: the fingerprints showing 2 whorls, 1 twinned loop, and 7 ulnar loops (right: U, W, W, U, U left: TL, U, U, U, U). The triradii a, b, c, d, and t were normally placed. There was a right hypothenar distal loop and a left hypothenar outer loop. There are no thenar patterns, a bilateral interdigital IV loop, and an incomplete single transverse palmar crease on the left. The left

hallucal area bore a distal loop, and the right hallucal area an open field.

Discussion

The nature and distribution of depigmentation are typical of hypomelanosis of Itô. The whorl-like patterning, and the zig-zag appearance, are quite extraordinary and no explanation is evident. There is a certain symmetry about the appearance on the back, but on the chest and abdomen the depigmentation is striking in the way it stops just short of the midline. Pattern asymmetry is well recognised in many lower animals, and there are reasons for thinking that even quite bizarre distributions of depigmentation may be under genetic control.³ McKusick's catalogue⁴ of inherited disease lists hypomelanosis of Itô as an autosomal dominant disorder, although the evidence for this mode of inheritance, or indeed for any genetic aetiology, is inconclusive. It is worth noting that parental consanguinity has been recorded twice before.⁵

It is interesting that the particularly severe left cerebral atrophy coincides with the predominantly right-sided depigmentation and right hemiplegia.⁶ Other examples of unilateral skin disorders with underlying defects are well known (for example the Sturge Weber syndrome, and the unilateral psoriasis and ectromelia syndrome), but the pathogenesis in this case is not so clear, particularly because of the symmetrical nature of the lesion on the back and asymmetrical distribution on the chest and abdomen. It has been suggested that this syndrome is due to a defect of neural crest development,⁷ although other disorders where a defect of neural crest development has been incriminated (for example Waardenburg's syndrome and Treacher Collins syndrome) are more notable for their bilateral symmetry.

Congenital heart disease does not appear to be associated with this syndrome, although in one case triphalangeal thumbs and a heart murmur suggested the possibility of the Holt Oram syndrome.⁸ In this case the dermatoglyphs were normal, and provided no evidence of the Holt Oram syndrome. Mental retardation and epilepsy are well recognised complications of hypomelanosis of Itô,² and computerised tomography is a useful investigation that may help to predict the outcome in newly diagnosed newborn infants.

Most of the reports of this condition are in black patients.² This is probably due to the fact that the condition is likely to be more difficult to detect in white-skinned people, although the use of a Wood's lamp may help.² Even if such cases were detected reporting might be deterred because of the difficulty of obtaining good illustrations.

There is debate about the precise histological findings, but the most common description is of a reduction of melanocytes without pigmentary incontinence. Thus the term incontinentia pigmenti achromians may be best avoided, although the whorl-like patterning does resemble the apparently unrelated disorder of incontinentia pigmenti. It has even been suggested that it is the *depigmented* areas in hypomelanosis of Itô which are normal, but this has not been generally accepted and in our patient the pigmentation of the rest of the skin was the same as that of the relatives and was appropriate for their racial extraction.

Hypomelanosis of Itô is another example of a neurocutaneous syndrome. The pathogenesis is unknown.

This case was reported at a clinical meeting of the Section of Dermatology, Royal Society of Medicine, in June 1980.

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