Incontinentia Pigmenti

ASSOCIATED WITH RAISED ALKALINE PHOSPHATASE AND DISTURBANCE OF THE PLASMA PROTEINS*

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SUMMARY

A case of incontinentia pigmenti in a 1-month-old infant girl is described. The patient had an associated raised alkaline phosphatase level, hyperphosphataemia, as well as abnormalities of the plasma proteins. These may possibly be a feature of incontinentia pigmenti. It is suggested that biochemical abnormalities should be sought in future cases of this syndrome.

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Incontinentia pigmenti (the Bloch-Sulzberger syndrome) is a rare, inherited disease characterized by striking cutaneous changes associated with other ectodermal and occasionally with mesodermal anomalies.

The cutaneous features of incontinentia pigmenti are well recognized. They consist of a vesicular-bullous eruption presenting in the early neonatal period, to be followed, or accompanied, by verrucous lesions and bizarre pigmentation. However, biochemical abnormalities have rarely been recorded in this condition. The purpose of this presentation is to report the association of elevation of the alkaline phosphatase level and abnormalities of the plasma proteins with this syndrome.

CASE REPORT

A Bantu infant girl was referred to hospital on the fifth day of life because of skin lesions. Dark patches were present on the trunk at birth. On the eighth day widespread vesicles appeared. This was followed a week later by raised pigmented lesions. The mother's pregnancy had been uneventful. She had not had any abnormalities relating to her skin during the course of her pregnancy, nor was she aware of any cutaneous lesions during her own infancy or childhood. There was no history of any abortions. Two male siblings, aged 10 and 1½ years, were healthy and had never had skin problems.

The patient was first seen in the dermatology department on the 29th day of life. Examination at that time revealed a healthy and vigorous infant who weighed 3 026 g. There was no jaundice. The liver was enlarged to 1½ finger-breadths below the right costal margin. Apart from this, and the cutaneous findings, there were no other physical abnormalities or congenital defects.

Chocolate-brown, blotchy pigmented areas were present on the trunk and limbs (Fig. 1). In addition, there were greyish-brown verrucous nodules and a few erythematous papules on the buttocks, thighs and legs. These had a striking linear grouping (Fig. 2). Similar nodular lesions

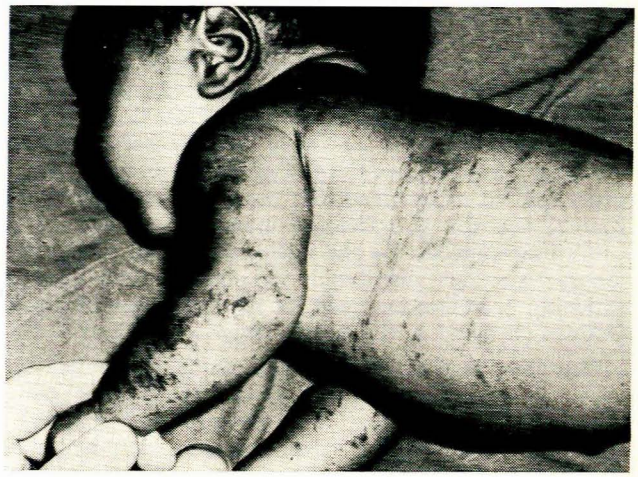

Fig. 1. Showing pigmentation of trunk and upper limbs. Note verrucous lesions on elbows and forearms.

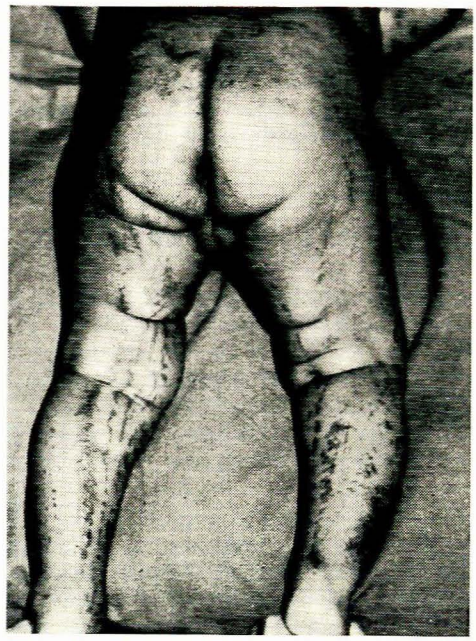

Fig. 2. Showing linear arrangement of lesions on lower limbs.

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were present on the arms and dorsae of the hands, but the linear arrangement was less obvious. The palms and soles were unaffected, and there was no nail dystrophy or alopecia. A tentative diagnosis of incontinentia pigmenti was made.

Laboratory Investigations

Haemoglobin concentration was 12·0 g/100 ml; white blood count and differential count were within normal limits; ESR (Wintrobe) was 18 mm in the first hour; the Wassermann reaction was negative; and serum electrolyte values were normal. Liver function tests were as follows: total bilirubin, less than 1 mg/100 ml; SGOT 30 units/ml; SGPT 6 units/ml; lactic dehydrogenase 7 units/ml; and alkaline phosphatase 47 King-Armstrong units/100 ml. Serum calcium was 4·9 mEq/litre; serum inorganic phosphorus 6·9 mg/100 ml; and blood glucose level 75 mg/100 ml.

Protein electrophoresis showed the following: total protein 6·0 g/100 ml; albumin 13% (0·8 g/100 ml); alpha-1 globulin 6% (0·4 g/100 ml); alpha-2 globulin 27% (1·6 g/100 ml); beta-globulin 27% (1·6 g/100 ml); gamma-globulin 27% (1·6 g/100 ml). Repeated estimation of the alkaline phosphatase remained elevated at 45 King-Armstrong units/100 ml.

Histology

Microscopical examination of skin biopsy specimens taken from plaques on a leg and arm was carried out by Dr James Notman of the School of Pathology, Johannesburg. This showed acanthosis, hyperkeratosis and intra-epidermal cornification. There was slight reduction of melanin pigment in the basal layer while there was abundant deposition of melanin in the melanophages of the upper dermis (Fig. 3). The histological findings confirmed the clinical diagnosis of incontinentia pigmenti. The patient was lost to follow-up.

DISCUSSION

The skin changes are the most striking features of incontinentia pigmenti. These occur in 3 phases:

1. Inflammatory Phase

This is characterized by crops of clear vesicles, bullae, papules or 'pustules' which appear on the limbs or trunk. These may be symmetrical in distribution and may have a linear arrangement. They may be present at birth or appear at any time up to the first 4 months of life, and may remain for periods varying from a few days to several months.

2. Hyperkeratotic Phase

This is characterized by nodules or verrucous-like plaques which appear either in areas previously affected by lesions of the inflammatory phase or on normal skin. The nodules and wart-like patches may have a linear grouping. They may last for about one year.

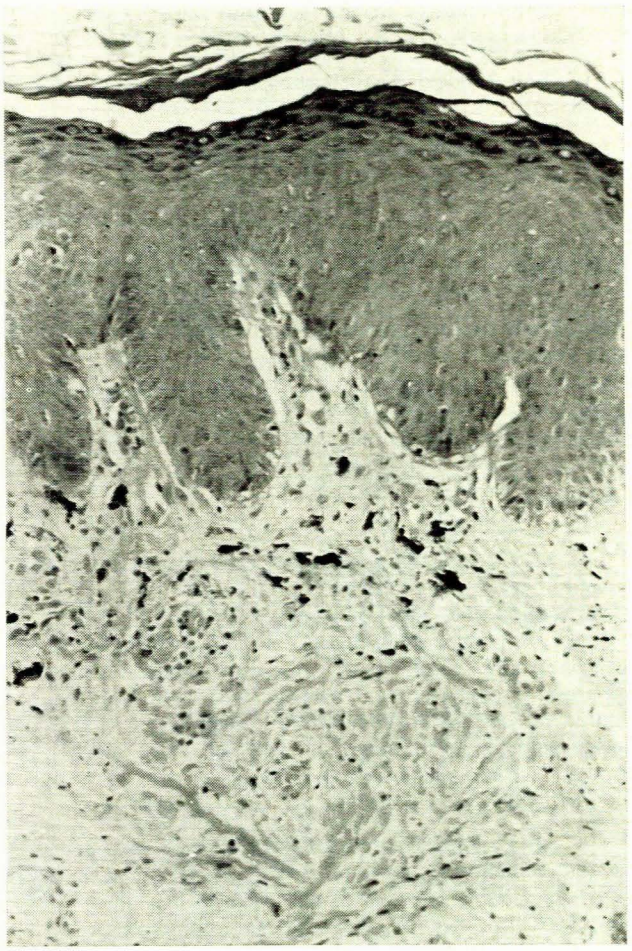

Fig. 3. Photomicrograph showing clumps of melanin in the upper dermis.

3. Pigmented Phase

This is characterized by greyish-brown pigmented patches which may have a 'splashed', whorled or dendritic arrangement. The bizarre pigmentation may occur in areas affected with active or regressing inflammatory or verrucous lesions or in previously uninvolved skin. Generally the pigmented areas persist for many years, gradually fading with time.

Although the skin lesions are the most striking manifestations of this syndrome, they are the least significant

since they are ultimately self-limiting. There may, however, be associated mesodermal and other ectodermal anomalies such as:

(i) Ocular abnormalities.[1] These include pseudo-glioma, optic nerve atrophy, retinal detachment, strabismus and a condition resembling retrolental fibroplasia.[2]

(ii) Dental abnormalities,[3] viz. cone-shaped teeth or partial anodontia.

(iii) Abnormalities of the hair and nails.[4] Bald patches and malformation of the fingernails may occur.

(iv) Neurological abnormalities.[5] These include spastic paresis, convulsions and mental retardation.

(v) Osseous malformations.[6] High palatal arch and other bony abnormalities may occur.

Aetiology

Although sporadic cases of incontinentia pigmenti have been reported without a family history of skin lesions, the frequent familial incidence of the disease suggests it is a hereditary syndrome.

Histology

The histological features were consistent with a diagnosis of incontinentia pigmenti. The finding in some cases of a reduction in the amount of melanin in the basal layer prompted earlier authors[7,8] to suggest that there was an abnormality in the basal cells in this condition rendering them unable to retain pigment which diffused into the dermis to be taken up by dermal histiocytes, hence the designation incontinentia pigmenti. It has since been shown that in some cases there is not a deficiency but in fact an excess of pigment in the basal layer.[9]

The cutaneous lesions in incontinentia pigmenti are usually self-limiting and the prognosis is good. Isolated fatal cases have, however, been reported during the early phase of the disease.[10,11] Those cases that have central nervous system and eye involvement usually have a more serious outcome.

Significance of the Biochemical Abnormalities

The raised alkaline phosphatase and inorganic phosphorus levels, as well as the disturbances in plasma proteins in this patient require elucidation.

Raised alkaline phosphatase and serum phosphorus. Significant hyperphosphatasia occurs, in addition to obstructive jaundice, with cholangitis, intrahepatic malignancy and other infiltrative lesions of the liver, none of which occured in this patient. Elevation of the alkaline phosphatase level also occurs with increased osteoblastic activity associated with the laying down of new bone as in the early period of life, at which time it causes a moderate elevation of this enzyme ranging from 15 - 20 King-Armstrong units/100 ml. Increased osteoblastic activity with raised alkaline phosphatase levels is also a feature of rickets, hyperparathyroidism and renal insufficiency.

The finding of hyperphosphataemia and hyperphosphatasia with normal serum calcium levels might suggest renal osteodystrophy due to progressive glomerular failure as a cause for these biochemical disturbances. However, the blood urea was not raised, there was no metabolic acidosis, as indicated by the normal plasma CO_2 content, and there were no radiological abnormalities of the skeleton, thus making a diagnosis of bone changes secondary to chronic renal failure very unlikely.

Abnormal plasma proteins. The low concentration of albumin might reflect decreased protein synthesis or increased loss, either as a result of renal disease or loss through the gastro-intestinal tract (protein-losing gastro-enteropathy). The finding of normal liver function tests, with the exception of the raised alkaline phosphatase, excludes a hepatic cause for the hypo-albuminaemia. There was no evidence of renal disease to which to attribute protein loss via the kidney. Investigations to establish protein-losing gastro-enteropathy were not carried out. The hyperglobulinaemia may have been due to hepatic inflammation. Although the liver was slightly enlarged clinically, none of the liver function tests support a finding of hepatocellular damage. Furthermore, hepatocellular disease gives rise mainly to a raised gammaglobulin fraction, while in this case there was, in addition to hypergammaglobulinaemia, also elevation of the alpha and beta fractions. Raised gammaglobulins also occur in a wide variety of infections, in the malignant lymphomata and in the connective tissue disorders. None of these conditions was responsible for the plasma protein abnormalities in the patient, and its cause remains an enigma.

It would indeed be of interest to establish whether the raised alkaline phosphatase level together with the hyperphosphataemia and the disturbances in the plasma proteins is a general feature of incontinentia pigmenti or whether it represents the manifestation of some complicating factor.

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