SEIP—LAWRENCE SYNDROME
(Three cases in a family)

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A rare episode of Seip-Lawrence syndrome manifesting in all three siblings of consanguinous parents is reported. Two children were male and one female. They exhibited low intelligence, gaunt facies, depressed bridge of nose, large low-set ears, thick lips and protruberant abdomen. Skin was showing hypermelanosis, hypertrichosis, absence of subcutaneous fat and acanthosis nigricans with very prominent perianal rugosities. In addition, the first child was short statured having hypertrophic clitoris, hepatomegaly, left ventricular hypertrophy, hyperglycaemia and glycosuria without ketoacidosis. The second child was having enlargement of penis, left ventricular hypertrophy, hepatosplenomegaly and abnormal GTT. The third and the youngest child was having only cutaneous changes and no visceromegaly or biochemical abnormality. None of these patients were having gigantism and advanced bone age.

Key words : Seip-Lawrence syndrome, Congenital total lipodystrophy, Acanthosis nigricans, Insulin resistant non-ketotic diabetes mellitus.

Seip-Lawrence syndrome (SLS) is a rare congenital or acquired total lipodystrophy characterised by complete absence of body fat, accelerated prepubertal growth, advanced bone age, muscular prominence, genital hypertrophy, visceromegaly and insulin resistant non-ketotic diabetes mellitus.[1,2] Skin manifestations reported with this disorder include acanthosis nigricans, generalised hypertrichosis and hyperpigmentation.[3-5] Only 50 patients of this peculiar anomaly have so far been documented in the literature.[6] The cases described from India had been very few.[7,8] We report an interesting episode of SLS manifesting in all the three siblings of consanguinous parents, associated with some unusual features.

Case Reports

Case 1

A 13-year-old girl was brought to us with retarded growth and dark, thickened skin on the body folds since her early childhood. The patient was the eldest of three children born to healthy consanguinous parents. She had delayed milestones and not yet attained menarche. Her two younger brothers had a similar skin problem with retardation of growth. The patient was of short stature (body height 108 cm and head circumference 52.5 cm), had gaunt facies, depressed nose bridge, large low set ears, thick lips, large crowded teeth, thick fissured and pigmented tongue and a prominent abdomen (Fig. 1). The subcutaneous fat was completely absent with normal skin elasticity, generalized hyperpigmentation, hypertrichosis and acanthosis nigricans involving all the major flexures. Nails were normal. Genital examination showed clitoral hypertrophy (Fig. 2). Hepatomegaly and tachycardia were alo present. A moderate mental retardation was recorded with an IQ of 30-80.

Laboratory examination showed persistent hyperglycaemia and glycosuria without ketoacidosis. Fasting blood sugar was 362 mg% ; post prandial blood sugar 566 mg% ; serum cholesterol 200 mg% and triglycerides 126 mg%. Estimation of serum protein-bound iodine (PBI), basal metabolic rate (BMR) and urinary 17-ketosteroids were normal. Liver and kidney function tests including intravenous pyelogram

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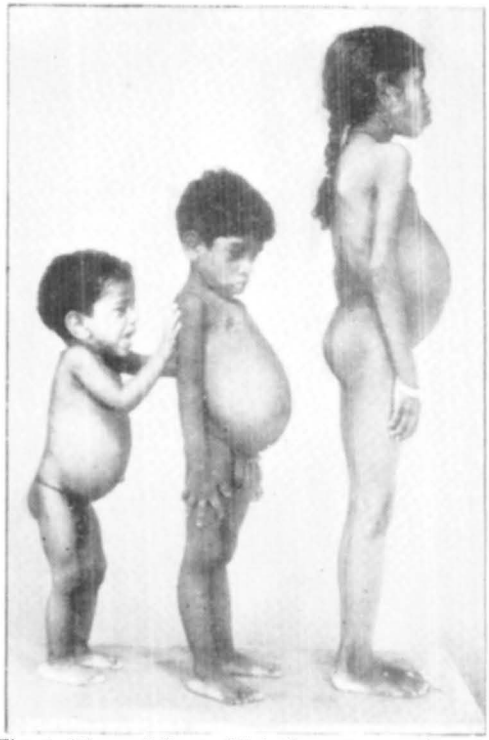

Fig. 1. Three siblings of Seip-Lawrence syndrome with the characteristic features of the disease (Case 1, 2, 3).

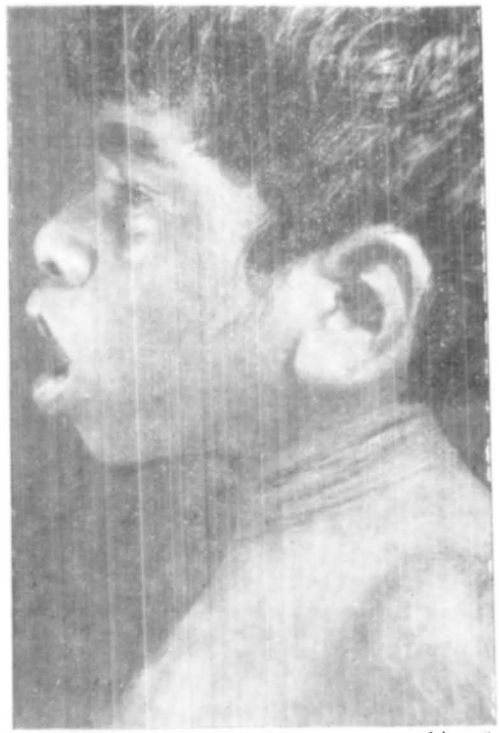

Fig. 3. Abundant dark scalp hair almost reaching the eyebrows, typical gaunt facies, prominent ears, marked hypertrichosis and hyperpigmentation over the face, body and arms with acanthosis nigricans over the neck and axilla (Case 2).

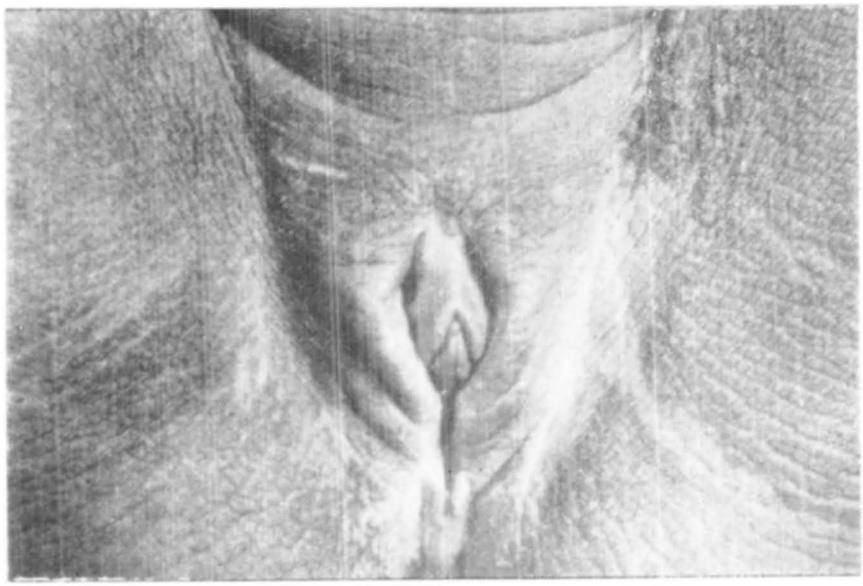

Fig. 2. Acanthosis nigricans in the groin and hypertrophy of the clitoris (Case 1).

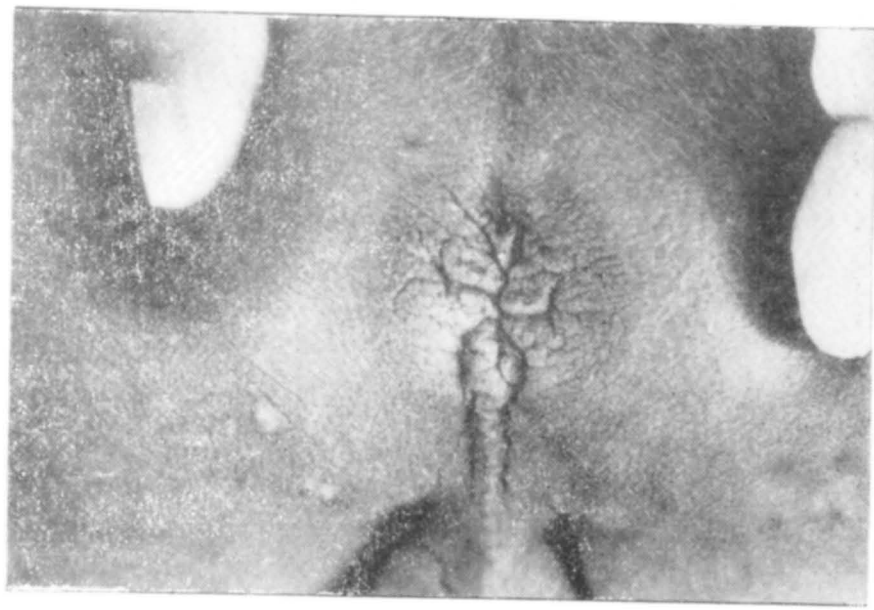

Fig. 4. Prominent perianal rugosities with hypertrichosis and hyperpigmentation (Case 2).

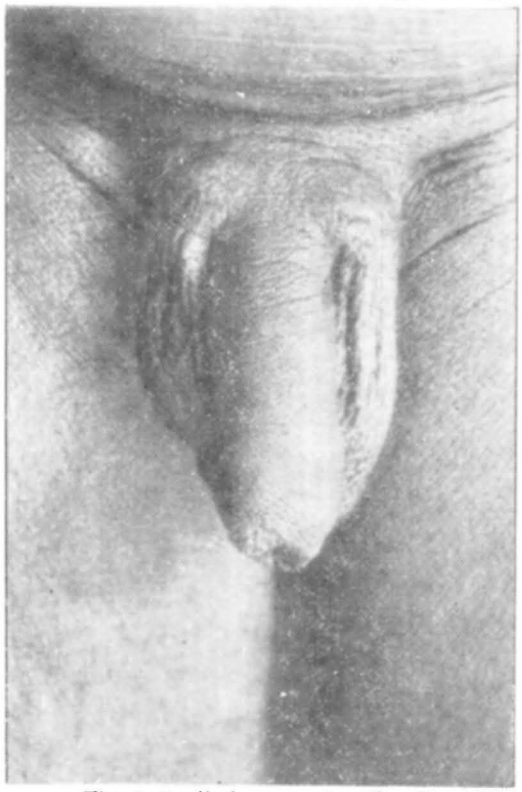

Fig. 5. Penile hypertrophy (Case 2)

were normal. ECG showed left ventricular hypertrophy with sinus tachycardia. X-ray chest demonstrated cardiomegaly and radiological assessment of her bone age was in accordance with chronological age. Administration of plain insulin upto 200 units per day was inconclusive.

Case 2

Case 2, a second of the three in the family, was aged four years and had delayed milestones. His height was 88 cm and head circumference was 46 cm. His physical presentation was quite similar to the earlier patient with total lipodystrophy and prominent cutaneous abnormalities (Figs. 1, 3, 4). Penile enlargement was conspicuous without pubic hair or testicular enlargement (Fig. 5). He had a mild degree of splenomegaly in addition to other systemic features present in his sister. Blood sugar was normal with no glycosuria. Nevertheless, he had an abnormal GTT. Serum triglycerides were 162 mg%, ECG showed left ventricular hypertrophy and sinus tachycardia. Cardiomegaly was detected on chest X-ray.

Case 3

Case 3, youngest of the three siblings was 2 years old. His height was 75 cm and head circumference was 45 cm. His physical appearance and skin manifestations were similar to case 1 and 2 but of a lesser degree (Fig. 1). Further, he had no splenomegaly or cardiomegaly. Investigations revealed neither hyperglycaemia nor glycosuria. Serum triglycerides were 107 mg%. GTT was within normal limits. ECG and X-ray chest also did not reveal any abnormality.

Histopathology

Haematoxyln-eosin stained sections revealed complete absence of subcutaneous fat and features of acanthosis nigricans from the anterior abdominal wall and axilla respectively.

Comments

The credit of recognising the syndrome appears to be shared equally by Lawrence[1] and Seip.[2] It is, however, worthwhile to point out that the former thought it to be acquired while the latter claimed it as congenital.

Reed et al[4] proposed the name of 'Seip-Lawrence Syndrome' (SLS) for this condition which combines both the congenital and acquired forms under one entity. Undoubtedly, our patients had the characteristic clinical and biochemical abnormalities suggestive of SLS, yet they displayed some variation in the disease presentation that deserve special mention.

Autosomal recessive mode of inheritance has been the usual pattern of transmission, affecting either one or two members in the family.[1,3,4] However, in our series, it manifested interestingly in all three siblings in the family with conspicuous parental consanguinity.

Prepubertal rapid growth resulting in gigantism and advanced bone has been described in a number of children with this disorder.[3] Remarkably, these features were absent in our patients. Based on the data from long term follow up studies of this condition, Reed et al[4] pointed out that these children may look normal or even appear shorter in later years of life due to sudden slowing of growth that occurs around tenth year. In fact, the first patient in our series was short statured confirming the above view.

Generalized loss of subcutaneous fat, hypertrichosis, hypermelanosis and acanthosis nigricans[4,5] were the cardinal clinical features amongst the patients under review. Increased perianal rugosity, a remarkable manifestation noted in the present study has never been reported earlier in SLS. However, such a feature was observed by Roth et al[10] in leprechaunism, a rare congenital disorder first reported by Donohue and Uchica,[11] which resembles closely with SLS. It is therefore imperative to appreciate the differentiating features in the two—namely muscular wasting, fasting hypoglycaemia, postprandial hyperglycaemia, insulin hypersensitivity, hyperplasia of the islets of Langerhans and depressed innate immunity with a high rate of mortality rarely surviving more than a year after birth in leprechaunism. Similarly, it is most unlikely that our patients are suffering from the syndrome described by Mendenhall[12] due to the absence of characteristic dental precocity, dysplastic thickened nails with no clinical or radiologic evidence of pineal hyperplasia.

The cutaneous manifestations seen in SLS appear quite early in life and are definitely helpful in suspecting the diagnosis during infancy. The exact pathogenesis of these abnormalities is not clear but speculated to be due to the hyperinsulinaemia and insulin resistance associated with this disorder. Insulin is a growth promoting factor and its effect on the skin may result in acanthosis nigricans.[9]

Patients with SLS develop insulin resistant non-ketotic diabetes mellitus around teens.[12] This is true in respect of our 13 year old firts

case, while her two younger brothers aged 4 and 2 are yet to develop this anomaly. The exact reason for insulin resistance is not known but considered to be due to the diminished binding of insulin to its receptors on the cell surface.[10]

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