Sjögren-Larsson syndrome in two sibs with peripheral nerve involvement and bisalbuminaemia

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SYNOPSIS Two sibs are described with Sjögren-Larsson syndrome. Another sib died in early life with signs which appear to be indicative of the same condition. In the two cases studied we have documented signs of peripheral nerve involvement (not previously reported in the literature) which point towards a pathological process acting on ectodermal structures to a greater extent than has previously been considered.

Ichthyosis, spastic tetraparesis, and mental retardation were first described as a syndrome by Sjögren (1956) and Sjögren and Larsson (1957) reporting on 33 patients from a Northern area in Sweden. This genetic and statistical study enabled those authors to postulate an autosomal recessive entity the mutation of which had occurred about 600 years earlier. Very soon similar cases were published from different parts of the world (Blumel et al., 1958; Link and Roldan, 1958; Richards, 1960; Baar et al., 1960; Zaleski, 1962; Heijer and Reed, 1965; Selmanowitz and Porter, 1967). Gomes da Costa and Menano (1963) were the first to report from Portugal on such an entity—a male child who presented at 15 days to a paediatric department in Lisbon as a ‘collodion baby’. One sister with similar skin lesions died at the age of 19 days and the family tree shows that their grandparents were half brothers.

The ichthyosis, as in Rud’s syndrome, is of congenital type (Wells and Kerr, 1965): the flexor surfaces are the site of predilection, the face is usually involved, and ectropion is very often present. In addition to the increased plate-like hyperkeratosis, there is erythema. Histology shows marked hyperkeratosis, the granular layer is increased, and perivascular infiltrates are present in the clinically evident areas of erythema (Schnyder, 1970), features which differentiate this type of ichthyosis from the other types.

No biochemical abnormality has been so far described in the Sjögren-Larsson syndrome, including the results of analysis of cutaneous lipids (Selmanowitz and Porter, 1967).

This report deals with two cases in a sibship. They have severe alterations in the peripheral nerves, lesions not previously reported in the literature. An interesting aspect of the condition is bisalbuminaemia, an asymptomatic dominant characteristic found in some of the members of the same family.

CASE 1

A female patient aged 20 years was born normally but with all skin covered by a severe erythema. On the second day of life scales began to appear and have become progressively thicker ever since. When she was about 2 years old her fourth and fifth fingers started forced flexion and, according to the family, the terminal phalanges were spontaneously expelled soon after. She began walking at 3 years of age and talking still later. No diseases were contracted in childhood and, apart from her skin trouble, she did well until the age of 7 years when her walking started to be difficult. At about the same time her toes became deformed and twisted. The walking got progressively worse but she was able to attend school on her own for four years: she could not, however, learn to read or write. She menstruated at 15 and periods have been normal ever since. At 7 years she started to wear glasses and these have already had to be changed three times because her vision has deteriorated.

On examination the patient’s skin was seen to be covered in scales all over her body, not sparing...
circumscribed osteoporosis, demonstrates that some of the phalanges had just disappeared.

Walking was still possible without help but was slow and of clearly spastic type. There was a tetraparesis with brisk reflexes and bilateral ankle clonus. The cutaneoplantar responses, when present were slightly extensor. The muscles in arms and legs seemed to be atrophic but this was difficult to determine because of the severe skin changes. Superficial sensation for touch, pin-prick, and temperature was completely normal. Two simultaneous stimuli showed no abnormality. Vibration sense and articular localization were also preserved. No signs of ataxia or incoordination could be elicited. There was no cranial nerve involvement and the fundi, apart from her high myopic disturbances, were normal without signs of macular pigmentation.

Her face was very extraordinary, mainly because of her ectropion (Fig. 9). In spite of her striking appearance and her IQ (37 on the Terman-Merrill test), she was rather sweet tempered.

The results of haemoglobin, white blood count, urea, and glucose tolerance test were normal. Serological tests for syphilis were negative. Urinalysis showed slight protein but urea clearance and phenolsulphonphthalein excretion were normal. Blood protein was increased (98 g/l.); on electrophoresis bisalbuminaemia was present. The CSF was normal with 0-39 albumin and 4 cells. CSF electrophoresis could not be performed as, unfortunately, the centrifuge tube broke during the procedure. No LE cells were found in peripheral blood and the antinuclear factor was negative.

The EEG showed discrete slow waves over the right temporal areas. There was a slight bilateral ventricular dilatation and a discrete cortical atrophy of the cerebral cortex in the pneumoencephalogram (Fig. 10) with a normal posterior fossa.

On EMG (performed on quadriceps, tibial anterior and extensor digitorium brevis muscles) no spontaneous activity was seen. The recruitment pattern appeared moderately reduced on volition. With a concentric needle electrode in extensor digitorium brevis no action potential could be obtained stimulating the lateral popliteal nerve at the fibular neck. Dr Canijo’s comment was ‘inconclusive results’.

Skin biopsy (Fig. 11) showed marked hyperkeratosis with granular layer increased and perivascular infiltrates with lymphocytes and histiocytes. On biopsy, the sural nerve showed variations and partial destruction of axons with vacuolization and fragmentation of myelin (Fig. 12).

**CASE 2**

Case 2 was a brother of case 1. He presented at 17
FIG. 2. Case 1. Scaling on back.

FIG. 3. Case 1. Scaling on thighs and back of knees.
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FIG. 4. Case 1. Deformities of hands.

FIGS 5 (left) and 6 (right). Case 1. Deformities of feet.
years of age, with a history of slowly progressive impairment in walking for the last three years.

On examination we observed a rather abnormal posture with a tendency to keep the head in slight flexion; there was a discrete dorsal scoliosis with a lumbar hyperlordosis. His gait was markedly spastic with very brisk knee reflexes. Ankle jerks were just present with bilateral extensor responses. There was an internal strabismus of the right eye with a slight impairment of abduction of both eyes. Fundi were normal. All modes of sensation were normal, as they were in his sister. No ataxia or incoordination could be detected. The skin appeared normal with no lesions of ichthyotic type and nothing abnormal was observed on general examination.

Radiography of the cervical area and examination of the CSF were normal. The EEG showed an alpha rhythm of 8 Hz with brief slower waves on the fronto-temporal regions which increased slightly during hyperventilation. His IQ (Terman-Merrill) was 52.

The EMG of the lateral rectus muscles, bilaterally,
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FIG. 11. Case 1. Skin biopsy, ×60.

was normal. Quadriceps, tibialis anterior and extensor digitorum brevis muscles showed no spontaneous activity with concentric needle electrode. On contraction there was a moderately reduced recruitment pattern due to a reduction in the number of units. The conduction velocity in the lateral popliteal nerve in the left side was 37 m/s (lower limit of normal) with a distal latency of 7.5 ms (upper limit of normal). These signs were suggestive of neuropathy in Dr Canijo's opinion.

Skin biopsy showed (Fig. 13) a slight but definite hyperkeratosis with an irregular increase of the granular layer and discrete perivascular infiltration. Histological examination of sural nerve showed vacuolization of myelin sheaths with partial tumefaction of axons (sausage appearance) (Figs 14 and 15).

**GENETICS** (Fig. 16)

Our patients IV<sub>2</sub> (case 1) and IV<sub>3</sub> (case 2) had a sib IV<sub>1</sub> with skin lesions similar to her sister who died when she was 3 months old. The youngest sib IV<sub>4</sub>, 11 years old, is entirely normal on clinical examination and doing well at secondary school.

We have then a sibship of four with three affected members. Their parents are first cousins and entirely normal on clinical examination. Bisalbuminaemia is present in the propositus IV<sub>2</sub>, in her mother III<sub>20</sub>, and in her normal sister IV<sub>4</sub>. The condition is indicated in Figure 16 by a ringed line. Protein electrophoresis was performed in those cases marked by a dotted line.

Three deaf-mutes (III<sub>4</sub>, III<sub>5</sub>, III<sub>21</sub>) and two cases with 'foot deformities' (II<sub>6</sub> and III<sub>17</sub>) were also referred.

**DISCUSSION**

According to Richards' extensive review (1972), about 100 cases of Sjögren-Larsson syndrome have been traced and 60 examined in the literature. No cases have hitherto been described with peripheral nerve involvement, but no nerve biopsy has so far been carried out.

A biopsy was carried out in case 2 because the
discrepancy between the knee and ankle jerks made us wonder if a peripheral component could be present. A rather strange feature was that, although the histological pictures were strongly indicative of severe nerve involvement, none of the patients showed any sensory changes on clinical examination. The only clinical signs of such involvement were the severe bone changes in case 1, which we believe are trophic disturbances. Of the 14 cases examined by Sjögren and Larsson, nine were said to have muscular atrophy in the legs, although none of them had any deformities or signs of motor neurone disease on electromyography (performed in two cases). Richards (1972) talks about irregularities in the length of the fingers and toes but does not give any details. The same author quotes Timpany’s personal communication (1962) but again without going further. Franceschetti et al. (1963) report on a peculiar case with bone lesions but these seem to be more dysplastic changes than trophic ones. This case, oddly enough, shows signs of incontinentia pigmenti on histological studies.

Sylvester (1969), reporting on a case that came to necropsy, did not examine the peripheral nerves. In the brain he found no macroscopic disturbance in the cortex but on histology

**FIG. 15.** Case 2. Sural nerve biopsy. Luxol fast blue staining, ×800.

**FIG. 16.** Family tree. Case 1: IV₂. Case 2: IV₃.
there was diffuse cell loss, particularly poverty of Betz cells in the motor cortex. It was, however, the white matter which showed mainly diffuse and widespread myelin loss. With the present findings at peripheral level, we may assume that the pathological process, whatever it might be in Sjögren-Larsson syndrome, affects both myelin in CNS and peripheral nerves as well as the skin. The disturbances in the skin manifest themselves at birth, and the peripheral nerve involvement, as suggested by the clinical history in case 1, appears very early. This may explain, bearing in mind the extraordinary adaptive capacity of the nervous system, the absence of sensory disturbances in our patients.

From the point of view of genetics, our cases fit an autosomal recessive inheritance pattern. Case 2, however, shows the congenital ichthyotic lesions only on histological study. We must remember that, of the 33 cases reported by Sjögren and Larsson, five of them who did not have ichthyosis were excluded for genetic and statistical analysis. Our results show the importance of doing skin biopsy on such a case.

Bearing in mind that two relatives were said to have had ‘foot deformities’, we could argue (in a family with a higher coefficient of inbreeding than the usual population) for another recessive characteristic. However, as we did not see the other cases, we cannot be sure of what sort of abnormalities they had and we believe, as pointed out above, that we are dealing with trophic disturbances secondary to peripheral nerve lesion.

In relation to bisalbuminaemia and quoting Weitkamp et al. (1967), at least 19 unrelated families have been so far described with such a condition. The pattern does not fit any defined entity. For instance, it has been found in normal people (Sandor et al., 1965), in some members of a family with goitre and deafness as well as the healthy ones (Fraser et al., 1959), and in a peculiar condition which presented as ‘blue hands’ (Franglen et al., 1960). It has therefore been considered as an asymptomatic autosomal dominant characteristic. Tárnoky et al. (1970) found eight types of albumin in eight unrelated families and we may assume that, with more sophisticated techniques, more knowledge will be gained.

I am much indebted to Dr Corino Andrade for his advice and stimulating help. I should like to thank Dr Pereira Guedes for the histological studies, Dr Canijo for the EMG, Dr Pinho Costa for the biochemical studies and help with the text, and Dr L. Wagner for the photographs.

REFERENCES


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*J Neurol Neurosurg Psychiatry* 1974 37: 1306-1315

doi: 10.1136/jnnp.37.12.1306

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