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# SJÖGREN-LARSSON SYNDROME

## *Diversity of Cutaneous Manifestations*

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*Abstract.* The Sjögren-Larsson syndrome consists of ichthyosis, spastic diplegia or paraplegia, retinal degeneration, and oligophrenia. The skin can provide a clue to the underlying systemic complications, although the cutaneous manifestations are variable. Usually, generalized hyperkeratosis is present from birth. Collodion babies are not present. The face, palms and soles, and scalp are variably involved. The pattern of hyperkeratosis in some cases resembles lamellar ichthyosis and in other cases resembles epidermolytic hyperkeratosis with a prominent parallel ridge pattern of the epidermis. The biopsy uniformly shows hyperkeratosis and a normal granular layer. Attention to fine details of the skin may aid detection of cases of this syndrome.

Sjögren-Larsson syndrome is an autosomal recessive, genetically determined disorder associated with ichthyosis, mental retardation, diplegia or paraplegia, and sometimes retinal degeneration. During the neonatal period and the early months of life the neurological manifestations of the Sjögren-Larsson syndrome (SLS) are usually not evident. The skin lesions may, therefore, be the only clue to potentially severe central nervous system disease. Since major advances in the nosology of ichthyosis have occurred since the last review of the dermatological manifestations (11) of the SLS it is useful to review these lesions to ascertain whether they have unique or diagnostic characteristics.

## CASE REPORT

The patient is the product of a non-consanguineous marriage; both parents are of French-Canadian ancestry. She was the third child of a 38-year-old mother, weighed 6 lb 4 oz at birth, and was delivered by a breech delivery. Dry, red, scaling skin was noted at birth which involved the entire body including the palms and soles. When seen by a dermatologist on the second day of life, generalized redness and hyperkeratosis were seen with areas of fissuring on the trunk and extremities. No ectropion or collodion baby appearance was described. At the age of six the patient was hospitalized for a gangrenous appendix and peritonitis. After an appendectomy she had a long post-operative course until final recovery. She goes to school daily, walks with a walker or when held by one hand, can write and identify letters, recites, sings, etc. Her mental ability was not formally evaluated. Ophthalmologic examination was negative. She had spasticity in the lower extremities with clonus and positive Babinski signs. She had generalized hyperkeratosis with minimal facial involvement; over the upper trunk and arms there was hyperkeratosis with the marked patterning of parallel rows of hyperkeratotic papules; the palms, soles, and distal legs had polygonal scales upto 0.5 cm in size. Small yellow scales were on the scalp. Nails and hair were normal. Skin biopsies from areas with both hyperkeratosis with a scaling pattern, and areas with a parallel row pattern were identical and showed hyperkeratosis and a normal granular layer with no evidence of epidermolytic hyperkeratosis. The family did not grant permission to publish clinical photographs.

## DISCUSSION

Skin manifestations in the reported cases of the SLS are shown in Table I. Some cases in which the diagnosis of the SLS was uncertain, such as that of Frazier (7), are not tabulated. In the majority of the cases, ichthyosis was present at birth, and in all by 1 year. The form of SLS seen among the Haliwas seems unique in that in the majority of those patients the disease did not start until the age of 6 to 8 months (28).

In all cases, there were hyperkeratotic skin lesions—in some, these were described only as "ichthyosis", "ichthyosiform rash" or other terms not providing complete description. In some cases

Table I. *Summary of the cutaneous manifestations in the Sjögren-Larsson syndrome*

?= not reported; *= clinical photograph in published report; 0= not present;
+ = mildly affected; + + = moderately affected; + + + = severely affected

| Year | Author | Author's case no. | Skin manifestations | Age at onset | Special areas involved: Palms & soles | Face | Scalp | Biopsy |
|---|---|---|---|---|---|---|---|---|
| 1932 | Pardo-Costello & Faz (16) | 1 | Large dry scales; periodic scaling | 20 days | ? | + | + | ? |
| 1934 | Pisani & Cacchione (17) | 1–3 | Polygonal scales; dirty-grey color; groin clear; dystrophic nails on feet | Birth-erythema | + | 0 | + | Hyperkeratosis; normal granular layer |
| 1957 | Sjögren & Larsson (22) | all | Pronounced in all except one case | Congenital | | | | |
| | | 1c and 1a | Furrowing of skin* with a "distinct" field pattern"; slight desquamation and a grey-blue hue | | + | 0 | 0 | Thick horny layer and areas of thinned stratum granulosum |
| | | 6a | Large thick lamellar-like scales | | ? | ? | + + + | ? |
| 1957 | Richards et al. (18) | 1 & 2 | Small scaling; no areas of accentuation* | Birth | + + | + | ? | Reported by Sylvester (23) Acanthosis; hyperkeratosis; granular layer prominent due to thickening and presence of increased number of granules |
| 1958 | Link & Roldan (14) | 1 | Generalized ichthyosis with minimal scaling | Birth (premature by 1 month) | ? | ? | ? | ? |
| 1958 | Blumel et al. (2) | 1 | Ichthyosiform erythroderma | Birth | ? | ? | ? | ? |
| 1959 | Greither (9) | 1 | *Marked parallel row of greyish scales; adherent pattern on abdomen & axillae; sharply deliniated borders; "Skin pattern is protruded by keratinization" | Less than 6 weeks | 0 ± (soles) | 0 | 0 | Acanthosis, hyperkeratosis |
| 1960 | Richards (19) | 1 | *Parallel rows on abdomen and scaling on legs | ? | ? | ? | ? | ? |
| 1960 | Williams & Tang (27) | 2 | Severe ichthyosis with parallel ridges on neck & arms | 1 month (premature birth) | 0 | + | 0 | ? |
| 1960 | Barr et al. (1) | 1 & 2 | Dry, rough, diffuse scaling | Birth | + +* | 0 | ? | Hyperkeratosis without parakeratosis well-developed stratum granulosum |
| 1960 | Wallis & Kalushiner (25) | 1 & 2 | "Distinct field pattern"; slight desquamation, increased in axillae; greyish hyperkeratosis | ? | 0 | 0 | 0 | Hypertrophic horny layer; granular layer present for the most part |
| 1961 | Mercu & Coreddu (15) | 1 | *Scaling with ridge-like accentuation on arms | 3 months (1 month premature) | ? | + | + | ? |

Table I (*Continued*)

| Year | Author | Author's case no. | Skin manifestations | Age at onset | Special areas involved: Palms & soles | Face | Scalp | Biopsy |
|---|---|---|---|---|---|---|---|---|
| 1962 | Timpany (24) | 1 & 2 | "Ichthyosis in general" | Birth | 0 | 0 | 0 | ? |
| 1962 | Francheschetti et al. (6) | 1 | Diffuse hyperkeratosis; greyish pigmentation | ? | ? | ? | ? | Pigmentary incontinence |
| 1962 | Zaleski (29) | 1 | Dry, rough, diffuse fine scales; increased pigmentation | Birth | + | 0 | + | Hyperkeratosis; no parakeratosis |
| 1963 | Chlond (4) | 1 | *Rough, desquamating, grey, tightly adherent scales; axillae, elbows, knees, clear | Birth | 0 | 0 | ? | ? |
| 1963 | Hanafy et al. (10) | 1 | "Scaly, dry, brownish rash" | 1 year | ? | + | ? | ? |
| | | 2 | "Dry, scaly, rough" | 9 months | ? | + | + | ? |
| | | 3 | "Dry, rough, ichthyosiform rash" | 4 months | ? | 0 | ? | ? |
| 1963 | Witkop & Henry (28) | 1–14 | Red, shiny, thickened skin and backs of hands; rough skin on trunk & shoulders *Poor | Birth (2/14) 4–8 months (12/14) | ? | ? | ? | ? |
| 1965 | Heijer & Reed (11) | Swedish 1 | *Generalized ectropion | Birth erythema | + | + | + | Hyperkeratosis and Acanthosis |
| | | Swedish 2 | *Generalized, esp. flexural | 3 months | + | + + | + | |
| | | Swedish 3 | Generalized, esp. flexural | Birth | + | + | ? | |
| | | Swedish 4 | Generalized, esp. flexural | Birth | 0 | + | 0 | |
| | | Calif 5 & 6 | Generalized, esp. flexural | Birth | + | 0 | 0 | |
| 1967 | Hooft et al. (12) | 1 | "Rough, exfoliative hyperkeratosis" | 1 week | + + | 0 | 0 | ? |
| 1967 | Selmanowitz & Porter (21) | 1–3 | *Hyperkeratotic folds verrucoid hyperpigmentation; fine desquamation on lower legs | Birth | 0 | ± | + + + | Hyperkeratosis |
| 1968 | Gilbert et al. (8) | 1 | Large black scales; "generalized ichthyosis with scaling"* | Birth | + + + | + | + | "Picture of lamellar ichthyosis" |
| 1969 | Sayli et al. (20) | 1–3 | Some scales and some accentuations of skin markings* | Birth | 0 | 0 | ? | "Confirmed skin findings" |
| | This case | 1 | Accentuation of skin markings with a ridge-like pattern; small polygonal scales on lower extremities | Birth | + | + | + | Hyperkeratosis; normal granular layer |

distinct large lamellar scales are seen, while in other cases there was marked accentuation of the ridge-like pattern of the skin producing a clinical picture similar to that seen in epidermolytic hyperkeratosis; however, no bullae or pustules were present. In our patient this ridge-like pattern was

prominent. Grayish pigmentation of the skin is sometimes present. Collodion babies are not described in the SLS. The scalp and palms and soles are variably involved in SLS, the face is sometimes involved, and only rarely was ectropion present. In some cases, intertriginous areas, such as the groin, have been clear.

Biopsies of this condition have constantly shown hyperkeratosis, a normal granular layer, and in some cases pigmentary incontinence.

Since varieties of ichthyosis which do not have the severe nervous system manifestations of SLS can be present at birth or in the neonatal period, the diagnosis of ichthyosis in the early months of life will be considered. This differential diagnosis is especially important considering the wide variety of skin manifestations of reported cases of SLS.

Conradi's disease (3) presents at birth with generalized hyperkeratosis often with a swirl-like pattern and shortened proximal extremities. A characteristic roentgenographic pattern of stippled epiphyses confirms the diagnosis. The harlequin fetus (5) also represents a form of ichthyosis present at birth—it has massive ectropion, eclabion, large thick keratinous plaques and its distinctive clinical picture is unmistakable.

The most common form of ichthyosis, autosomal dominantly inherited ichthyosis vulgaris, is not present at birth and in only 37 % of cases is it present by the age of 3 months (26). The scales in that disorder are small, branny, and neither large lamellar scales or ridge-like accentuation is seen. The next most common form of ichthyosis, X-linked ichthyosis, is sometimes (17 % of cases) present at birth, and 84 % of the cases are present at 3 months (26). Only males are affected; flexures, face, palms, and soles are usually spared. Epidermolytic hyperkeratosis and lamellar ichthyosis present the two most difficult differential diagnoses. Both are present at birth, the latter often presenting as a collodion baby. In epidermolytic hyperkeratosis a prominent ridge pattern is present, bullae may be present and there is a distinctive histopathology.

Patients with lamellar ichthyosis have a clinical appearance and histopathology similar to many of the patients with SLS (13). The face, scalp, and palms and soles are more consistently involved than in the SLS. Ectropion is very frequent in lamellar ichthyosis but rare in SLS, and most patients with lamellar ichthyosis are collodion babies at birth. Therefore, cases which appear to be atypical for lamellar ichthyosis should have careful neurological, ophthalmologic examinations and follow-up for SLS, and the prognosis should be somewhat guarded during the first few months of life.

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