CASE REPORT

# Stiff skin syndrome - Case report

## Síndrome stiff skin - Relato de caso

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**Abstract:** Stiff skin syndrome is a rare scleroderma-like disorder of unknown etiology characterized by stone-hard indurations of skin, mild hypertrichosis and limited joint mobility. No effective treatment has yet been found. Exercises and rehabilitative therapy are important in maintaining the patient's quality of life. The authors present a case of a two-year-old boy with progressive skin hardening since he was eight-month old and secondary restricted joint mobility, diagnosed as Stiff skin syndrome.
Keywords: Contracture; Fascia; Mucopolysaccharidoses; Rare diseases; Scleroderma, systemic

**Resumo:** Síndrome *stiff skin* é doença rara, esclerodermiforme, de etiologia desconhecida, caracterizada por endurecimento pétreo da pele, hipertricose leve e limitação da mobilidade articular. Não há tratamento efetivo até o momento. Exercícios e reabilitação são importantes para manter a qualidade de vida do paciente. Os autores apresentam caso de um menino de dois anos de idade com endurecimento cutâneo progressivo desde os oito meses de idade e restrição secundária da mobilidade articular, diagnosticado como Síndrome *stiff skin*.
Palavras-chave: Contratura; Doenças Raras; Escleroderma sistêmico; Fascia; Mucopolissacaridoses

## INTRODUCTION

Stiff skin Syndrome (SSS) is a rare disease that is present at birth or early infancy, characterized by stone-hard skin, especially in areas with abundant fascia like buttocks and thighs, limitation of joint mobility secondary to the skin thickening and mild hypertrichosis. [1] The cutaneous involvement is not associated to visceral, muscular, immunological or vascular changes. [2] We report a case of child with clinical and histopathological characteristics of SSS.

## CASE REPORT

Two year old male black infant, original from Niterói, Rio de Janeiro. He was sent to the Dermatology service for the evaluation of asymptomatic skin hardening on the upper abdomen and thighs, noticed by the mother since the age of eight months. The patient was born at term after an uneventful pregnancy. He was the only child of healthy, non-consanguineous parents. There was no history of previous traumas to the affected areas, frequent use of any medication, infectious diseases or convulsions. The patient´s cognitive development was appropriate for his age but his height and weight were below the expected. There was no report of Raynaud's phenomenon and no familiar case of diabetes, scleroderma or similar cutaneous findings.

At physical examination the patient had a small, hard, non folding plaque on the skin of the upper abdomen and a rock-hard indurated area around the thighs, close to the knees, as well as slight thickening of the skin on the buttocks, without hypertrichosis. There was a noticeable shortening of the left leg in relation to the right, "genu varum" deformity and joint stiffness with restriction of the amplitude of the movement of the legs and hips (Figure 1). On standing position the child would show fixed flexion of the knees and accentuation of the lumbar lordosis (Figure 2). There was no alteration at the neurological exami-

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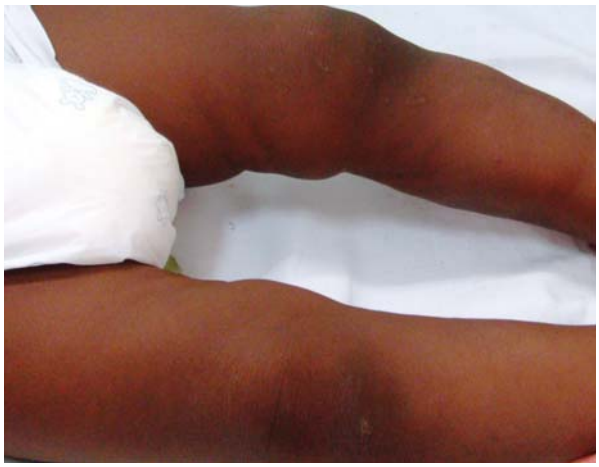

**Figure 1:** Shortening of the left leg and "genu varum" deformity

nation. Routine blood tests including complete haemogram, erythrocyte sedimentation rate (ESR), glucose, urea, creatinine, lipoprotein panel, C-reactive protein, SGPT, SGOT, bilirrubines, alkaline phosphatase, glutamyl transferase, albumin, protein electrophoresis, thyroid tests, antistreptolysin O, stool and urine exams were all within normal range. Dosages of mucopolysaccharides (on blood and urine), muscle enzymes, anti-double stranded DNA antibody, anti-centromere, anti-Scl-70, anti-Ro, anti-La and chest x-ray were normal. Due to the age of the patient computerized tomography and electromyography were not performed. Ultrasound and Doppler of the abdomen and pelvis were normal, except for the thickening of the soft tissues, up to the aponeurosis, which was also present on the ultrasound of soft tissues on the lower limbs.

Histopathological examination of biopsied samples from lesions on the abdomen and right thigh stained by haematoxylin and eosin (HE) showed normal epidermis, thickening of the collagen on the dermis with normal appendages and vessels and no inflammatory infiltrate (Figure 3). Staining by Alcian Blue at ph 2.5 revealed moderate deposits of mucopolyssacharides on the dermis between the collagen bundles, making it impossible to visualize the fascia. The combined histological and clinical findings were suggestive of Stiff Skin Syndrome (Figure 4).

The therapeutic plan for the patient included physiotherapy and physical exercise. Initially the mother did not follow the recommendations and after eight months of the diagnosis the deformity of the patient´s legs worsened. Treatment based on physiotherapy was started once a week and physical exercise like soccer was encouraged, which led to an improvement in walking. After one year expanding of the lesions around the knees and involvement of almost the entire abdomen, with the aspect of “cobblestone” were noticed at physical examination (Figure 5). The mother was instructed to increase the physiotherapy sessions and come back in three months, but she discontinued the treatment despite phone calls and medical recommendation.

## DISCUSSION

SSS is an uncommon connective tissue disease similar to scleroderma, described in 1971 by Esterly and Mc Kusik. Visceral and muscular involvement, vascular hyperactivity and immune abnormalities are absent. The clinical presentation is heterogeneous and there are no pathognomonic histological or laborator-

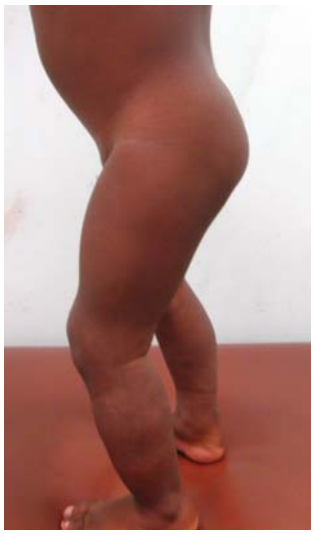

**Figure 2:** Typical posture of patients with this syndrome: flexion of the knees and accentuation of the lumbar lordosis

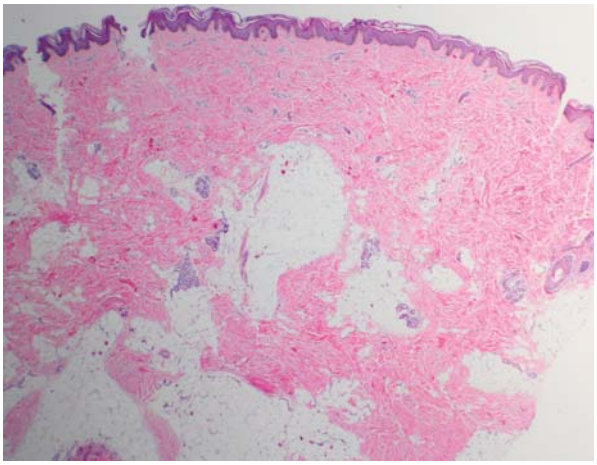

**Figure 3:** H.E.: Disorganization and thickening of the collagen bundles on the dermis without inflammatory infiltrate and with unaltered appendages

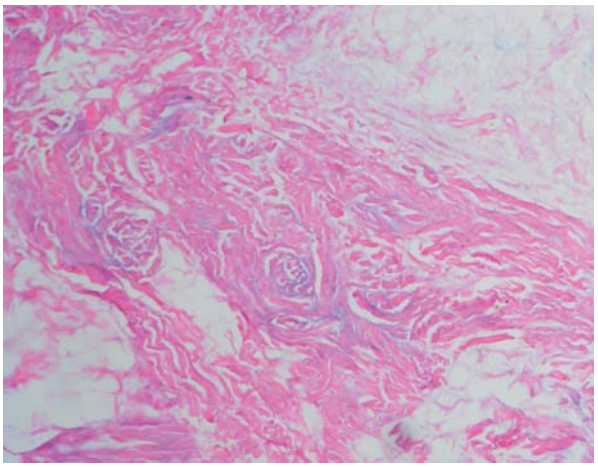

**Figure 4:** Alcian Blue pH 2,5: Presence of moderate amount of mucin on the dermis

ial findings, thus being a diagnostic of exclusion. The age of the start of the symptoms varies from birth to childhood and there is no predilection for sex or race. The clinical criteria that support the diagnosis of the syndrome are: 1-hereditary condition, 2-stone-hard thickening of the skin more prominent in areas with abundant fascia like buttocks and thighs, 3-limitation of joint mobility secondary to the thickening of the overlying skin, 4-absence of urinary mucopolysaccharides, 5- mild and variable hypertrichosis. The patients might have a delayed growth with normal neuropsychomotor development, typical "tiptoe´´ posture, accentuation of the lumbar lordosis, cutaneous lesions with the ´´cobblestone´´ pattern and restrictive pulmonary abnormalities secondary to the stiffening of the thoracic skin. [1, 3, 4, 5]

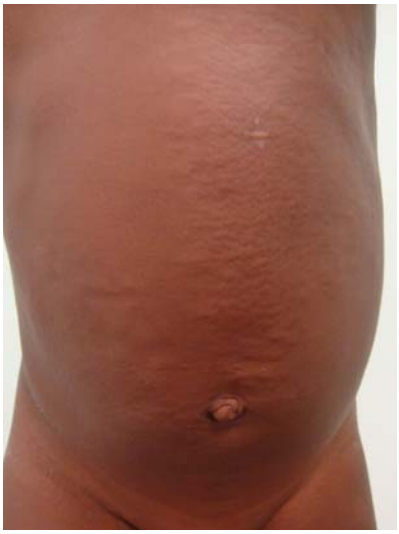

**Figure 5:** Abdominal plaque: "cobblestone" or "orange peel" aspect. On the first consultation the lesion was restrict to the site of the biopsy (see scar on the superior abdomen)

The pathogenesis of SSS remains unknown. The two main pathogenic hypotheses are: a primary abnormality of the fascia with increased production of collagen VI or a congenital abnormality of the fibroblasts leading to a non-inflammatory dermal fibrosis due to a defective synthesis of mucopolysaccharides. [2,3,6-8] Some authors have detected high levels of proinflammatory cytokines (tumor necrosis factor-alpha, Inteleukin-6 and transforming growth factor- $\beta$2) suggesting that the fibrosis might be related to the inflammatory process. However, systemic corticosteroids and immunosuppressant drugs do not modify the progress of the syndrome. [2, 4, 9]

There are familial and consanguineous reports in 30% of the cases, which suggests the possibility of genetic transmission. [1, 2, 6] Loeys and collaborators presented the results of a genetic study with evidence that a mutation of the locus 15q21.1 of the FBN1 gen that regulates the production of the profibrotic cytokine transforming growth factor- $\beta$2 (TGF- $\beta$2) causes the SSS.[9]

Two variants of SSS have been described: The Parana Syndrome, which has a worse clinical progress, with diffuse cutaneous involvement, restrictive pulmonary abnormalities, slow growth and consanguinity, and the congenital fascial dystrophy, that involves isolated areas of abundant fascia. [2, 4, 7, 10-13]

The histology might show various levels of fibrosis on the dermis and subcutaneous tissue, with the presence of mucopolyssacharides amongst the collagen fibers at earlier stages, absence of inflammatory infiltrate and preservation of the blood vessels and cutaneous appendages. The fascia might or might not be thickened.[4]

The patient fulfilled the clinical criteria for SSS although he did not have hypertrichosis, which is a variable finding, developing over hardened skin areas. He had the abdominal lesions with the characteristic ´´cobblestone´´ pattern as well as an accentuation of the lumbar lordosis and flexion of the knees, typical of SSS. There was no report of consanguinity or familial cases. The laboratory and image tests did not show any signs of immunological, inflammatory, muscular or visceral alteration. The histopathology probably represents the initial stage of the syndrome with the presence of mucin on the dermis, since at advanced stages there is sclerosis of the deep dermis.

The main differential diagnosis of SSS are the systemic scleroderma, which is rare in childhood and is associated with cutaneous lesions on the face and hands, Raynaud's phenomenon, periungual telangectasias and visceral and immunological abnormalities, which were absent in this patient. [4, 14] The localized scleroderma, also known as morphea, presents with mostly cutaneous involvement and only rarely

involves the joints, causing contractures and retraction of the limbs. [15] The histology differs from SSS, with lymphocytic infiltrate on the dermal-epidermal junction and abnormally sclerotic collagen on the reticular dermis, and it responds favorably to treatment with anti inflammatory medication. Neonatal scleredema is more related to prematurity, and the histology shows lesions to the adipocytes, which were absent on the actual patient. [16] Scleredema usually starts abruptly and results from infiltration of mucin into the dermis, causing the clinical aspect of non-pitting edema and more uniform cutaneous hardening, not as well defined as in SSS, predominantly on the upper trunk, neck and face (unusual locations for the syndrome), and develops mostly in adults. Sclerodermatomyositis has characteristics of both scleroderma and dermatomyositis, with the elevation of muscular enzymes, auto antibodies and vascular hyper reactivity. Scleromyxedema, or lichen myxedematosus, shows progressive thickening of the face, neck, ears, upper limbs and upper trunk, as well as a papulous eruption. [17] The mucopolysaccharidosis can present with nodules and plaques on the extremities or upper trunk, with the ''orange peel'' aspect and the presence of mucopolysaccharides on the urine and blood.[5, 8]

The treatment described on the literature, based on motor physiotherapy, was proposed during the ambulatory follow-up and provided an improvement on the quality of life of the patient, but the cutaneous thickening progressed slowly, as seen on the literature. There are many reports of treatments aiming at slowing down the progression of the disease, like immunosuppressant drugs, corticotherapy, psoralens and penicillamine, however the patients have not shown any clinical improvement. [5] The authors have found 43 cases of SSS on the world literature, five of which reported in Brazil. ❑

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