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Case Report
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# Segmental Stiff Skin Syndrome: a Rare Case Report from Indonesia

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**ABSTRACT**

**Background:** This paper reports a segmental Stiff Skin Syndrome (SSS) case in a four-year-old girl. SSS is a rare disease characterized by skin hardening and joint stiffness due to a mutation of the fibrillin-1 (*FBN-1)* gene encoding the fibrillin protein. The effective therapies for this disease are limited. **Case Report:** The patient presented with hardened skin and a limping gait. Clinically, there were hard, hyperpigmented patches with hypertrichosis on the skin of the left femur and left gluteal. The left coxae and left genu joint were in fixed flexion, causing a limping gait. The SSS histology revealed thickened collagen fibers, trapping adipocytes between them, but no inflammatory cells. The UV-A phototherapy and physiotherapy session resulted in a modest improvement. **Discussion:** This case's segmental SSS diagnosis was based on clinical and histological findings. Establishing a diagnosis of SSS is a challenge for clinicians because it can resemble other skin disorders, particularly sclerosing diseases. The recommended management for SSS remains limited. In this case, after the UV-A phototherapy and physiotherapy, complaints of hardened skin were said to soften.

**Keywords:** fibrillin, fibrosis, hardened skin, joint contractures, stiff skin syndrome.

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## BACKGROUND

The term Stiff Skin Syndrome (SSS) and its alternate name, Congenital Fascial Dystrophy, was initially coined by Esterly and McKusick in 1971. It is characterized by hardened skin and fascia, mild hypertrichosis, and limited joint mobility.[1] Consanguinity and a positive family history are found in 30% of cases, indicating that SSS can be inherited.[2,3]

SSS is a rare disease with an estimated global incidence of 1:1,000,000. Its prevalence varies depending on geography and population.[1]only about 130 cases have been reported worldwide, and none originated from Indonesia.[3]

Diagnosis of SSS requires a thorough evaluation, encompassing the patient's medical history, physical examination, imaging studies, and histological examination. Physical examination is essential for determining primary manifestations of skin stiffness, limited joint mobility, contractures, subcutaneous fibrosis, or fasciitis.[1]

Clinicians face challenges in establishing the diagnosis of SSS due to its clinical similarities with other sclerosing diseases and its scarcity. Misdiagnosis can harm patients through unnecessary therapy and its side effects. Unfortunately, effective therapeutic options to suppress the progression of SSS have not yet been identified. Disease progression and complications due to skin stiffness can interfere with daily activities and decrease the patient's quality of life. [4]

This case report aimed to enhance comprehension of SSS and disseminate experience regarding treatments of this disease.


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**CASE REPORT**

A four-year-old girl presented to the Dermatology and Venereology Clinic at Dr. Sardjito General Hospital with hardened skin. The skin lesion began two and a half years earlier as a hardened lump on the front of the left thigh. There was no itchiness, pain, or fever. The lump gradually spread across the left thigh to the skin of the left waist and left buttock, with the affected skin becoming rigid wood. The patient maintained a normal posture but exhibited a limping gait.

The patient demonstrated average growth and development for her age. She was born as a singleton, following a normal full-term delivery without complications. The patient's family did not have any comparable conditions, nor was there any family history of scleroderma or other autoimmune diseases. Figure 1 depicts the family pedigree.

The patient's general condition was good, with normal vital signs. Physical examination revealed a hyperpigmented patch with indistinct boundaries and overlying hypertrichosis on the left thigh up to the left waist (Figure 2). Upon palpation, the patch showed a firm consistency. Hyperpigmented nodules with a cobblestone appearance were observed in the left gluteal area. Her standing posture and gait were abnormal, potentially due to fixed flexion on the left coxae and left genu joint. Nevertheless, passive examination of the coxae and genu joints revealed that their range of motion (ROM) was within normal limits. We observed no periungual telangiectasis, microstomia, or salt and pepper skin appearance.

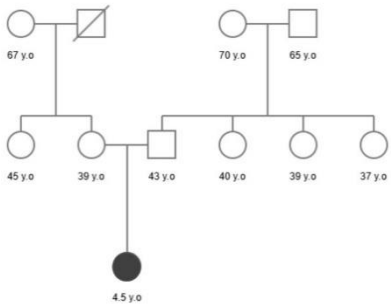


**Figure 1.** Family pedigree of the patient.

The patient is a singleton with non consanguineous parents. None of the patient's family members have a similar condition (Figure 1).

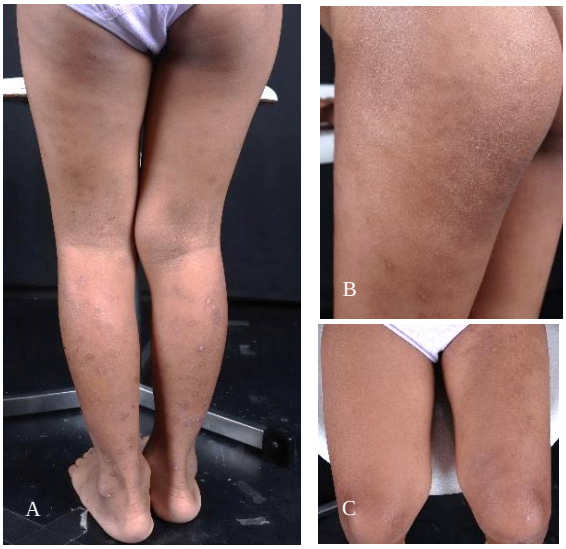


**Figure 2**. The patient's clinical appearance.

A) The patient's posture and gait are abnormal due to skin hardening, causing limited joint mobility; B) The left waist and gluteal area show an irregular cobblestoning skin texture with nodular hardening upon palpation. C) A well-defined hyperpigmented patch with hypertrichosis overlying the lesion is visible on the anterior left thigh. On palpation, the skin feels rigid with the consistency of a wooden board.

Magnetic resonance imaging of the lateral aspect of the proximal left femur region showed an intense lesion with a thickness of 0.76-0.77 cm from the skin surface, indicating fibrosis. An X-ray examination using a long-length stitching image view revealed that the length of the lower extremities was normal (Figure 3). Histological examination using hematoxylin-eosin staining showed normal epidermis. However, the dermis showed thickened collagen fibers with adipocytes trapped between them. The hair follicles and adnexa appeared normal, with no inflammatory cells or vascular changes. Alcian blue staining revealed no mucopolysaccharide deposition in the dermis (Figure 4). The patient's hematology test, liver function test, complete blood count, and glucose levels were within normal limits. The results of antinuclear antibody (ANA) and anti-dsDNA examinations were normal.

A) No scoliosis was found on the vertebral X-ray examination; B) On the long leg stitch view examination, there was no difference in the length of the lower leg bones; C)1-4: On MRI examination of the right thigh, an isointense lesion was found on the skin of the lateral aspect of the femur region with a depth of

0.76-0.77 cm from the skin, indicating fibrosis. There was no fascia or muscle involvement.

The patient was diagnosed with SSS. UVA phototherapy and physiotherapy managed the disease. The skin of the anterior thigh mildly softened after 46 sessions of UVA phototherapy and 20 sessions of physiotherapy.

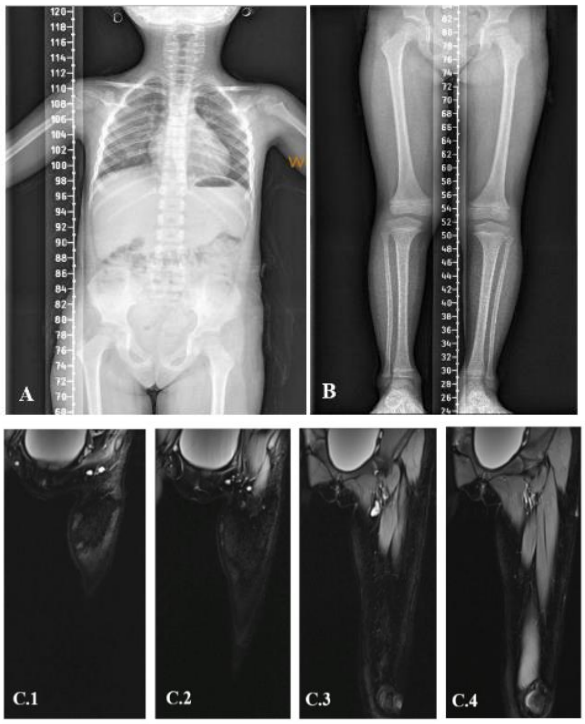


**Figure 3.** Patient's X-ray and MRI examination.

A) The histological examination using hematoxylin-eosin staining showed a normal epidermal layer (yellow arrow). Thickened collagen fibers were found, many arranged horizontally amianthoid-like (blue arrow). The thickened collagen traps some adipose tissue (red arrow). The adipose tissue contains terminal hair follicles, a sign of hypertrichosis (green arrow). There was no inflammatory cell infiltrate in the dermis. B) Negative direct immunofluorescence examination shows this disease is not an autoimmune process.

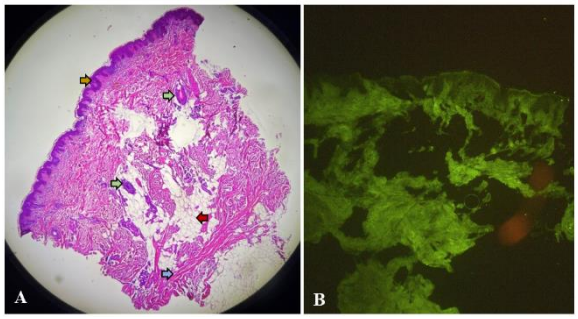


**Figure 4.** The patient's histological examination.

## DISCUSSION

SSS may be widespread or segmental; both variants are genetic and heritable. The clinical manifestations of widespread SSS are more severe, with decreased ROM in more joints and earlier onset than the segmental variant. Usually, segmental SSS is distributed unilaterally and does not progress to the widespread form.[5] SSS can appear from birth through the first six years of life. Initially, it presents as hardened skin with clear boundaries and no visible alterations to the skin surface. Hypertrichosis, hyperpigmentation, subcutaneous nodules, and skin lesions with cobblestone and pseudocellulite patterns may manifest in certain instances. The predilection of SSS is for limb-girdle areas such as the shoulder, pelvis, and proximal thigh areas; however, involvement of more unusual areas, such as the abdomen and eye, has been reported. SSS does not involve muscular, vascular, or internal organs.[1,6] The onset of symptoms in our patient occurred at around the age of two years. This manifested as a firm lump on the front of the left thigh, which expanded to include the gluteal region and waist. The presence of hypertrichosis, hyperpigmentation, and subcutaneous nodules with cobblestone and pseudo cellulitis patterns supports a diagnosis of SSS.[2]

The main physical impediment for patients with SSS is the secondary limitation of joint movement. Skin induration and fascial fibrosis may cause contracture of large joints over time, resulting in scoliosis, lordosis, or tiptoe. Some cases of extensive SSS, particularly in the chest area, can reduce lung capacity.[2,6,7] Our patient experienced fixed flexion in the left coxae and left genu joints, causing gait abnormalities, but the ROM of those joints was normal. The bones of our patient were unaffected, and an X-ray examination showed that the length of both lower extremities was normal.

The hallmark of the histological pattern of SSS is the thickening of collagen fibers, which form an amianthoid-like shape and adipocyte trapping. In addition, there is adnexal preservation and no dermal inflammatory infiltrates. SSS inconsistently exhibits thickening of the fascia and mucopolysaccharide deposition. The histological examination of our patient showed adipocytes trapped between thickened collagen, which had a horizontal amianthoid-like shape. Inflammatory infiltrates were absent, and the skin's adnexa remained intact. These findings were consistent with SSS.[1,6]

The doctor who referred the patient to our hospital suggested morphea, a more common sclerosing disease, as the differential diagnosis in this case.

However, young patients typically do not exhibit morphea, and sclerotic skin changes are usually visible. The characteristic histology of morphea is dense inflammatory cell infiltration at the perivascular and peri adnexal levels, with abnormal sclerotic collagen in the reticular dermis. Adnexal structures are atrophic or absent. Our patient did not exhibit these morphea manifestations, making this diagnosis inappropriate.[1,7] Another differential diagnosis is Becker's nevus, which resembles SSS in terms of indurative plaques with hypertrichosis and hyperpigmentation. Like SSS, Becker's nevus predominantly appears in children and adolescents. However, lesions from Becker's nevus typically affect the chest, shoulders, upper back, and lateral arms, with some cases also reported in the gluteus and lower extremities. The histology of Becker's nevus included a normal epidermis with acanthosis, papillomatosis, elongation of the rete ridge, and an increase (hamartoma) in smooth muscle fibers.[8] This histological pattern is easily differentiated from that of SSS.

SSS is caused by mutations in the FBN-1 gene encoding human fibrillin-1, a 350-kDa glycoprotein that polymerizes to form microfibrils. Fibrillin microfibrils serve various functions, including structural support of tissue, scaffolding for elastin deposition during elastogenesis, and the regulation of transforming growth factor-β (TGF-β) activities through the sequestering of latent-TGF-β (LTGF- β). Mutations in the FBN-1 gene cause abnormal fibrillin microfibrils, releasing free TGF-β, which has a profibrotic effect. As a result, there is greater collagen deposition in the deeper regions of the dermis, the subcutaneous tissue, and the muscle fascia. In addition, fibroblasts in SSS lesions show upregulation of the profibrotic genes and a decrease in matrix metalloproteinase-2 (MMP-2) enzyme activity. This combination of factors leads to fibrosis and skin hardening in SSS. Widespread SSS is known to be associated with mutations in the FBN-1 gene, while the pathogenesis of segmental SSS remains less well understood. It is postulated that somatic variants in FBN-1 may cause segmental SSS.[9,10] Unfortunately, we could not perform a genetic analysis of our patient due to limited resources.

At present, there is no effective therapy for SSS. The recommended management of the condition is physiotherapy to prevent the development or reduce the severity of motor disorders due to skin thickening.

Researchers have also tried immunosuppressive drugs and UVA phototherapy in SSS, but the results remain controversial. Losartan has also been reported to provide mild clinical improvement by reducing TGF-β signaling.[11] Our patient showed mild clinical improvement after 46 sessions of UVA phototherapy and 20 sessions of physiotherapy, with some softening of the lesion on the anterior side of the thigh.[6]

This paper reports a case of segmental SSS in a four-year-old girl. The diagnosis of SSS was established based on its characteristic clinical and histological features, which can be distinguished from sclerosis diseases. Therapy with UVA phototherapy and physiotherapy resulted in mild clinical improvement.

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