

Case presentation

A 7-year-old with indurated skin and unilateral progressive joint immobility: A case of stiff skin syndrome

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Abstract

Stiff skin syndrome is a rare sclerotic condition that presents during infancy or early childhood. It has an insidious chronic course and may lead to significant co-morbidity and reduced quality of life. Often, affected individuals experience impaired ambulation and immobilization related to joint involvement. Clinically, it may resemble other sclerotic diseases, so histopathological evaluation is necessary to establish a diagnosis. As it is a condition with limited treatment options, prompt diagnosis and early initiation of physical therapy is crucial to prevent joint restriction and maintain quality of life. We describe a case of a 7-year-old with stiff skin syndrome, and review the literature to discuss the clinical presentation, histological findings, and management of this condition.

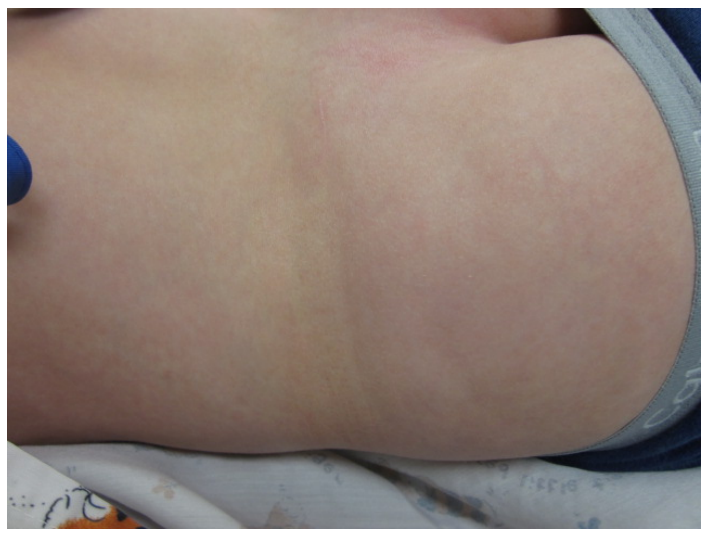
Keywords: Stiff skin syndrome, scleroderma, fibrillin-1, histology, treatment

Introduction

Stiff skin syndrome (SSS), sometimes known as congenital scleroderma or congenital fascial hemidystrophy, is an uncommon scleroderma-like condition first described in 1971 by Esterly and McKusick [1]. It is characterized by induration of areas abundant in fascia such as the thighs and buttocks [1-4]. Patients often present with mild hypertrichosis and hyperpigmentation overlying the affected area, abdominal protuberance, and a characteristic lordotic stance [1,4]. There is no predilection for race or sex. SSS lacks visceral, vascular, and muscular abnormalities [2], but involvement of tissue overlying joints may result in immobilization and contracture formation. We report a case of a 7-year-old boy with clinical and histological findings consistent with stiff skin syndrome.

Case synopsis

A 7 year-old boy presented to our clinic with bound-down, indurated flesh-colored plaques on his right thigh and left buttock that had slightly increased in size over the past year. The plaque on his right thigh was a 12.3 x 3.4cm linear plaque with mild hypertrichosis extending from the right medial mid-thigh to the inguinal fold (Figure 1). An ill-defined 3.2 x 2.4cm firm plaque was noted on his upper left buttock (Figure 2). There was no involvement of the upper extremities or head and neck. There was no evidence of Raynaud phenomenon on examination or from history. No sclerodactyly or cuticular changes were noted. The patient denied dyspnea, chest pain, dysphagia, odynophagia, or abdominal pain. Prior to his presentation, he had not been evaluated by another physician or received any treatment for this condition. His past medical history was positive for ADHD and fetal alcohol syndrome but was otherwise insignificant. His family history was unknown, as he was adopted.



Figure

1. Poorly circumscribed flesh-colored linear plaque with mild hypertrichosis on medial thigh. The erythematous plaque is a scar from the biopsy. **Figure 2.** Ill defined flesh-colored plaque on left upper buttock

Following examination, our differential diagnosis included linear morphea and evolving Becker nevus. Hematoxylin and eosin stain of a 4mm punch biopsy of the right thigh revealed haphazardly arranged spindle cells that infiltrated dermal collagen fibers (Figure 3,4). There was a slight increase in mucin, which was highlighted with colloidal iron (Figure 5). Trichome staining revealed normal collagen bundles. There was no lymphoplasmocytic infiltrate and the adnexal structures were normal, without inflammation or collagen trapping. No fascia was examined in the specimen. Serologic examination was not performed.

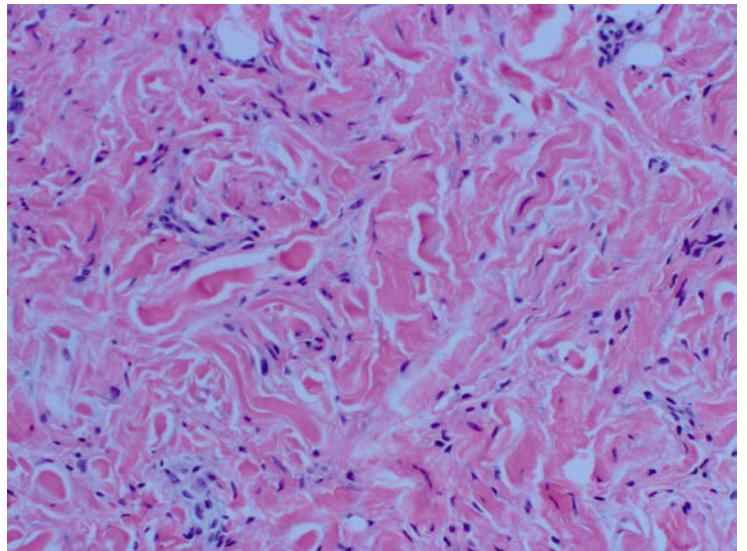
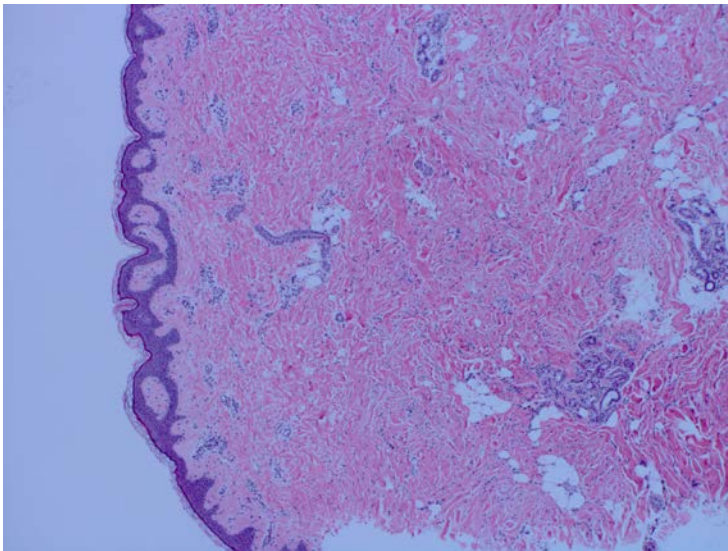


Figure 3 and 4. Demonstrate thickened collagen fibers infiltrated by haphazardly arranged spindle cells and normal adnexal structures without collagen trapping.

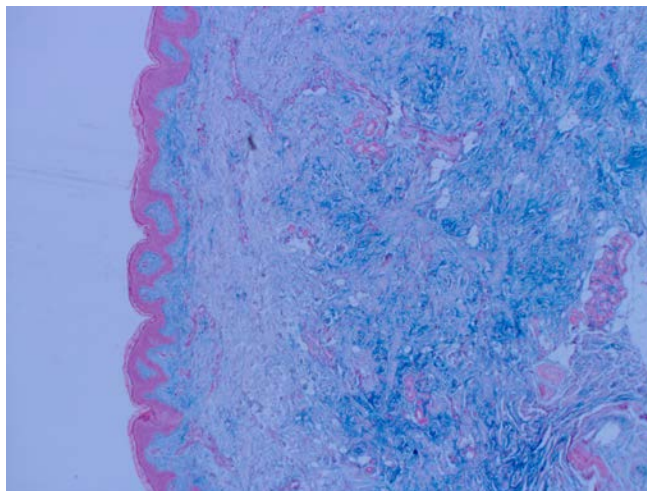


Figure 5. Colloidal iron reveals increase in dermal mucin

Clinicopathological evaluation supported a diagnosis of SSS. The patient was started on triamcinolone 0.1% topical cream BID. No systemic therapies were initiated at the time as the patient's parents were apprehensive of side effects and opted for conservative management.

At three month follow up, the patient complained of stiffness and decreased mobility of his right hip. On physical examination, the indurated plaque on his right thigh was now noted to involve the skin overlying the right ileofemoral joint. We referred the patient to physical therapy in an effort to prevent joint restriction. At six month follow-up, the patient presented with slight progression of the lesions and worsened mobility of his right hip despite weekly physical rehabilitation. At that time, we recommended that the patient increase physical therapy sessions and he was started on oral methotrexate 7.5mg PO weekly, which was later increased to 10mg weekly in an attempt to achieve disease stability. Light therapy was impractical, as the patient resided in a rural area.

Discussion

Stiff skin syndrome is a rare scleroderma-like disorder that may be congenital or occur early in childhood [1]. Recent studies have elucidated that it is caused by heterozygous missense mutations in the FBN1 gene encoding fibrillin-1 [5,6]. Mutations in fibrillin-1 lead to increased activation and signaling of TGF- β , resulting in fibroblast proliferation and the development of a profibrotic phenotype [5-8]. Reports have revealed familial recurrences, which suggest an autosomal dominant mode of inheritance [1,2,5]. SSS may clinically resemble several other sclerotic conditions, particularly morphea and systemic sclerosis, which may make its diagnosis challenging. However, there are some clinical and histopathological findings that may aid in distinguishing this condition from similar entities.

In SSS, patients present with unilateral, indurated, bound-down plaques in areas abundant in fascia such as the buttocks, and thighs. The overlying epidermis may be normal or mildly hyperpigmented, and often mild hypertrichosis is present on the affected sites [1-4]. Cutaneous stiffness may lead to joint immobilization and contracture formation, especially of large joints, which results in a characteristic lordotic stance with hip and knee flexion, and a protuberant abdomen [1-4]. Rarely, patients may experience dyspnea secondary to restriction of the thoracic cavity, but it is not associated with visceral organ involvement, immunological abnormalities, or vascular hyperactivity [2]. SSS has a stable to slowly progressive course but is non-fatal.

In contrast, systemic sclerosis is very rare in childhood and characteristically presents with symmetric involvement of the face and bilateral hands [9]. It is progressive and associated with the presence of auto-antibodies, Raynaud phenomenon, sclerodactyly, and capillary nail fold abnormalities [9,10]. Internal organ involvement is present and is a cause of significant morbidity and mortality. Morphea, particularly linear morphea, is clinically difficult to distinguish from stiff skin syndrome as it similarly presents as unilateral indurated plaques on the thighs of children, that are persistent and difficult to treat [11]. It may have underlying fascial and muscular involvement that results in impaired joint mobility and limb asymmetry [11], making it clinically indistinguishable from SSS. However, histological examination may yield information to differentiate between the two entities.

On histological examination, morphea and systemic sclerosis are characterized by dense thickened dermal collagen that may extend to the subcutis or fascia. There is decreased fibroblast cellularity and adnexal structures are often diminished and entrapped by collagen [12]. A lymphoplasmocytic infiltrate is often noted perivascularly. In contrast, SSS has a more heterogenous histological presentation. It may demonstrate fibroblast cellularity, with normal or thickened dermal collagen in a horizontal or haphazard arrangement, and fascial thickening and hyalinization [4,13]. Mucin may or may not be present. The adnexal structures are normal and without collagen trapping. There is no inflammatory infiltrate [2,4,14]. One study [13] proposed that a subcutaneous lattice-like array of thickened collagen and lack of inflammation suggests a diagnosis of stiff skin syndrome.

Becker nevus may similarly present as a unilateral indurated plaque with overlying hypertrichosis and hyperpigmentation, when associated with an underlying smooth muscle hamartoma. Lesions are typically located on the chest, shoulder, upper back, or lateral arm, though cases have been reported of lesions on the buttocks and lower extremities. Becker nevus usually presents during childhood or adolescence as opposed to birth through childhood, as seen in SSS. On histopathological examination, the epidermis may be normal, or reveal acanthosis, papillomatosis, and elongated rete ridges [15]. Increased bundles of smooth muscle are noted in the reticular dermis when associated with a smooth muscle hamartoma, which makes it easy to distinguish from SSS.

In our case, histopathological evaluation revealed haphazardly arranged spindle cells infiltrating normal collagen bundles and mild mucin deposition. No inflammation or adnexal changes were noted. These findings, along with the clinical presentation, led us to the diagnosis of stiff skin syndrome.

One could also consider diabetic stiff skin, also known as diabetic cheiroarthropathy; patients with this condition similarly present with taut skin and joint immobility. However, it may be readily distinguished from SSS owing to its clinical presentation. In contrast to stiff skin syndrome, patients with diabetic stiff skin are often older as this condition is secondary to longstanding diabetes. Additionally, patients with this condition present with thickened and taut skin limited to the dorsal hands and feet. These skin changes often result in limited mobility of the underlying interphalangeal joints and patients are often unable to approximate the volar surfaces of their fingers and palms while pressing both hands together, resulting in a characteristic "prayer sign." Other sclerotic conditions like sclerodermatomyositis, scleredema, nephrogenic systemic fibrosis, and eosinophilic fasciitis may similarly be considered when evaluating patients with SSS. However, these entities can typically be readily distinguished from SSS based on clinical and histopathological examination.

There are no effective treatment options for stiff skin syndrome. One study reported stability of disease with monthly IV methylprednisolone (20mg/kg) for 3 months with concurrent weekly subcutaneous doses of 25mg methotrexate [4]. However, long term follow-up revealed further disease progression. Reports of treatment with PUVA, oral penicillamine, calcipotriene, and topical corticosteroids have also failed to prove successful [4]. This is possibly related to the lack of inflammation and the presence of an underlying defect in fibrillin-1. Recently, a study revealed improvement of skin lesions and joint motility in a patient with stiff skin syndrome and smouldering myeloma when the patient was treated with hematopoietic stem cell transplant [16]. Although this was appropriate treatment for the reported patient, and yielded interesting results, hematopoietic stem cell transplant is not a reasonable treatment option for the typical SSS population who lack underlying malignancy. Physical therapy has been shown to improve joint mobility and prevent contracture formation, and remains the mainstay of therapy.

Conclusion

Stiff skin syndrome is a rare cutaneous disorder that is difficult to distinguish from other sclerotic diseases. Clinical and histopathological correlation is important when making the diagnosis as it is often one of exclusion. There are no effective treatments for this condition, though some anecdotal improvement has been reported with certain immunosuppressants. Physical rehabilitation should be initiated early as it is important to improve joint mobility, prevent contractures, and preserve quality of life.

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