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ESCLEROSIS SISTÉMICA EN UN PACIENTE EN EDAD PREESCOLAR: UNA MANIFESTACIÓN INUSUALMENTE TEMPRANA DE UNA ENFERMEDAD AUTOIMMUNE

Melissa Carrillo Hernández
Hospital General ISSSTE

Braulio Esteban López Reyes
Hospital General ISSSTE

Karime Giselle Sandoval Enriquez
Hospital General ISSSTE

Daniela Nicolle Gómez Narváez
Hospital General ISSSTE

Gloria Jimena Coello Uribe
Hospital General ISSSTE

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Systemic Sclerosis in a Preschool-Aged Patient: An Unusually Early Presentation of an Autoimmune Disease

Melissa Carrillo Hernández[1]
dra.melissa44carrillo@gmail.com
https://orcid.org/0009-0002-5196-1269
Hospital General ISSSTE Aguascalientes, Servicio de Medicina Interna, Aguascalientes, México.

Braulio Esteban López Reyes
brauliol.reyes1203@gmail.com
https://orcid.org/0009-0003-3547-2243
Hospital General ISSSTE Aguascalientes, Servicio de Pediatría, Aguascalientes, México.

Karime Giselle Sandoval Enriquez
kgse1124@gmail.com
https://orcid.org/0009-0003-4952-7209
Departamento de Medicina, Universidad Cuauhtémoc Plantel Aguascalientes, México

Daniela Nicolle Gómez Narváez
dra.nicollegomez@gmail.com
https://orcid.org/0009-0004-7086-1858
Hospital General ISSSTE Aguascalientes, Servicio de Cirugía General, Aguascalientes, México.

Gloria Jimena Coello Uribe
jimena_coello@hotmail.com
https://orcid.org/0009-0000-7659-1546
Hospital General ISSSTE Aguascalientes, Servicio de Cirugía General, Aguascalientes, México.

ABSTRACT

Introduction: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by skin fibrosis, vascular alterations, and specific autoantibodies. Onset during childhood is uncommon, and presentation at preschool age is exceptional. Case report: We describe an 8-year-old female presenting with a progressive indurated plaque on the left leg, refractory to topical treatments. Laboratory tests revealed positive antinuclear antibodies (ANA) and anti-topoisomerase I (Scl-70). Skin biopsy demonstrated epidermal atrophy and dermal sclerosis consistent with scleroderma. Nailfold capillaroscopy showed a scleroderma pattern, while chest CT, pulmonary function tests, and echocardiography revealed no visceral involvement. A diagnosis of juvenile systemic sclerosis was established. Methotrexate therapy was initiated, along with multidisciplinary follow-up, leading to clinical stabilization at six months. Discussion: Pediatric SSc accounts for less than 5% of all cases, with localized morphea being the most common subtype. Systemic disease at preschool age is exceedingly rare and poses diagnostic challenges. Capillaroscopy and systemic screening are essential for assessing progression risk. Methotrexate is considered first-line therapy in children, although long-term follow-up is mandatory to detect cardiopulmonary complications. Conclusions: This case contributes to the international literature by documenting an unusual presentation of SSc in preschool age, highlighting the importance of early diagnosis, immunomodulatory therapy, and multidisciplinary management.

Keywords: systemic sclerosis, pediatrics, autoimmunity, capillaroscopy, methotrexate.

[1] Autor principal
Correspondencia: dra.melissa44carrillo@gmail.com

Esclerosis sistémica en un paciente en edad preescolar: una manifestación inusualmente temprana de una enfermedad autoimmune

RESUMEN

Introducción: La esclerosis sistémica (ES) es una enfermedad autoinmune poco frecuente caracterizada por fibrosis cutánea, alteraciones vasculares y autoanticuerpos específicos. Su aparición durante la infancia es poco habitual, y su presentación en edad preescolar es excepcional. Caso clínico: Describimos el caso de una niña de 8 años que presentaba una placa indurada progresiva en la pierna izquierda, refractaria a los tratamientos tópicos. Las pruebas de laboratorio revelaron anticuerpos antinucleares (ANA) y anti-topoisomerasa I (Scl-70) positivos. La biopsia cutánea mostró atrofia epidérmica y esclerosis dérmica compatibles con esclerodermia. La capilaroscopia del lecho ungueal mostró un patrón de esclerodermia, mientras que la TC torácica, las pruebas de función pulmonar y la ecocardiografía no revelaron afectación visceral. Se estableció un diagnóstico de esclerosis sistémica juvenil. Se inició un tratamiento con metotrexato, junto con un seguimiento multidisciplinar, lo que condujo a la estabilización clínica a los seis meses. Discusión: La esclerosis sistémica pediátrica representa menos del 5 % de todos los casos, siendo la morfea localizada el subtipo más común. La enfermedad sistémica en edad preescolar es extremadamente rara y plantea dificultades diagnósticas. La capilaroscopia y el cribado sistémico son esenciales para evaluar el riesgo de progresión. El metotrexato se considera el tratamiento de primera línea en niños, aunque es obligatorio realizar un seguimiento a largo plazo para detectar complicaciones cardiopulmonares. Conclusiones: Este caso contribuye a la literatura internacional al documentar una presentación inusual de la ES en edad preescolar, lo que destaca la importancia del diagnóstico precoz, el tratamiento inmunomodulador y el manejo multidisciplinario.

Palabras clave: esclerosis sistémica, pediatría, autoinmunidad, capilaroscopia, metotrexato

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic, multisystem autoimmune disease characterized by cutaneous fibrosis, vascular abnormalities, and the presence of specific autoantibodies against nuclear and cytoplasmic antigens[1]. Although its pathogenesis is not fully understood, it is recognized as the result of interactions among genetic, epigenetic, immunological, and environmental factors[2,3].

SSc is considered a rare disease, with an estimated prevalence ranging from 7 to 489 cases per million inhabitants and an annual incidence varying from 0.6 to 122 cases per million, with significant geographic differences[1,4]. The average age of onset is between 30 and 50 years, with a clear female predominance[5].

In the pediatric population, systemic sclerosis is extremely rare. Fewer than 5% of cases occur before the age of 16, and when it does, it usually manifests as localized scleroderma in the form of morphea, while the systemic variant at preschool age is even less common[6,7,8]. These cases pose diagnostic and therapeutic challenges due to the lack of validated clinical criteria for children and the limited cumulative experience available in the literature[9].

The prognosis of SSc largely depends on visceral involvement, particularly cardiopulmonary disease. Complications such as pulmonary hypertension and interstitial lung fibrosis account for most of the mortality, which may be up to eight times higher than in the general population[10,11].

The present report describes a case of systemic sclerosis in a preschool-aged patient, representing a particularly unusual manifestation of the disease and contributing to the available literature on this entity in childhood.

Case Presentation

We report the case of an 8-year-old female patient, originally and resident of Mexico. She was the third child of a pregnancy complicated by maternal gestational diabetes, delivered via cesarean section at 38 weeks of gestation, with a birth weight of 3100 gr and length of 50 cm, both appropriate for gestational age. Psychomotor development was normal, and immunizations were up to date for age.

Family history

The mother had a history of type 2 diabetes mellitus and systemic arterial hypertension. The maternal grandparents had oncological histories (gastric and stomach cancer), and the paternal grandfather had pancreatic cancer. The father had no known chronic illnesses.

Personal history

The patient denied medication allergies, genetic conditions, or chronic diseases. There was no history of recurrent infections or previous hospitalizations.

History of present illness

At 8 years of age, her mother noticed the appearance of an indurated skin lesion on the anterior aspect of the left leg, measuring approximately 5 cm in diameter, non-painful, without erythema or associated systemic symptoms. The lesion gradually progressed in size over the following months, despite multiple topical treatments prescribed by different physicians (including corticosteroids, emollients, and topical antibiotics) without improvement, which led to referral for pediatric dermatology evaluation.

Physical examination

Dermatological examination revealed a localized dermatosis on the anterior surface of the left leg, characterized by an indurated plaque measuring 10 × 7 cm, with a rough, shiny surface, light brown hyperpigmentation, loss of skin elasticity, and difficulty in pinching the lesion. There was no tenderness on palpation or local inflammatory signs. No additional cutaneous lesions or mucosal abnormalities were identified. Facial telangiectasias and Raynaud's phenomenon were not observed at that time.

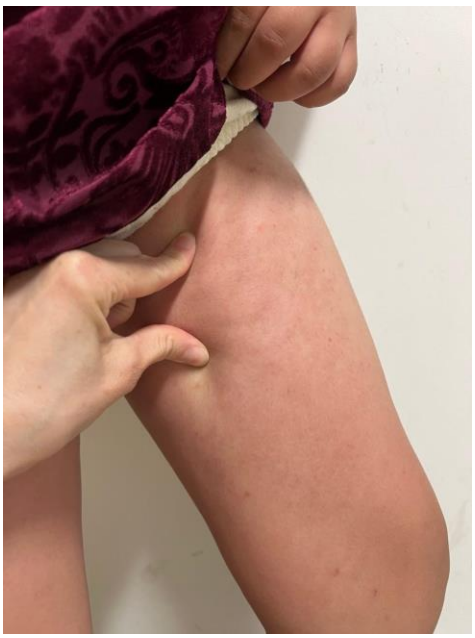

Figure 1. Clinical examination of the right lower limb showing soft edema on the thigh with evident pitting on digital pressure.

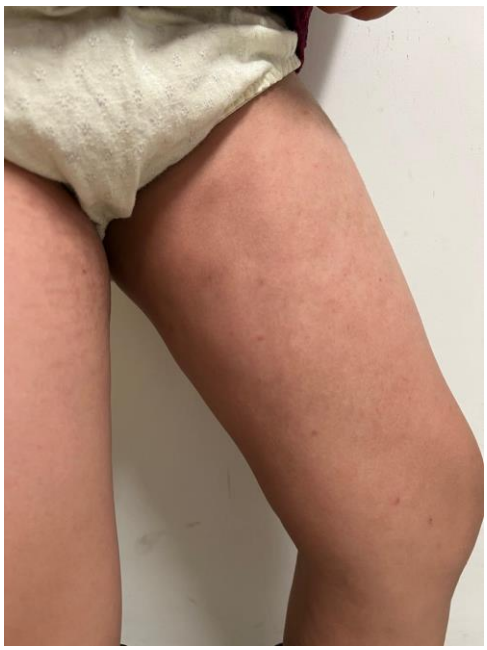

Figure 2. Same limb at rest, showing mild diffuse erythema and persistence of proximal edema.

General physical examination showed weight and height appropriate for age, blood pressure of 90/60 mmHg, heart rate of 88 bpm, respiratory rate of 18 breaths per minute, and temperature of 36.7 °C. No signs of respiratory or cardiovascular involvement were observed on initial examination.

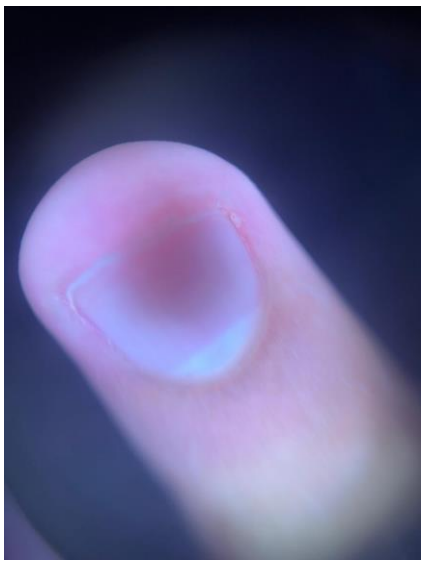

Figure 3. Nail evaluation under dermoscopy revealing periungual inflammatory changes and a small lateral fissure.

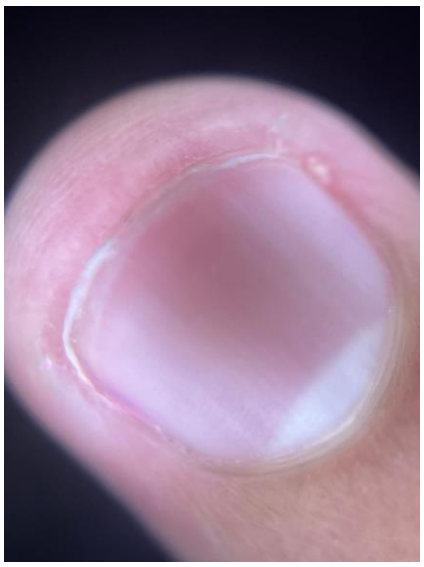

Figure 4. Magnified view of the nail demonstrating mild hyperkeratosis of the proximal nail fold and periungual groove, consistent with chronic inflammatory involvement.

Laboratory studies Initial laboratory tests revealed the following:	**Immunologic profile:**
● **Complete blood count:** hemoglobin 12.4 g/dL, leukocytes 6,500/µL, platelets 280,000/µL. ● **Serum chemistry:** glucose 88 mg/dL, urea 28 mg/dL, creatinine 0.5 mg/dL. ● **Liver function tests:** AST 25 U/L, ALT 21 U/L, ALP 180 U/L. ● **Erythrocyte sedimentation rate:** 36 mm/h. ● **C-reactive protein:** 1.2 mg/dL.	● ANA positive, speckled pattern, at a titer of 1:320. ● Anti–topoisomerase I (Scl-70) antibodies positive. ● Anti-centromere antibodies negative. ● Anti-Smith and anti-RNP antibodies negative. ● Rheumatoid factor and anti-CCP antibodies negative. ● Complement C3 and C4 within normal ranges.

Imaging and complementary studies

- **Skin biopsy:** a 0.9 × 4 cm specimen from the left leg showed focal epidermal atrophy, hyalinization and dermal sclerosis, with adnexal atrophy, consistent with scleroderma.
- **Nailfold capillaroscopy:** demonstrated decreased capillary density with avascular areas and the presence of megacapillaries, findings compatible with a scleroderma pattern.
- **Plain radiograph of the left leg:** no evidence of calcinosis or bone involvement.
- **High-resolution chest CT (HRCT):** no evidence of interstitial lung fibrosis.
- **Transthoracic echocardiogram:** preserved ventricular function, no estimated pulmonary hypertension.
- **Pulmonary function tests:** within normal parameters for age.

Clinical course and management

Based on the clinical, serological, and histopathological findings, a diagnosis of juvenile systemic sclerosis, localized form with risk of systemic progression, was established. The case was discussed with pediatric rheumatology, and treatment with oral methotrexate at 10 mg/m²/week was initiated, along with folic acid supplementation and photoprotection measures. Multidisciplinary follow-up was recommended, including periodic cardiopulmonary evaluations for early detection of complications.

At the 6-month follow-up, the patient demonstrated stabilization of the cutaneous lesion, with no development of new plaques or systemic involvement.

Discussion

Systemic sclerosis (SSc) is a heterogeneous disease with a clinical spectrum that differs widely between adult and pediatric populations. In children, the most frequent form is localized scleroderma (morphea), while the systemic variant accounts for less than 5% of cases, with onset usually occurring during adolescence[6,7]. Presentation at preschool age, as in this case, is exceedingly rare and has only been reported sporadically in the literature[12,13].

Characteristic	Adults	Pediatric
Age of onset	Peak between 30–50 years[1,2]	<16 years in <5% of cases[6,7]
Predominant sex	Female-to-male ratio 3–6:1[2,3]	Female predominance also observed, but with a lower ratio (≈2:1)[7]
Most frequent clinical form	Systemic, either diffuse or limited (CREST)[1,2]	Localized (morphea) much more common; systemic form very rare[6,8]
Initial cutaneous manifestations	Raynaud's phenomenon, distal skin thickening, telangiectasias[2,4]	Indurated plaques, linear or localized morphea; Raynaud's phenomenon less frequent[7–9]
Associated autoantibodies	ANA >90%, anti-centromere (limited), anti–Scl-70 (diffuse)[2,4]	ANA frequent, but specific autoantibodies less consistent; Scl-70 may be positive in some juvenile systemic cases[7,9]
Visceral involvement	Pulmonary (interstitial fibrosis), pulmonary hypertension, gastrointestinal, renal, cardiac[2,5]	Less frequent at onset; risk of pulmonary and cardiac involvement increases during

		adolescence[6,7,9]
Prognosis	Mortality 5–8 times higher than the general population; main causes: pulmonary hypertension and pulmonary fibrosis[10,11]	Overall better prognosis, but systemic cases may progress with severe complications[7,9]
Standard treatment	Immunosuppressants (methotrexate, mycophenolate, cyclophosphamide), vasodilators, antifibrotic agents[2,5]	Similar to adults, adjusted to age and tolerance; methotrexate most commonly used as first-line in juvenile forms[8,9]

Early diagnosis in pediatric patients is challenging due to clinical overlap with other indurated dermatoses and the lack of validated diagnostic criteria specifically for children. Nevertheless, positivity for ANA and anti–topoisomerase I (Scl-70), along with compatible histopathological findings, provide strong evidence to support the clinical suspicion and differentiate it from other entities such as localized morphea or cutaneous lupus erythematosus[3,8,14].

Nailfold capillaroscopy, as performed in our patient, is a non-invasive tool that allows the detection of early microvascular alterations and is highly useful for identifying patients at risk of progression to systemic involvement[15]. Recent studies confirm that typical SSc capillaroscopic patterns can be present from the earliest phases of the disease, even in childhood[16].

With respect to systemic assessment, it is recommended to rule out visceral involvement from the outset, particularly pulmonary and cardiac. In this case, high-resolution chest CT and pulmonary function tests were normal, and echocardiography showed no evidence of pulmonary hypertension. These findings are consistent with pediatric cohorts, where initial visceral involvement is uncommon, but its incidence increases over time, justifying close follow-up[7,9,17].

Immunosuppressive therapy remains the cornerstone of management. Methotrexate is considered first-line treatment for progressive cutaneous forms or localized disease at risk of systemic involvement in children, with documented efficacy in several studies and an acceptable safety profile[18,19]. In refractory

cases, mycophenolate mofetil, cyclophosphamide, or biologic agents such as tocilizumab have been used, although evidence in children is limited and largely extrapolated from adult experience[20,21].

The prognosis in pediatric patients is generally more favorable than in adults, especially when there is no initial visceral involvement. Nonetheless, mortality associated with cardiopulmonary complications remains significant, underscoring the importance of multidisciplinary follow-up involving pediatric rheumatology, dermatology, and pulmonology[10,11,21].

Finally, this case contributes to the literature by documenting a rare presentation of systemic sclerosis in preschool age, reinforcing the need for comprehensive management and the creation of international pediatric registries to improve understanding of the disease in this population[21].

CONCLUSIONS

Systemic sclerosis in childhood is an uncommon condition, and its presentation at preschool age is exceptional. This case highlights the importance of considering the disease in the differential diagnosis of indurated dermatoses in children, particularly when accompanied by positive autoantibodies and compatible histopathological findings.

A multidisciplinary approach, including dermatology, rheumatology, and pediatric pulmonology, is essential for the early detection of potentially severe systemic complications. Nailfold capillaroscopy and systemic screening studies allow for close monitoring and timely management.

Immunomodulatory treatment with methotrexate represents the first-line therapy in this age group and may stabilize cutaneous disease, although long-term follow-up is required due to the risk of progressive cardiopulmonary involvement.

Finally, this case expands the existing literature on juvenile systemic sclerosis, underscoring the need for international multicenter registries to better understand the clinical course, prognostic factors, and optimal therapeutic strategies in the pediatric population

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