CASE REPORT

Pediatrics Sciences Journal (*PedScij*) 2024, Volume 5, Number 1: 17-21
P-ISSN: 2722-0427, E-ISSN: 2722-1474

Pediatric Sciences Journal

Published by
Pediatrics Sciences Journal

Challenging diagnostic of juvenile systemic sclerosis in limited sources: a case report

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Received: 2024-03-10
Accepted: 2024-05-01
Published: 2024-05-27

ABSTRACT

Background: Juvenile Systemic Sclerosis (JSSc) is a rare chronic-autoimmune rheumatic disease leading to potential delay in diagnosis, especially in limited sources due to lack of knowledge and facility. This case report aimed to present a rare case of JSSc in limited sources of medical facilities.

Case presentation: A 15-year-old girl was earlier suspected of having congenital heart disease due to the presentation of bluish fingers without any detectable clinical heart disease manifestation, including normal electrocardiography as well as echocardiography. The patient experienced pain and difficulty executing wrist endorotation, representing limited joint movement action. Further physical examinations showed pale, cold fingers and toes, bluish color in the peripheral represented sclerodactyly and arthritis. Skin showed multiple erythema-hypopigmentation papuls, in accordance with gottorn papule, gottorn sign. The antinuclear antibody titer was 1:320. Chest CT-Scan result was a fibrotic line at the inferior lobe of the left lung with the left diaphragm tenting due to a chronic inflammatory process. Skin biopsy shows an acanthotic epidermis, dermafibrocollagenous tissue with extensive fibrosis, and sclerosis with vascular proliferation. These findings meet JSSc PRES, ACR, and EULAR standard classification criteria, including 1 major and 4 minors. The treatment regimen was started with methylprednisolone 2 mg/kg/day, then tapering off once clinical manifestation alleviated, methotrexate 10 mg/BSA, and folic acid 1 mg a day. Long-term monitoring plans are also scheduled.

Conclusion: Recognizing early symptoms of JSSc would provide a better outcome.

Keywords: juvenile systemic sclerosis, Raynaud's phenomenon, autoimmune rheumatic disease.
Cite This Article: Ronaldi, M., Wati, K.D.K., Gunawijaya, E., Yantie, N.P.V.K., Anandasari, P.P.Y. 2024. Challenging diagnostic of juvenile systemic sclerosis in limited sources: a case report. *Pediatrics Sciences Journal* 5(1): 17-21. DOI: 10.51559/pedscij.v5i1.88

INTRODUCTION

Children with chronic illnesses experience significant effects on their social, academic, psychological, and physical development. A rare chronic autoimmune rheumatic disease known as juvenile systemic sclerosis (JSSc) is rarely documented in the literature. The incidence and prevalence of systemic sclerosis in the US were 15.1 and 25.9 per 100,000 person-years, respectively.[1] Although the precise number of scleroderma cases in Indonesia is unknown, six instances were found between 1986 and June 2006, according to a case report from Dr. Cipto Mangunkusomo Hospital.[2] Rare cases led to potential diagnosis delays, especially in limited sources due to lack of knowledge and facility. This case report aimed to present a rare case of JSSc in limited sources of medical facilities.

CASE PRESENTATION

A 15-year-old girl is referred from SH Hospital to the emergency unit of Prof. I.G.N.G Ngoerah Central Hospital with a diagnosis of suspected cyanotic congenital heart disease with a differential diagnosis of Raynaud Phenomenon. The patient came with a chief complaint of cyanotic fingers 4 months before being admitted to the hospital without shortness of breath with activity or when lying down, rapid or irregular heartbeat, and chest pain. Her fingers worsened when it was cold and got better when it was warmer.

The patient also complained that her joint was painful and making a sound every time she moved for years. This condition affected her routine because she was limited to sports activities and small joint movements like opening jars and cans, but she could write well. Her eyes were blurring for months, but it did not affect her routine.

A week before admission, the patient had a fever with the highest temperature, 38.5°C, and a day later, the patient had a cough and cold. The patient was brought to the midwife and general practitioner, but it was not improving. The patient was referred to a cardiologist at SH Hospital with suspected cyanotic congenital heart disease and then was referred to Prof. I.G.N.G Ngoerah Hospital.

The patient could eat well without difficulty swallowing with regurgitation symptoms like a burning sensation in the chest, backwash of food or sour liquid, and an unpleasant sensation in the throat. History of diarrhea or constipation was denied.

Six months before admission, the

patient complained of painless red rashes in whole fingers and ulcers at the top of her fingers. She was brought to the hemato-oncology pediatrician and was diagnosed with iron deficiency anemia. Then, she was given iron supplements for 3 months. Ulcers dried, the skin became discolored, and the patient was unaware of another discolored skin lesion on her body. The history of this complaint also occurred when she was 8 years old for 3 months, and this complaint never occurred until admission.

The patient did not have tears when 3-month-old to 3 years old. The patient was diagnosed with congenital cataracts and had cataract surgery at 5 years old. After surgery, the patient could see clearly and had tears.

The patient is the second child of two children. Her brother has the same complaints: His finger becomes pallor and cyanotic in cold temperatures and improves in warm temperatures. His brother has not been treated yet. The family history of autoimmunity was denied. There is consanguinity in her parents.

The patient was born spontaneously, a full term without complication, even though the mother had no antenatal examination. She grew well until the complaint started at 3 years old. History of diaphoresis, longer breastfeeding time, poor weight gain, and bluish or purple discoloration of the skin or mucous membranes are denied.

Now, the patient is in first-grade high school. The patient has good academic scores in Mathematics and English. The patient is easygoing and friendly. The patient does not have any history of being bullied.

The physical examination shows the patient's nutritional status is mild protein energy malnutrition (Body mass index < -1 SD). From eye examination, visual acuity at both eyes is 6/60 and intraocular lens at both eyes. Teeth examination revealed malaligned teeth, dentures, gangrene radix, and necroes of pulp, pulpitis (Figure 1). From Skin efflorescence, there are multiple rounded macula hypopigmentation with diameter 0.3-0.6 cm, multiple rounded erythema plaque with diameter 0.3–0.4 cm, multiple

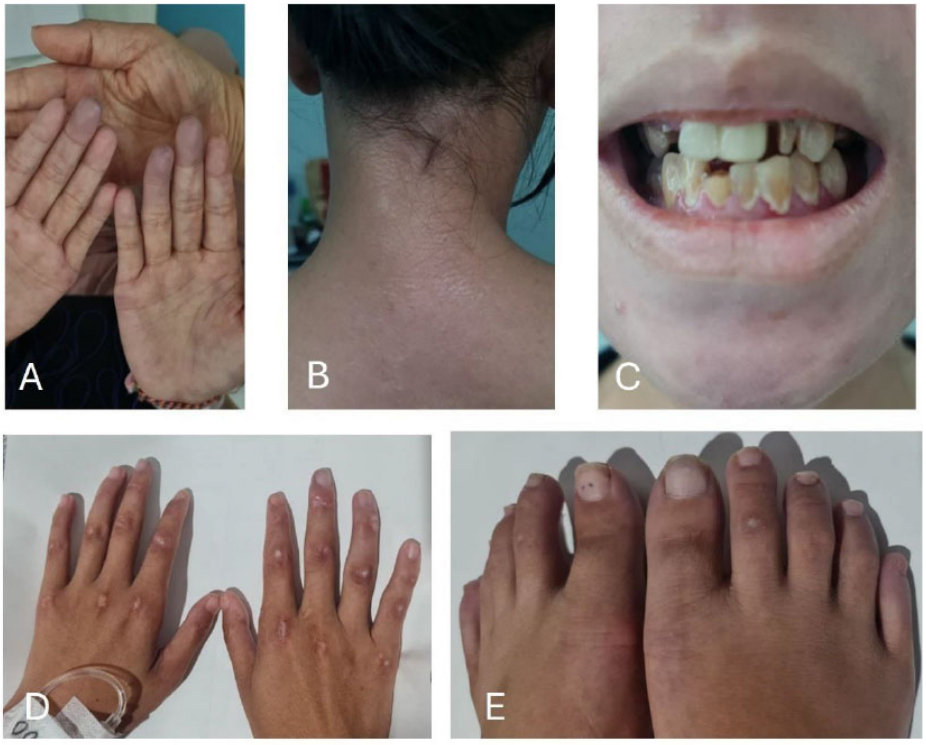

Figure 1. Clinical manifestation of the patient. (A) Raynaud Phenomenon; (B) Salt and Paper appearance; (C) Malalignment teeth; (D) and (E) Hypopigmentation macule and thickening.

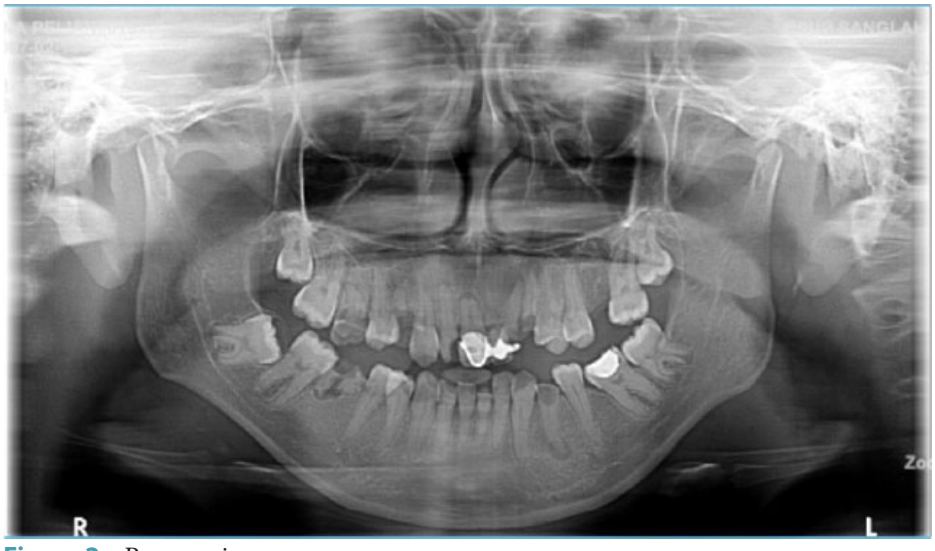

Figure 2. Panoramic x-ray.

erythemas – hypopigmentation papules with diameter 0.2- 0.4 cm, gottorn papule (+), gottorn sign (+) at digit I-V manus dextra et sinistra, digit II pedis dextra et sinistra (Fig. 4-5). Raynaud phenomenon at digit I-V manus dextra et sinistra (Figure 1). Multiple rounded - geographic macula hypopigmentation with sized 0.5 – 0.8 cm. Multiple macula depigmentation forms a salt and pepper appearance measured 0.5x0.8 cm at the back of the neck (Figure 1). The modified Rodnan Skin Score (MRSS) was 25, and the Childhood Myositis Assessment Scale (CMAS) was 46.

Complete blood count and renal function examination, we found normal results with eGFR 149.28 ml/min/1.73m^2. Indirect immunofluorescence ANA result showed a speckled pattern with titer 1:320. Complement C3 result is 119,7. ANA Profile result is negative. Spirometry

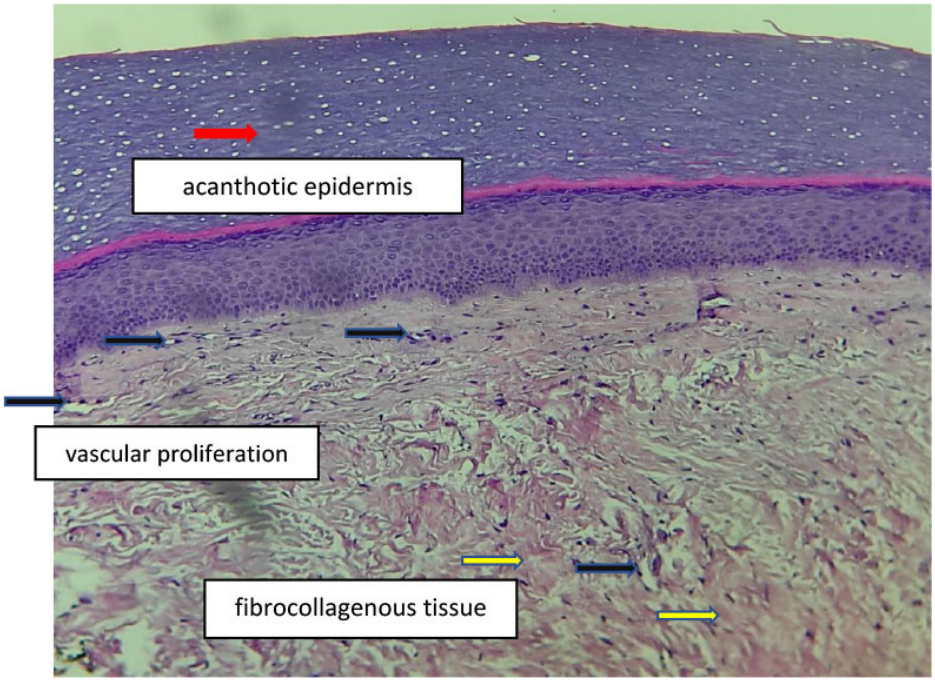

Figure 3. Skin biopsy.

Table 1. Preliminary classification criteria for JSSc[11]

Major criterion - proximal sclerosis/induration of the skin
Minor criteria
Skin
Sclerodactyly
Vascular
Raynaud's phenomenon
Nailfold capillary abnormalities
Digital tip ulcers
Gastrointestinal
Dysphagia
Gastroesophageal reflux
Renal
Renal crisis
New-onset arterial hypertension
Cardiac
Arrhythmias
Heart failure
Respiratory
Pulmonary fibrosis (high-resolution computed tomography/ radiograph)
Diffusing lung capacity for carbon monoxide
Pulmonary hypertension
Musculoskeletal
Tendon friction rubs
Arthritis
Myositis
Neurological
Neuropathy
Carpal tunnel syndrome
Serology
Antinuclear antibodies.
SSc-selective autoantibodies (anticentromere, anti topoisomerase I, anti fibrillarin, anti-PM-Scl, ant-fibrillin or anti-RNA polymerase I or III)

result was moderate restriction and no obstruction with Force Vital Capacity (FVC 62%). Panoramic x-ray shows occlusal caries teeth, interproximal caries, periapical cysts, pulpitis, and unerupted teeth (Figure 2). The electrocardiography result was sinus rhythm, and the echocardiography result was mild pulmonary regurgitation with a Left Ventricular Ejection Fraction (LVEF) of 69.7%. Chest high-resolution CT Scan result was a fibrotic line at the inferior lobe of the left lung with left diaphragm tenting due to chronic inflammatory process, emphysema at the apical segment of superior lobe right lung, and multiple lymph node sub-centimeter at left and right axilla region, right upper-lower paratracheal and subaortic. Skin biopsy shows an acanthotic epidermis, derma fibro collagenous tissue with extensive fibrosis, and sclerosis with vascular proliferation differential diagnosis acral angiofibroma (Figure 3).

Using classification criteria from the Rheumatology European Society (PRES), the American College of Rheumatology Pediatric (ACR), and the European League Against Rheumatism (EULAR), from all findings, we established the diagnosis of JSSc and the clinical features suggested limited cutaneous type. Considering the natural course of the disease, which is mild but also progressive, the availability of medication from where she lived, and potential long-term side effects, we decided to give methylprednisolone at 2 mg/kg body weight, then tapering off once clinical manifestation alleviated. The patient also consumes methotrexate 10 mg/body surface area once a week and folic acid 1 mg a day. Along with medication, the patient takes more fluid intake for connective tissue hydration and exercise for joint mobility. Long-term monitoring plans for eyes, teeth, muscles, and joints are scheduled. The patient was informed regarding treatment adherence for good outcomes.

DISCUSSION

The 15-year-old girl featured in this paper has been diagnosed with JSSc. There are no precise epidemiological data on the frequency or prevalence of JSSc, making this case extremely uncommon. The

Table 2. JSSc Severity Score[11]

	O (normal)	1 (mild)	2 (moderate)	3 (Severe)	4 (end-stage)	Maximum possible score
General	BMI ³ baseline Hgb >11.5 gm/dl	BMI < 1st centile Hgb 10–11.4 gm/dl	MI < 2nd centile Hgb 9–9.9 gm/dl	BMI < 3rd centile Hgb 7–8.9 gm/dl	BMI < 4th centile Hgb < 7 gm/dl	4
Vascular	No Raynaud's	Raynaud's requiring vasodilators	Digital tip scars	Digital tip ulcerations	Digital gangrene	4
Skin	MRSS 0	MRSS 1–14	MRSS 15–29	MRSS 30–39	MRSS 40	4
Osteoarticular	No articular involvement		presence of limited range of motion		Presence of arthritis or tendon friction rub	2
Muscle	normal proximal muscle strength	CMAS 39–51	CMAS 26–38	CMAS 13–25	CMAS 0–12	2
GI	Normal results of proximal GI tract investigations	GI symptoms Distal esophageal hypomotility GERD on 24-hour Ph-metry or scintiscan	Medium or high esophageal hypomotility	Malabsorption syndrome	Hyperalimentation	4
Respiratory	DLCO >80% FVC >80% Normal HRCT sPAP <30 mm Hg	DLCO 70–79% FVC 70–79% Ground glass changes on HRCT sPAP 31–45 mm Hg	DLCO 50–69% FVC 50–69% Honeycomb changes on HRCT sPAP 46–75 mm Hg	DLCO 50% FVC 50% Fibrosis on radiography sPAP 75 mm Hg	O_2 dependence	8
Cardiac	Normal EKG LVEF >50%	EKG conduction defect LVEF 45–49%	Arrhythmia LVEF 40–44%	Arrhythmia requiring treatment LVEF 30–39%	Congestive heart failure LVEF 30%	8
Renal	GFR >90 ml/minute	GFR 75–89 ml/minute	GFR 50–74 ml/minute	GFR 10–49 ml/minute	End-stage renal failure	4

estimated mean age of systemic sclerosis is 8,8 years, and 3–10% of patients are thought to have started the disease before turning 18 years old.[3] From the report of a multinational, worldwide cross-sectional questionnaire-based survey of 135 JSSc patients from 34 pediatric rheumatology centers reported that 122 patients were Caucasian and 100 were female patients.[2] Childhood systemic sclerosis affected females more than males.[3-5] Skeletal muscle involvement occurred more than twice in the childhood-onset compared to the adult onset. Systemic sclerosis survival in childhood-onset was better than adult onset.[6]

In our case, the patient was female, corresponding with the worldwide incidence. Females are more likely to have this condition compared to males. The onset for this patient was 8 years old, corresponding with epidemiological data, which stated that the mean onset age was 8.8 (±3.3) years.

An autoimmune condition called scleroderma affects the skin and other body organs in certain situations. The main symptoms of localized scleroderma are skin tightness and thickness.[7,8] It can cause inflammation and damage when it spreads to internal organs, including the heart, kidneys, lungs, and digestive tract. In contrast, systemic sclerosis affects internal organs such as the heart, lungs, and kidneys, leading to symptoms such as dysphagia, heartburn, dyspnea, hypertension, and pulmonary hypertension.[8] Raynaud's syndrome, characterized by paleness or blueness in the extremities and occasionally the face due to restricted blood flow, is common in children with systemic sclerosis.[8] It is noteworthy that one of the most serious rheumatologic disorders identified in children is systemic sclerosis, which manifests differently in children than in adults.[8-10]

The American College of Rheumatology (ACR), the European League Against Rheumatism (EULAR), and the Pediatric Rheumatology European Society (PRES) comprised the Committee on Classification Criteria for JSSc. The committee's goal was to standardize the conduct of clinical, epidemiological, and outcome research for this uncommon pediatric disease, which is frequently underdiagnosed, as indicated in Table 1.[11]

In our case, the diagnosis of JSSc was established from one major criterion: sclerosis, and 4 minor criteria: digital tip ulcers, Raynaud's phenomenon (vascular), arthritis (musculoskeletal), pulmonary fibrosis (respiratory), and positive antinuclear antibody (serology). La Torre *et al.* proposed a severity score for JSSc because there is no severity score ever validated in pediatrics with SSc, as shown in Table 2.[12] In our case, the patient severity

score using JSSc severity score was 14.

Eighty-one percent of JSSc patients have antinuclear antibodies (ANA), and thirty-four percent also have anti-topoisomerase I (anti-Scl-70) antibodies. Anticentromere antibodies, which are seen in 7-8% of children, and anti-topoisomerase I (anti-Scl-70) may be less common in children (20–30%) compared to adults (30–40%).[11,12] The patient in our instance had 1/320 ANA positivity and negative anti-Scl-70 results.

SSc treatment should be according to organ involvement. By controlling the disability and loss of function, the treatment seeks to improve the patient's quality of life while slowing or stopping the disease's course.[12] Methotrexate (MTX) is recommended by EUSTAR for the treatment of recent diffuse types of SSc. 0.3 mg/kg per week is the maximum suggested dosage, which can be administered subcutaneously or orally.[13] From multi-center, randomized, double-control studies suggested using immunosuppressive treatments. The most classical and common immunosuppressive drugs are corticosteroids, although these agents have not been widely accepted for treating SSc.[14] Takehara uses low-dose corticosteroid therapy starting with 20 mg/day and decreasing to 2.5-10 mg/day of prednisolone for maintenance. This research found that 16 of 23 patients with SSc show good to excellent reducing MRSS.[14]

In our case, the patient received oral methotrexate 10 mg/body surface area and methylprednisolone at 2 mg/kg body weight, which tapered off as the skin sclerosis improved. In two weeks, MRSS was reduced.

Our limitation in this case report writing is that we did not include testing for all SSc-selective autoantibodies because of the limited sources.

CONCLUSIONS

A comprehensive examination is needed to diagnose JSSc early. Recognizing early symptoms of JSSc would improve patients' outcomes.

CONFLICT OF INTEREST

None declared.

FUNDING

The authors receive no specific grant from any public, commercial, or not-for-profit funding agency.

INFORMED CONSENT

Written informed consent has been obtained from the patient's parents.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this study.

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