

### Juvenile Localized Scleroderma: A Very Rare Case

Nibedita Paul<sup>1</sup>, Md. Rafiqul Islam<sup>2</sup>, Nadia Nusrat<sup>3</sup>, Lazina Sharmin<sup>4</sup>, Md. Mahamudul Hasan<sup>5</sup>

#### Abstract

*Juvenile localized scleroderma (JLS) is a rare chronic inflammatory and fibrosing disorder. It can result in significant morbidity, disfigurement, and severe functional, aesthetic and psychological disabilities. Patients with JLS should be identified early, evaluated extensively, treated aggressively, and monitored carefully. Here the case of a 2 year old boy is reported who was admitted into the department of Paediatrics of Delta Medical College & Hospital, Dhaka, Bangladesh with painful swelling of all fingers of both hands for 6 months and blackish patches over the fingers for the last one and half months. Left little finger was the first finger affected and there was flexion contracture of both left little and index fingers. The boy was diagnosed as a case of juvenile localized scleroderma and was confirmed by skin biopsy. We treated the child with methotrexate and prednisolone. It is very essential to raise awareness about this disease among clinicians and also parents for early diagnosis and treatment.*

**Keywords:** Scleroderma; localized scleroderma; juvenile localized scleroderma

*Delta Med Col J. Jul 2015;3(2):96 – 101*

#### Introduction

Scleroderma is a chronic systemic autoimmune disease characterized by hardening (sclero) of the skin (derma). In the more severe form, it also affects internal organs.<sup>1,2</sup> Scleroderma is characterized by increased synthesis of collagen (leading to the sclerosis), damage to small blood vessels, activation of T lymphocytes and production of altered connective tissues.<sup>3</sup> The aetiology of scleroderma is unknown but the mechanism of disease appears to be a combination of vasculopathy, autoimmunity, immune activation and fibrosis.<sup>1,4</sup> Strong associations with certain mutations in the HLA gene have been

identified.<sup>5,6</sup> Environment influences have also been implicated in the aetiology of scleroderma.<sup>7,8</sup>

Scleroderma is found worldwide and is less common in the Asian population.<sup>1,2,9</sup> The approximate female to male ratio of paediatric localized scleroderma is 2:1.<sup>10</sup> Estimated prevalence of juvenile scleroderma is 1/100,000. Localized scleroderma is the predominant type seen in paediatric population. Ratio of localized and systemic scleroderma is 10:1. Juvenile localized scleroderma (JLS) is the major form of scleroderma in the paediatric population.

1. Assistant Professor, Department of Paediatrics, Delta Medical College & Hospital, Dhaka, Bangladesh.
2. Professor & Head, Department of Paediatrics, Delta Medical College & Hospital, Dhaka, Bangladesh.
3. Resident Physician, Department of Paediatrics, Delta Medical College & Hospital, Dhaka, Bangladesh.
4. Assistant Professor, Department of Paediatrics, Enam Medical College & Hospital, Savar, Bangladesh.
5. Assistant Registrar, Department of Paediatrics, Delta Medical College & Hospital, Dhaka, Bangladesh

**Correspondence:** Dr. Nibedita Paul. e-mail: dr.nibedita.bd@gmail.com

Because JLS presents in young children and can dramatically affect limb and/or craniofacial growth, it is associated with high morbidity and lifelong disability. Localized scleroderma is divided into several subgroups: plaque morphea, generalized morphea, bullous morphea, localized scleroderma and deep morphea. Localized scleroderma (LS)/morphea is largely limited to the skin.<sup>11-14</sup>

The onset of scleroderma is generally insidious and manifestation varies according to disease subtype. The initial skin manifestation of localized disease includes early oedema and erythema followed by indurated, hypopigmented or hyperpigmented, atrophic lesion. Upto 25% of children with LS have extracutaneous manifestations most commonly arthritis (47%) and neurologic symptoms (17%) associated with en coup de sabre.<sup>3</sup> Localized scleroderma, also known as 'morphea', has a different pattern of skin involvement than systemic sclerosis (SSc) and encompasses several subtypes classified by depth and pattern of the lesion(s). The group of disorders is characterized by fibrosis that is mainly confined to the skin and subcutaneous tissue; however, deeper forms also involve the fascia, muscle, tendon and joint capsule.<sup>14</sup> Various autoimmune conditions are associated with scleroderma. In general, the most frequently reported conditions are Hashimoto thyroiditis, vitiligo, and insulin dependent diabetes mellitus (IDDM).<sup>15,16</sup>

We describe a case of a child affected by juvenile localised scleroderma which we encounter rarely.

## Case report

A 2 years old male child hailing from Mohakhali, Dhaka was admitted into the department of Paediatrics of Delta Medical College & Hospital on 25-2-2014 with painful swelling of all fingers of both hands for 6 months and blackish patches over the fingers for the last one and half months. Left little finger was the first finger affected. Mother also gave history of recurrent attack of fever. But there were no respiratory, gastrointestinal or neurological problem. There

was no history suggestive of associated endocrine problem. He was the second issue of his parents and his parents were first degree cousins. His elder sister was healthy. His father was a day labourer.

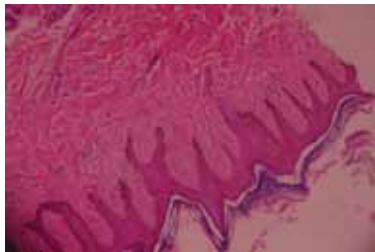
On examination the child was fretful, moderately pale. His weight was 8.2 kg and height 79 cm. His anterior fontanelle was open. Eye examination revealed no abnormality. All the fingers of both hands were swollen, tender and hot. There were several blackish patches on the fingers and flexion contracture of both left little and index fingers. Both heels were also hardened. There was no organomegaly. He had no neurological abnormality. There was no feature suggestive of endocrine disorder.

Laboratory investigations: CBC with PBF showed microcytic hypochromic anaemia with eosinophilia. Hb% was 9.3 gm/dL, eosinophil count 28%, ESR 10 mm in the 1st hour, CRP < 6mg/dL, ANA - moderately positive and serum ferritin level was 2.6 ng/mL. Random blood sugar was within normal limit. Thyroid function, kidney function and liver function tests revealed normal values. Urine for R/M/E revealed no abnormality. X-ray right hand showed osteopenia and X-ray chest was normal. There was moderate hyperkeratosis and acanthosis in the epidermis on skin biopsy. The dermis revealed increased collagenization and mild infiltration of inflammatory cells. Features were suggestive of scleroderma. Hb electrophoresis revealed haemoglobin E trait. The child was diagnosed as a case of localized scleroderma deep morphea type with nutritional anaemia, protein energy malnutrition and haemoglobin E trait.

The parents were properly counseled. We started treatment with oral prednisolone and inj. methotrexate to be continued for one year. Dietary advice and micronutrients supplementations were also given. In addition he was advised for physiotherapy. The parents were very poor and illiterate. They did not put him on physiotherapy and he was on irregular follow up. After 6 months of treatment blackish pigmentation disappeared and hardening of the fingers and heels were softened. Follow up laboratory findings were also suggestive of control of disease (e.g. eosinophil count 2%).



**Fig 1:** Showing sclerodermatous change of hands of 2 years old male child



**Fig 2:** Skin biopsy showing features of scleroderma

## Discussion

The most common form of JLS in children is linear scleroderma.<sup>17-19</sup> Our patient was diagnosed to have juvenile localized scleroderma of deep morphea variant which is a rare subset of localized scleroderma affecting only 1-2% patients.<sup>14</sup>

The mean age of onset for both localized and systemic forms of paediatric scleroderma is between 7.3 and 8.8 years of age. Although less than 5% of all patients with SSc have paediatric onset, the majority of patients with LS have childhood onset.<sup>10,12,20,21</sup> No significant race predilection has been reported;<sup>14</sup> however Christien-Zaech et al.<sup>17</sup> observed a higher prevalence in Caucasian population.

The disease is usually considered a benign and self-limited condition; but the course and prognosis of JLS is unpredictable and depends on the variant of the disease. Average disease duration is of 3-5 years but there are reports of active disease lasting up to 20 years. Localized scleroderma can result in significant morbidity, disfigurement, disability especially with the linear and deep subtype and severe functional, aesthetic and psychological disabilities.<sup>4,22</sup>

Our patient had LS of deep morphea variant affecting both the hands. There were flexion contracture of both left little and index fingers and the heels were also hardened. Deep morphea is typically disabling. It initially involves the extremities, but later may migrate to the trunk, only sparing the face and distal areas of fingers and toes. There is a rapidly progressive fibrosis of the

deep dermis, subcutis, fascia, and muscles, with occasional bone involvement. This leads to significant contracture of joints, muscle atrophy, cutaneous ulcerations and sometimes restrictive pattern respiratory insufficiency if the trunk is involved.<sup>14</sup>

Extracutaneous manifestations (ECM) are not uncommon in LS and occur in approximately one-quarter of the patients throughout the course of disease.<sup>18</sup> But there were no respiratory, gastrointestinal or neurological problem in our case and there was no feature suggestive of endocrine problem.

Laboratory investigations in this case showed eosinophilia though ESR and CRP were not raised. In a review of a large number of JLS patients, 16 patients with deep morphea were reported and 62.5% of them had eosinophilia.<sup>10</sup> In another case series about 18% patient had eosinophilia.<sup>23</sup>

Autoimmunity, as one of the components propagating LS, is supported by the auto-antibody profile, concurrent associated autoimmune diseases, and family history of autoimmune disease observed in patients with LS. ANA is a classic serologic marker of autoimmune disease and is found in a high frequency of LS patients, with a reported range between 42 and 73%.<sup>10,24</sup> It is thought that higher titers are associated with early disease and increased risk for extracutaneous manifestations.<sup>10,25,26</sup> Our patient was also moderately positive for ANA.

Zulian et al.<sup>10</sup> reported positive family history for rheumatic and/or autoimmune diseases in 12.1% patients with JLS in their case series. But in our case the parents were poor and did not have that level of awareness or education to give family history for autoimmune disease.

Zulian et al.<sup>10</sup> also reported significant environmental factors, as possible triggers for disease onset, in 13.8% of the patients in their series. Local mechanical factors, including accidental trauma, insect bite and vaccination, were reported in 10.4% and 12.5% of the patients

with JLS and DM respectively. In this case there was no such triggering factor.

Optimal therapy for JLS is not known. A variety of therapeutic strategies have been proposed; however, the majority of published reports are case series with only a few comparative or placebo-controlled studies described. For treatment of JLS there is no universal agreement. Treatments have included topical and systemic corticosteroids, topical and systemic calcipotriol, topical tacrolimus, interferon- $\gamma$  and methotrexate.<sup>27-30</sup>

Approach to the treatment of LS initially depends on the severity of the disease which is characterized by the subtype of LS, potential involvement of deeper tissue and structures (such as joints), location of LS and disease activity state.<sup>14</sup> There is a profound lack of consensus on treatment among clinicians involved in the care of patients with JLS. There is a substantial division in therapeutic choices between subspecialty services receiving referrals for JLS, with pediatric rheumatologists treating disease beyond superficial circumscribed plaque morphea primarily with methotrexate and systemic corticosteroids, while dermatologists commonly utilize topical agents and phototherapy.<sup>28,31-35</sup>

Superficial morphea may benefit from topical corticosteroid or ultraviolet therapy. For lesions involving deeper structures, systemic therapy is recommended. Treatment regimen includes 3 months of either monthly high dose intravenous corticosteroids for 3 consecutive days in every month or high daily oral corticosteroids. In addition, methotrexate is given at 1 mg/kg dose weekly. Recently a double-blind randomized controlled trial in patients with pediatric-onset JLS, the combination of methotrexate and a short course of prednisone was confirmed as a beneficial and well tolerated treatment.<sup>33</sup>

We started treatment with oral prednisolone and inj. methotrexate to be continued for one year with dietary advice and micronutrients supplementations. After 6 months of treatment

blackish pigmentation disappeared and hardening of the fingers and heels were softened. Similar improvement with corticosteroid and methotrexate treatment was also reported by some other studies.<sup>17,30</sup>

Physical and occupational therapies are important adjunct to pharmacologic treatment.<sup>4</sup> Vigorous physiotherapy is helpful for maintaining range of joint movement.<sup>36</sup> Intensive physical and occupational therapy in conjunction with systemic immunosuppressive therapy is recommended for those with linear or deep scleroderma of the extremity to help avoid and or minimize joint contractures.<sup>14</sup> In addition to medication this patient was advised for physiotherapy but the poor parents could not avail it.

## Conclusion

Patients with juvenile localized scleroderma should be identified early, evaluated extensively, treated aggressively, and monitored carefully as localized scleroderma in childhood is not just a skin disease. It causes significant disfigurement and disability. One fourth of this group of children has extracutaneous manifestations. They are also at low risk in developing systemic scleroderma.

## References

1. Jimenez SA, Cronin PM, Koenig AS, O'Brien MS, Castro SV. Scleroderma. Medscape [Internet]. 2012 Feb [cited 2014 March 5]. Available from: <http://emedicine.medscape.com/article/331864-overview>.
2. Hajj-ali RA. Systemic Sclerosis. Merck Manual Professional. Merck Sharp & Dohme Corp [Internet]. 2013 June [cited 2014 March 5]. Available from: <http://www.merckmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/autoimmune-rheumatic-disorders/systemic-sclerosis>.
3. Valančienė G, Jasaitienė D, Valiukevičienė S. Pathogenesis and Treatment Modalities of Localized Scleroderma. Medicina. 2010;46(10):649-56.

4. Mater HAV, Rabinovich CE. Scleroderma and Raynaud Phenomenon. In: Kliegman RM, Stanton BF, Schor NF, St. Geme III JW, Behrman RE, editors. Nelson Textbook of Paediatrics. 19th ed. Philadelphia PA: Elsevier; 2011. p.850-53.
5. Balbir-Gurman A, Braun-Moscovici Y. Scleroderma - New Aspects in Pathogenesis and Treatment. Best Practice & Research Clinical Rheumatology. 2012;26(1):13-24.
6. Greenblatt MB, Aliprantis AO. The Immunopathogenesis of Scleroderma: Context is Everything. Current Rheumatology Reports. 2013;15(1):297.
7. Barnes J, Mayes MD. Epidemiology of Systemic Sclerosis: Incidence, Prevalence, Survival, Risk Factors, Malignancy, and Environmental Triggers. Current Opinion in Rheumatology. 2012;24(2):165-70.
8. Dospinescu P, Jones GT, Basu N. Environmental Risk Factors in Systemic Sclerosis. Current Opinion in Rheumatology. 2013;25(2):179-83.
9. Gelber AC, Manno RL, Shah AA, Woods A, Le EN, Boin F, et al. Race and Association with Disease Manifestations and Mortality in Scleroderma: A 20-Year Experience at the Johns Hopkins Scleroderma Center and Review of the Literature. Medicine. 2013;92(4):191-205.
10. Zulian F, Athreya BH, Laxer R, Nelson AM, Feitosa de Oliveira SK, Punaro MG, et al. for the Juvenile Scleroderma Working Group of the Pediatric Rheumatology European Society (PRES). Juvenile Localized Scleroderma: Clinical and Epidemiological Features in 750 Children. An International Study. Rheumatology. 2006;45:614-20.
11. Fett N, Werth VP. Update on Morphea: Part I. Epidemiologyclinical Presentation, and Pathogenesis. J Am Acad Dermatol. 2011;64:217-28.
12. Scalapino K, Arkachaisri T, Lucas M, Fertig N, Helfrich DJ, Londino AV Jr, et al. Childhood Onset Systemic Sclerosis: Classification, Clinical and Serologic Features, and Survival in Comparison with Adult Onset Disease. J Rheumatol. 2006;33(5):1004-13.
13. Li SC, Torok KS, Pope E, Dedeoglu F, Hong S, Jacobe HT, et al. and The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Localized Scleroderma Workgroup. Development of Consensus Treatment Plans for Juvenile Localized Scleroderma A Roadmap Toward Comparative Effectiveness Studies in Juvenile Localized Scleroderma. Arthritis Care Res (Hoboken). 2012;64(8):1175-85.
14. Torok KS. Pediatric Scleroderma - Systemic and Localized Forms. Pediatr Clin North Am. Pediatr Clin North Am. 2012;59(2):381-405.
15. Lee HJ, Kim MY, Ha SJ, Kim JW. Two Cases of Morphea Associated with Hashimoto's Thyroiditis. Acta Derm Venereol. 2002;82:58-59.
16. Dervis E, Acbay O, Barut G, Karaoglu A, Ersoy L. Association of Vitiligo, Morphea and Hashimoto's Thyroiditis. Int J Dermatol. 2004;43:236-37.
17. Christen-Zaech S, Hakim MD, Afsar FS, Paller AS. Pediatric Morphea (Localized Scleroderma): Review of 136 Patients. J Am Acad Dermatol. 2008;59(3):385-96.
18. Zulian F, Vallongo C, Woo P, Russo R, Ruperto N, Harper J, et al.; Juvenile Scleroderma Working Group of the Pediatric Rheumatology European Society (PRES). Localized Scleroderma in Childhood is Not Just a Skin Disease. Arthritis Rheum. 2005;52:2873-81.
19. Zulian F. Systemic Sclerosis and Localized Scleroderma in Childhood. Rheum Dis Clin N Am. 2008;34:239-55.
20. Martini G, Foeldvari I, Russo R, Cuttica R, Eberhard A, Ravelli A, et al. Systemic Sclerosis in Childhood: Clinical and Immunologic Features of 153 Patients an International Database. Arthritis Rheum. 2006;54(12):3971-78.
21. Foeldvari I, Zhavania M, Birdi N, Cuttica RJ, de Oliveira SH, Dent PB, et al. Favourable Outcome in 135 Children with Juvenile Systemic Sclerosis: Results of a Multi-National Survey. Rheumatology (Oxford). 2000;39(5):556-59.
22. Uziel, Black CM. Prognosis and Management of Sclero-Derma and Scleroderma-Like Disorders in Children. Clin Exp Rheumatol. 1994;12:S75-81.

23. Marzano AV, Menni S, Parodi A, Borghi A, Fuligni A, Fabbri P, et al. Localized Scleroderma in Adults and Children. Clinical and Laboratory Investigations on 239 Cases. *European Journal of Dermatology*. 2003;13(2):171-76.
24. Uziel Y, Krafchik BR, Silverman ED, Thorner PS, Laxer RM. Localized Scleroderma in Childhood: A Report of 30 Cases. *Semin Arthritis Rheum*. 1994;23:328-40.
25. Takehara K, Moroi Y, Nakabayashi Y, Ishibashi Y. Antinuclear Antibodies in Localized Scleroderma. *Arthritis Rheum*. 1983;26(5):612-16.
26. Arkachaisri T, Fertig N, Pino S, Medsger TA Jr. Serum Autoantibodies and Their Clinical Associations in Patients with Childhood- and Adult-Onset Linear Scleroderma. A Single-Center Study. *J Rheumatol*. 2008;35(12):2439-44.
27. Chung L, Lin J, Furst D, Fiorentino D. Systemic and Localized Scleroderma. *Clin Dermatol*. 2006;24:374-92.
28. Fett N, Werth V. Update on Morphea. part II. Outcome Measures and Treatment. *J Am Acad Dermatol*. 2011;64:231-42.
29. Santos Vilela F, Carneiro S, Ramos-e-Silva M. Treatment of Morphea or Localized Scleroderma: Review of the Literature. *J Drugs Dermatol*. 2010;9:1213-19.
30. Corradin MT, Fiorentino R, Giulioni E, Russo I, Alaibac M, Fortina AB. Linear Juvenile Localized Scleroderma: A Case Based Review [Internet]. 2013 Jan [cited 2014 March 5];1(4):216-18. Available from: [http://www.clinicaldermatology.eu/materiale\\_cic/719\\_1\\_4/6211\\_linear/article.htm](http://www.clinicaldermatology.eu/materiale_cic/719_1_4/6211_linear/article.htm).
31. Weibel L, Sampaio M, Visentin M, Howell K, Woo P, Harper J. Evaluation of Methotrexate and Corticosteroids for the Treatment of Localized Scleroderma (Morphea) in Children. *Br J Dermatol*. 2006;155:1013-20.
32. Li S, Feldman B, Higgins G, Haines K, Punaro M, O'Neil K. Treatment of Pediatric Localized Scleroderma: Results of a Survey of North American Pediatric Rheumatologists. *J Rheumatol*. 2010;37:175-81.
33. Zulian F, Martini G, Vallongo C, Vittadello F, Falcini F, Patrizi A, et al. Methotrexate Treatment in Juvenile Localized Scleroderma. *Arthritis Rheum*. 2011;63:1998-2006.
34. Uziel Y, Feldman B, Krafchik B, Yeung R, Laxer R. Methotrexate and Corticosteroid Therapy for Pediatric Localized Scleroderma. *J Pediatr*. 2000;136:91-95.
35. Zwischenberger B, Jacobe H. A Systematic Review of Morphea Treatments and Therapeutic Algorithm. *J Am Acad Dermatol*. 2011;65:925-41.
36. Davidson J, Cleary AG, Bruce C. Disorders of Bones, Joints and Connective Tissues. In: McIntosh N, Helms P, Smyth R, Logan S, editors. *Forfar & Arneil's Textbook of Paediatrics*. 7th ed. New York: Elsevier; 2008. p.1526-89.