Clinicohistopathological correlations in juvenile localized scleroderma: Studies on a subset of children with hypopigmented juvenile localized scleroderma due to loss of epidermal melanocytes

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Background: Localized scleroderma or morphea is a connective tissue disorder characterized by fibrosis of the skin and subcutaneous tissue. Excessive accumulation of collagen underlies the fibrosis, yet the pathogenesis is unknown. A subset of localized scleroderma/morphea, juvenile localized scleroderma (JLS), affects children and adolescents.

Objectives: The clinical and microscopic features of JLS have not been fully characterized. The goal is to better characterize the microscopic features of JLS.

Methods: We collected a distinctive data set of 35 children with JLS, 19 (54%) of whom presented with hypopigmented lesions, and performed a retrospective chart and pathology review. We had adequate tissue for immunostaining studies on 8 of these individuals.

Results: We found that: (1) CD34 and factor XIIIa immunostaining, reported previously in adult morphea and scleroderma, when used with clinical information, is valuable for confirming a diagnosis of JLS; and (2) presence of hypopigmented lesions in JLS correlates with immunostaining studies. Decreased numbers of MelanA$^+$ melanocytes were present at the dermoepidermal junction in lesional skin in two of 3 children with hypopigmented JLS and in two of 4 children with nonhypopigmented JLS.

Limitations: The number of cases is small, a function of the small number of children who have biopsy specimens with material sufficient for multiple immunostaining procedures.

Conclusions: These results provide a useful immunostaining method for confirmation of the diagnosis of JLS. They suggest a complex autoimmune phenotype in some children with JLS. (J Am Acad Dermatol 2011;65:364-73.)

Key words: CD34; dermatology; dermatopathology; factor XIIIa; hypopigmentation; immunostaining; juvenile localized scleroderma; morphea; pediatric.

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Supported in part by the Dermatology Foundation and the National Institutes of Health (NIH). Dr Amy E. Gilliam was supported by a Dermatology Foundation Medical Dermatology Career Development Award. Dr Anita C. Gilliam was supported by NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) R01 AR 049284 and the NIH NIAMS Case Skin Diseases Research Center P30-AR. The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

Conflicts of interest: None declared.

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Presented in 2007 at the American Society for Dermatopathology (Baltimore, MD, October 18-21, 2007) and the Society for Pediatric Dermatology (Chicago, IL, July 12-15, 2007).

Reprints not available from the authors.

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Published online May 13, 2011.
0190-9622/$36.00

doi:10.1016/j.jaad.2010.02.065

Localized scleroderma or morphea is a connective tissue disorder characterized by fibrosis of the skin and subcutaneous tissue. Excessive accumulation of collagen underlies the fibrosis, yet the pathogenesis is unknown. Previous studies have focused on the vascular changes, immune dysfunction, and dysregulated collagen synthesis as possible causes for localized scleroderma.[1-4] The skin lesions can be variable—localized scleroderma/morphea can present as a small well-circumscribed, indurated plaque, or it can involve large areas, resulting in significant cosmetic and functional deformity. A subset of localized scleroderma/morphea, juvenile localized scleroderma (JLS), affects children and adolescents. JLS includes linear scleroderma, plaque-type morphea, generalized morphea, and deep morphea.[5] Hypopigmented lesions occur in all of these subsets. The clinical and microscopic features of JLS have not been fully characterized. The lack of histopathological data may be a result of several factors, including the rarity of the condition, its variable presentation and subtypes, delays in recognition and diagnosis, the obvious clinical diagnosis in linear scleroderma (eg, coup de sabre), and the reluctance of physicians to perform skin biopsies on children.

Recently, members of the Pediatric Rheumatology European Society published a multicenter study of 750 children with JLS that led to new, more comprehensive clinical classification criteria and a better understanding of clinical and epidemiologic features.[6] Histopathology results and incidence of dyspigmented skin lesions were not included in that study. Other recent publications have focused on the imaging and serologic features of children with JLS.[2,7-9] Despite the latest advances in the clinical characterization of JLS, the histopathologic information is incomplete.

Skin lesions of JLS are often nonspecific and described as "bruiselike" or "hypopigmented and hyperpigmented plaques." These hypopigmented lesions can be misdiagnosed as vitiligo before induration, fibrosis, or atrophy develops fully. Because children with JLS may develop extracutaneous complications that can lead to significant morbidity,[10,11] it is imperative to have an early correct diagnosis to initiate treatment for JLS.

CAPSULE SUMMARY

- In a retrospective chart review on 35 children with juvenile localized scleroderma (JLS), 19 (54%) presented with hypopigmented lesions. We studied 8 with sufficient biopsy specimen material for immunostaining studies.
- We found that: (1) anti-CD34 and anti-factor XIIIa help confirm a diagnosis of JLS; and (2) there were decreased MelanA$^+$ melanocytes at the dermoepidermal junction in lesional skin in two of 3 children with hypopigmented JLS and two of 4 children with nonhypopigmented JLS.

Clinical and laboratory data collected from the University of California at San Francisco (UCSF) pediatric dermatology clinic were used to generate a data set of 35 children with JLS for a retrospective chart review and evaluation of histopathology. Eight of them had skin biopsy specimens with adequate material for study by routine histology and immunostaining. Biopsies were performed for diagnostic purposes, and specimens were taken from indurated areas clinically suggested to be morphea. In the children with hypopigmented lesions, the biopsy specimens were taken from hypopigmented indurated areas (A. E. G.). Based on previous studies of adult morphea and scleroderma,[12,13] we selected CD34 and factor XIIIa (FXIIIa) for immunostaining. We hypothesized that CD34 staining would be lost and FXIIIa gained in a reciprocal fashion in fibrotic areas as described for adult morphea.[12,13]

We also hypothesized that the hypopigmented lesions of morphea would have decreased epidermal melanocyte density, not simply loss of epidermal melanin, because of the clinical similarity to vitiligo, mainly perifollicular hyperpigmentation in hypopigmented lesions. We used MelanA immunostaining for melanocytes and Fontana-Masson histochemical staining for melanin to test this hypothesis.

METHODS

Patient selection and clinical data

Children with JLS (n = 35) were recruited from the pediatric dermatology division of UCSF from 2003 to 2006 (Table I) using UCSF Committee on Human Research guidelines and informed consent for collection of patient information (A. E. G.). To be included in this study, individuals were required to be 21 years of age or younger with one of the recognized subtypes of JLS as determined by an experienced pediatric dermatologist (A. E. G.) and defined by the following:

- Linear scleroderma: linear induration or fibrosis of the skin that involves the dermis, subcutaneous tissue and, in some cases, the underlying muscle or bone. This includes en coup de sabre and Parry-Romberg syndrome (progressive hemifacial atrophy).