Discrete Papular Form of Lichen Myxedematosus: A Case Report and Review of the Literature

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GOAL

To gain a thorough understanding of lichen myxedematosus (LM)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss the clinical presentation of LM.
2. Explain the histologic features of LM.
3. Describe the various forms of LM.

CME Test on page 92.

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Drs. Sulit, Harford, and O'Neill report no conflict of interest. The authors report off-label use of pimecrolimus for the treatment of discrete papular lichen myxedematosus. Dr. Fisher reports no conflict of interest.

The discrete papular form of lichen myxedematosus (LM) is a rare idiopathic skin disorder. We present a case of this type in an 80-year-old African American woman. She was treated with pimecrolimus cream, which resulted in symptomatic relief. To our knowledge, this is the first report of the discrete papular form of LM occurring in an African American, as well as the first report on the disorder's response to pimecrolimus therapy. We also review the English medical literature on this rare disease and examine and summarize the findings.

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Lichen myxedematosus (LM), also called *papular mucinosis*, was first described by Dubreuilh[1] in 1906 and later classified by Montgomery and

Underwood[2] in 1953. LMs are a group of localized or generalized papular eruptions of unknown etiology categorized as cutaneous mucinoses in which dermal mucin deposition is the distinctive histologic feature.[3-5] LM has no relation to endocrine gland disorders, particularly thyroid disease.[2,3,6]

In their landmark paper, Montgomery and Underwood[2] classified 4 clinical types of LM: (1) generalized lichenoid papular eruption, which is also called *scleromyxedema,* (2) discrete papular form, (3) localized to generalized lichenoid plaques, and (4) urticarial plaques and nodular eruptions that usually evolve into the generalized lichenoid form. In 2001, Rongioletti and Rebora[6] updated the classification system. The articles by Montgomery and Underwood[2] and Rongioletti and Rebora[6] both agree with the existence of the discrete papular form, also called *discrete papular LM* (DPLM). According to Rongioletti and Rebora,[6] DPLM has only been reported in the medical literature 8 times,[1,2,7-12] This is unlike scleromyxedema, the most common type of LM, which has been documented in more than 110 cases.[6] In this case report, we describe an interesting case of DPLM

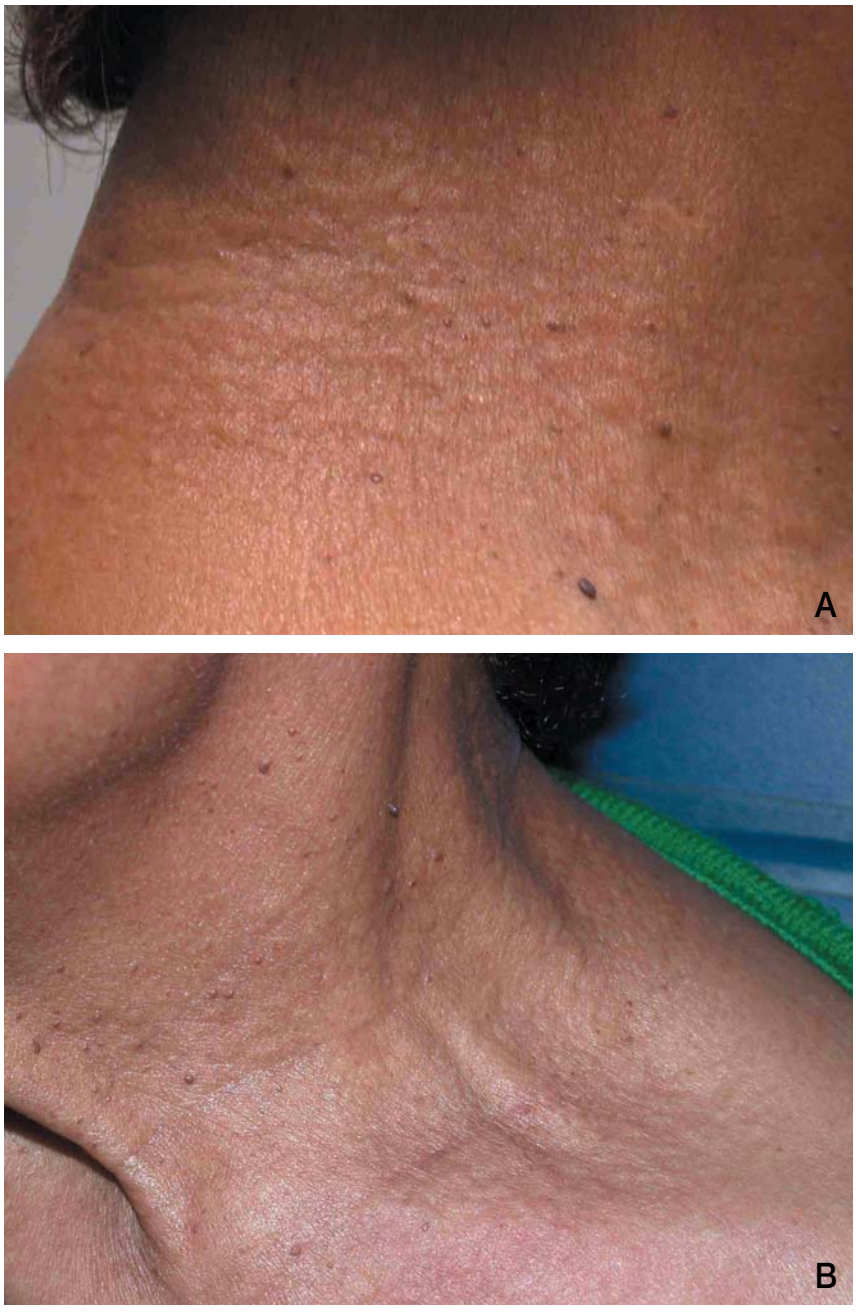

Figure 1. Right (A) and left (B) neck with multiple 2- to 3-mm discrete, firm, flesh-colored papules.

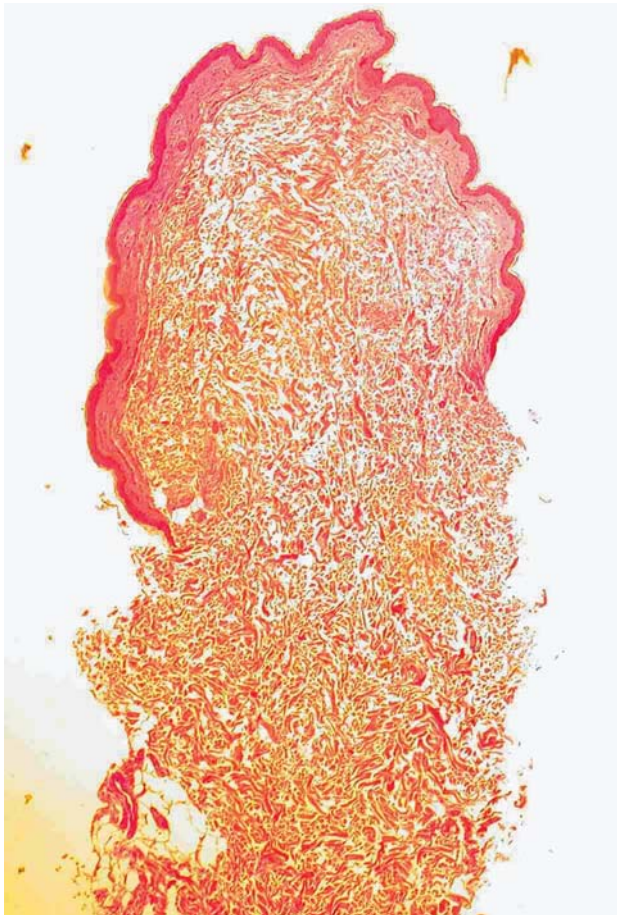

Figure 2. Results of a 4-mm punch biopsy show spaces between the collagen fibers and no increase in the number of fibroblasts (H&E, original magnification ×4).

that was localized to the neck of our patient, and we review the English medical literature.

Case Report

An 80-year-old black woman presented to our clinic with a 2-month history of a pruritic eruption localized to her neck. Multiple topical steroids and antihistamines had been used without any decrease in the eruption or the pruritus. The woman's medical history was significant for gastric cancer status post a partial gastrectomy 7 years prior, pseudotumor cerebri, hypertension, and osteoporosis. She is followed regularly for these conditions, which are stable. Her medications included acetazolamide, atenolol, nifedipine, rabeprazole sodium, fluoxetine, oxybutynin chloride, alendronate sodium, docusate calcium, and a multivitamin. Prior to the onset of this eruption, the patient had a change in the acetazolamide formulation, which was initially thought to be the culprit. Although she returned to the original formulation for longer than a month, she had no resolution of the symptoms. At that time, she sought evaluation in our clinic.

On physical examination, multiple 2- to 4-mm discrete, flesh-colored shiny papules without scale were present over the patient's bilateral and posterior neck (Figure 1). Results of 2 punch biopsies showed splaying of the collagen with mucin present diffusely throughout the dermis. No increase in the number of fibroblasts was seen (Figure 2). Results of colloidal iron stain showed positive results in the papillary dermis and showed mucin mildly throughout the deep dermis (Figure 3), supporting the diagnosis of LM. Complete blood count, chemistry panel, liver function, thyrotropin, and serum protein test results were all within reference range. Pimecrolimus cream has been effective in treating our patient's pruritus. We have followed her for 14 months, and the lesions have remained localized to her neck, with continued normal thyrotropin and serum protein values.

Comment

In 2001, Rongioletti and Rebora[6] revised the classification system of LM, categorizing it into 3 broad subsets: (1) generalized papular and sclerodermoid, (2) localized LM, and (3) atypical forms.

The first subset, generalized papular and sclerodermoid, represents scleromyxedema. Diagnosis requires a generalized papular and sclerodermoid eruption, monoclonal gammopathy (paraproteinemia), no evidence of thyroid dysfunction, and a histologic triad of fibroblast proliferation, fibrosis, and mucin deposition.[6] Scleromyxedema is associated with many systemic disorders that may include numerous organ systems.[6,13] Although spontaneous resolution has been reported,[14] scleromyxedema typically is a long-term and disfiguring disease[6,13] associated with variable morbidity and mortality.[15,16]

The criteria for diagnosing the subset of localized LM requires a papular eruption, deposits of mucin with variable fibroblast growth, absence of paraproteinemia, and absence of thyroid dysfunction.[6] There are 5 subtypes[6]: DPLM,[2,7-9,17-21] acral persistent papular mucinosis (APPM),[22-27] cutaneous mucinosis of infancy,[28-31] self-healing papular mucinosis (SHPM),[32-36] and nodular LM.[37,38] All subtypes show small, firm, waxy papules limited to a few areas of the skin, which may coalesce and form nodules or plaques. DPLM can involve any site on the body. APPM exclusively involves both extensor surfaces of the distal upper extremities. Cutaneous mucinosis of infancy is a pediatric variant of DPLM or APPM. SHPM has spontaneous resolution. Nodular LM is characterized by a

predominance of nodules.[6] All subtypes except for SHPM typically persist long-term. Systemic symptoms were only reported in SHPM.[32,33] In general, localized LM is self-limited and associated with a good prognosis.[6]

The histologic features of LM are summarized in Table 1.[5] The pathology lies within the dermis for all types of this disease, and the epidermis is essentially normal.[5] The types of LM can be distinguished from one another by 3 histologic clues: (1) mucin distribution pattern, (2) dermal level of mucin deposits, and (3) some extra findings.[5] Differentiation can be additionally aided by observing the number of fibroblasts. Common mucin stains include colloidal iron, mucicarmine, and alcian blue at pH 2.5 (but not pH 0.5); common metachromatic mucin stains include toluidine blue, thionine, and methylene blue.[3]

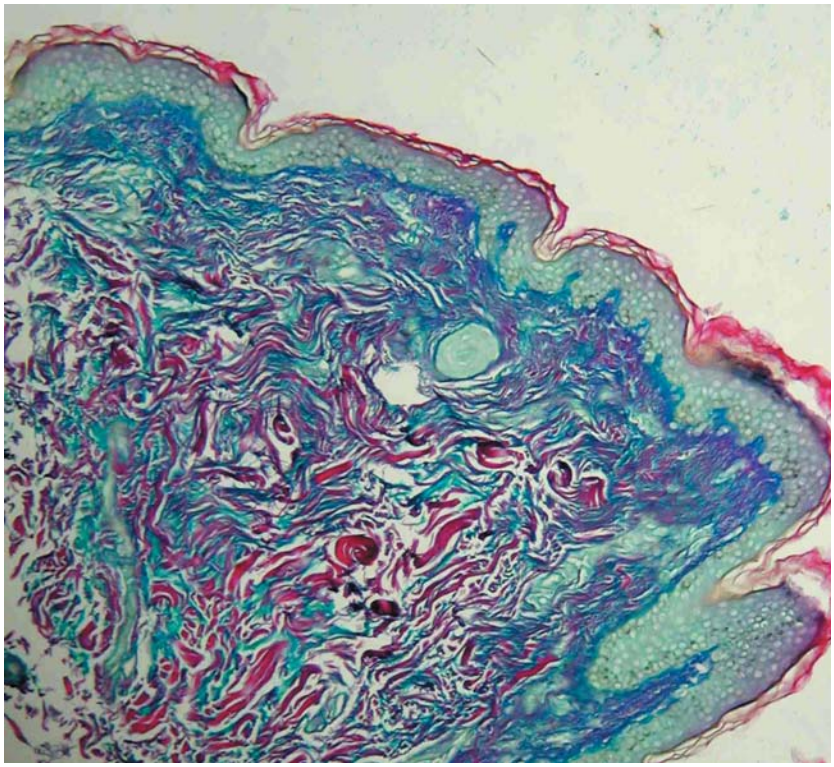

Figure 3. Biopsy specimen stained with colloidal iron exhibits ample mucin between the collagen fibers (original magnification ×10).

DPLM is a subtype of localized LM.[2,6] Although the lesions can involve any site, DPLM is typically distributed symmetrically to the trunk and limbs. The skin lesions have been described as a variable number of firm, smooth, waxy, or flesh-colored papules 2 to 5 mm in size. Normal serum protein and thyroid function test results verify the diagnosis of DPLM.[6] Because Montgomery and Underwood[2] originally defined LM as having no relation to any endocrine gland disturbance, we recommend additional random chemistry panel or fasting blood glucose laboratory tests if there is any question that a patient may have diabetes mellitus.

Histologically, DPLM may have a diffuse or local pattern of mucin distribution involving the upper and mid reticular dermis. The involved dermis typically shows edema. The amount of fibroblast proliferation is variable. When compared with scleromyxedema, DPLM has no collagen deposition or sclerosis and a lesser amount of fibroblast proliferation.[5-7]

Some argue that DPLM and APPM are closely related variants.[25,27] However, we believe that DPLM and APPM are distinct subtypes of localized LM. DPLM typically affects men (Table 2) and its lesions may be erythematous, larger, and include areas other than the distal upper extremities.[4,23,24] In comparison, APPM has an overwhelming female-to-male ratio of 4.7:1.[6] APPM also exclusively involves the back of the hands, extensor surface of the wrists, and sometimes the distal forearms.[4,6,23] Histologically, APPM typically has more focal mucin deposits, which spare a subepidermal grenz zone, and a normal number of fibroblasts; DPLM has mucin deposits that are more diffuse (compared with APPM), have a variable number of increased fibroblasts, and have an irregular arrangement of collagen bundles.[4-6,23]

Table 2 summarizes the main features of the 10 DPLM cases reported in the English medical literature.[2,7-9,17-21] Our criteria required there be no evidence of paraproteinemia, no history or laboratory evidence of any endocrine disease, no history of human immunodeficiency virus infection, histologic proof of dermal mucin deposits, and specific gross descriptions consistent with DPLM. It should be noted that only 4 of the 8 DPLM cases originally cited by Rongioletti and Rebora[6] were included in Table 2. Four cases were excluded because 2 reports were written in French,[1,12] 1 report included a patient with diabetes mellitus,[10] and another did not perform a necessary laboratory test to rule out thyroid disease.[11] Other cases were excluded because they did not fulfill our criteria.[39,40]

Table not available online

Among the 10 DPLM patients summarized, 7 were men. The mean age of the group was 51.3 years. Only 3 of the 10 cases reported information on the patient's ethnicity: one was Caucasian,[7] one was Asian,[8] and our patient was African American. Nine of the 10 cases reported no evidence of paraproteinemia. The single case[2] that did not report this finding was published before an association between LM and paraproteinemia was known in the 1960s.[41] All 10 cases reported thyroid function test results within reference range. Only 3 of the 10 patients had symptomatic skin lesions, which were mainly pruritus. No systemic symptoms were noted. Three of the 10 patients had solitary skin lesions on areas other than the typical trunk and limbs. One patient had skin lesions only on his lumbar region, another had facial lesions, and our patient had lesions on her neck. Seven of the 10 patients had comorbid medical disorders, including hypertension, migraines, psoriatic erythroderma, psoriasis, seizures, gastric cancer in remission, pseudotumor cerebri, osteoporosis, and hepatitis C. Only hepatitis C was comorbid with more than one DPLM patient.[17,20] This may be a coincidence because one patient developed DPLM after contracting hepatitis C,[20] while the other patient developed it before contracting hepatitis C.[17] Psychiatric illness was limited to depression and was found in 2 cases.[20,21] No DPLM cases progressed to scleromyxedema, and none have been reported in the literature.[5,6]

DPLM rarely resolves on its own. Spontaneous resolution did not occur in any of the 10 reported DPLM cases, and only 2 patients were treated successfully. In Reynolds et al,[18] the patient responded to therapy with intralesional corticosteroid injections and flurandrenolide-impregnated tape. In Kaymen et al,[19] a patient was treated with a CO_2 laser and postoperative intralesional corticosteroid injections. There was no growth after one year. All the other DPLM cases did not have effective therapy, lacked specific details of improvement, or did not report this

Table 2.

Summary of Patients With Discrete Papular Lichen Myxedematosus*

Reference	Age, y (Sex)	Symptoms	Location of Lesions	Course After Initial Medical Visit	Treatments	Other Notable Findings
Montgomery and Underwood[2]	38 (F)	NR	Dorsal surface of forearms, wrists, hands, and medial aspects of knees	Mild enlargement in size of skin lesions after 10 y	NR	None
Coskey and Mehregan[7]	22 (M)	AS	Left deltoid, right arm	No change after 8 y	NR	None
Tay and Khoo[8]	41 (M)	AS	Trunk, shoulders, and extensor surfaces of arms and forearms	No change after 2 y	Failed therapy with oral thyroxine	None
Enerback and Mobacken[9]	46 (M)	Symptomatic	Chest, back, shoulders, neck, and upper arms	Stable with mild changes after 9 y	Failed therapy with topical corticosteroids	None
Rongioletti and Rebora[17]	59 (F)	AS	Both upper extremities (upper arms and forearms)	Spreading of new lesions to shoulders, thighs, and trunk after 1 mo of interferon therapy for hepatitis C	None	DPLM worsened with interferon therapy; onset of DPLM occurred before acquiring hepatitis C
Reynolds et al[18]	32 (M)	NR	Chest, back, upper extremities more than lower extremities	Stable after therapy; exact period NR	Intralesional and topical cortico-steroids	Successful therapy
Kaymen et al[19]	63 (M)	NR	Face only	Stable 1 y after treatment with CO_2 laser	CO_2 laser and intralesional corticosteroids	Successful therapy
Montesu et al[20] `	70 (M)	Symptomatic	Face, neck, and clavicle area (stable for 2 y)	New lesions develop on back of hands and buttocks; period NR	Some improvement with topical corticosteroids and emollients	Onset of DPLM occurred after acquiring hepatitis C
Poswig et al[21]	62 (M)	AS	Back (lumbar region)	No change after 18 mo	NR	None
Our patient	80 (F)	Symptomatic	Posterior and lateral surfaces of neck	No change after 14 mo	Failed therapy with topical corticosteroids and antihistamines; successful symptomatic relief with pimecrolimus	No gross changes in skin lesions, but symptomatic relief from pruritis with topical pimecrolimus therapy

*F indicates female; NR, not reported; M, male; AS, asymptomatic; DPLM, discrete papular lichen myxedematosus.

information.[2,7-9,17,20,21] Only Tay and Khoo,[8] Enerback and Mobacken,[9] and Kaymen et al[19] commented on which therapies failed (oral thyroxine, topical corticosteroids, and shave excision, respectively). Our patient complained of persistent itching that did not respond to initial treatment with topical steroids and antihistamine medications. She later received pruritic relief with pimecrolimus cream therapy. However, the skin lesions remained. To our knowledge, this is the first report of pimecrolimus therapy in the treatment of pruritis secondary to DPLM.

It is difficult to treat a rare disease such as DPLM when the pathogenesis is unknown, and many treatments have failed. Fortunately, DPLM and the other localized forms of LM are usually self-limited to the skin and have very little or no morbidity, leading some experts to believe that the disorder is unnecessary to treat.[6] We believe that treatment is sometimes helpful. In our patient, the DPLM lesions were pruritic and located at a cosmetic area of the neck. The patient and dermatology staff decided to pursue a treatment plan. Therefore, even though localized LM lesions are typically benign, sometimes it is beneficial to treat them, especially if they cause irritating symptoms or cosmetic issues.

Conclusion

DPLM is a rare variant of localized LM. DPLM can be diagnosed by a thorough history and physical examination; histologic proof of dermal mucin deposits; and ruling out other diseases with laboratory tests for serum protein, thyroid function, and, if the patient is at risk of diabetes mellitus, blood glucose levels. DPLM is a self-limited skin disease, and prognosis is generally good, but it typically persists long-term and may slowly progress. Treatment is usually unnecessary, but it may be recommended if the lesions are symptomatic or cause cosmetic issues. Unfortunately, few treatment plans have been shown to successfully treat DPLM.

REFERENCES

1. Dubreuilh W. Fibromes miliaries folliculaires: sclerodermie consecutive. *Arch Dermatol Syph.* 1906;7:569-570.
2. Montgomery H, Underwood LJ. Lichen myxedematosus (differentiation from cutaneous myxedemas or mucoid states). *J Invest Dermatol.* 1953;20:213-236.
3. Truhan AP, Roenigk HH Jr. The cutaneous mucinoses. *J Am Acad Dermatol.* 1986;14:1-18.
4. Rongioletti F, Rebora A. The new cutaneous mucinoses: a review with an up-to-date classification of cutaneous mucinoses. *J Am Acad Dermatol.* 1991;24:265-270.
5. Rongioletti F, Rebora A. Cutaneous mucinoses: microscopic criteria for diagnosis. *Am J Dermatopathol.* 2001;23:257-267.
6. Rongioletti F, Rebora A. Updated classification of papular mucinosis, lichen myxedematosus, and scleromyxedema. *J Am Acad Dermatol.* 2001;44:273-281.
7. Coskey RJ, Mehregan A. Papular mucinosis. *Int J Dermatol.* 1977;16:741-744.
8. Tay CH, Khoo OT. Papular mucinosis in chronic psoriatic erythroderma. report of a case. *Arch Dermatol.* 1970;102:304-308.
9. Enerback L, Mobacken H. Lichen myxedematosus of urticarial type without paraproteinaemia. *Dermatologica.* 1976;152:309-315.
10. Abd El-Aal H, Salem SZ, Salem A. Lichen myxedematosus: histochemical study. *Dermatologica.* 1981;162:273-276.
11. Woerdeman MJ. Is collagenome erupt if a separate entity? *Br J Dermatol.* 1960;72:217-220.
12. Podglajen-Wecxsteen O, Ehrsam E, Mailfer C, et al. Apropos of papulous mucinosis: acral persistent papular mucinosis or minor form of scleromyxedema [in French]. *Ann Dermatol Venereol.* 1992;119:834-836.
13. Pomann JJ, Rudner EJ. Scleromyxedema revisited. *Int J Dermatol.* 2003;42:31-35.
14. Boffa MJ, Ead RD. Spontaneous improvement of scleromyxoedema. *Clin Exp Dermatol.* 1995;20:157-160.
15. Godby A, Bergstresser PR, Chaker B, et al. Fatal scleromyxedema: report of a case and review of the literature. *J Am Acad Dermatol.* 1998;38:289-294.
16. Webster GF, Matsuoka LY, Burchmore D. The association of potentially lethal neurologic syndromes with scleromyxedema (papular mucinosis). *J Am Acad Dermatol.* 1993;28:105-108.
17. Rongioletti F, Rebora A. Worsening of lichen myxedematosus during interferon alfa-2a therapy for chronic active hepatitis C. *J Am Acad Dermatol.* 1998;38:760-761.
18. Reynolds NJ, Collins CM, Burton JL. Discrete papular mucinosis responding to intralesional and topical steroids. *Arch Dermatol.* 1992;128:857-858.
19. Kaymen AH, Nasr A, Grekin RC. The use of carbon dioxide laser in lichen myxedematosus. *J Dermatol Surg Oncol.* 1989;15:862-865.
20. Montesu MA, Cottoni F, Sanna R, et al. Lichen myxedematosus associated with chronic hepatitis C: a case report. *Acta Derm Venereol.* 2001;81:67-68.
21. Poswig A, Hinrichs M, Megahed M, et al. Discrete papular mucinosis—a rare subtype of lichen myxoedematosus. *Clin Exp Dermatol.* 2000;25:289-292.
22. Rongioletti F, Rebora A, Crovato F. Acral persistent papular mucinosis: a new entity. *Arch Dermatol.* 1986;122:1237-1239.
23. Fosko SW, Perez MI, Longley BJ. Acral persistent papular mucinosis. *J Am Acad Dermatol.* 1992;27:1026-1029.
24. Coulson IH, Mallett RB, Holden CA. Acral persistent papular mucinosis. *Br J Dermatol.* 1992;126:283-285.
25. Espana A, Mosquera O, Idoate MA, et al. Acral persistent papular mucinosis. *Int J Dermatol.* 1993;32:600-601.

26. Menni S, Cavicchini S, Brezzi A, et al. Acral persistent papular mucinosis in two sisters. *Clin Exp Dermatol*. 1995;20:431-433.
27. Naeyaert JM, Geerts ML, Kudsi S, et al. Acral persistent papular mucinosis: a peculiar variant of the discrete papular form of lichen myxedematosus. *Arch Dermatol*. 1990;126:1372-1374.
28. Lum D. Cutaneous mucinosis of infancy. *Arch Dermatol*. 1980;116:198-200.
29. McGrae JD Jr. Cutaneous mucinosis of infancy. a congenital and linear variant. *Arch Dermatol*. 1983;119:272-273.
30. Calza AM, Masouye I, Saurat JH. An unusual case of infantile dermal mucinosis. *Pediatr Dermatol*. 1994;11:252-255.
31. Stokes KS, Rabinowitz LG, Segura AD, et al. Cutaneous mucinosis of infancy. *Pediatr Dermatol*. 1994;11:246-251.
32. Aydingoz IE, Candan I, Dervent B. Self-healing juvenile cutaneous mucinosis. *Dermatology*. 1999;199:57-59.
33. de las Heras ME, Perez B, Arrazola JM, et al. Self-healing cutaneous mucinosis. *Dermatology*. 1996;192:268-270.
34. Suhonen R, Niemi KM. Cutaneous focal mucinosis with spontaneous healing. *J Cutan Pathol*. 1983;10:334-339.
35. Cannata G, Gambini C, Ciaccio M. Self-healing localized cutaneous mucinosis. *Dermatology*. 1994;189:93-94.
36. Kwon OS, Moon SE, Kim JA, et al. Lichen myxoedematosus with rapid spontaneous regression. *Br J Dermatol*. 1997;136:295-296.
37. Suter L, Vakilzadeh F, Macher E. Atypical tuberous myxedema Jadassohn-Dossekker. report of a case. *Dermatologica*. 1980;161:265-269.
38. Schneider BV, Hohl D, Schnyder UW. Nodular cutaneous mucinosis—an unusual multiple type of euthyreotic focal mucinosis. *Dermatologica*. 1991;183:73-76.
39. Banno H, Takama H, Nitta Y, et al. Lichen myxedematosus associated with chronic hepatitis C. *Int J Dermatol*. 2000;39:212-214.
40. Saez-Rodriquez M, Garcia-Bustinduy M, Lopez-Alba A, et al. Localized lichen myxoedematosus (papular mucinosis) associated with morbid obesity: report of two cases. *Br J Dermatol*. 2003;148:165-168.
41. McCarthy JT, Osserman E, Lombardo PC, et al. An abnormal serum globulin in lichen myxedematosus. *Arch Dermatol*. 1964;89:446-450.