

Scleromyxedema Presenting With Neurologic Symptoms: A Case Report and Review of the Literature

Kathleen Marshall, MD; Stacy A. Klepeiss, MD; Michael D. Ioffreda, MD; Klaus F. Helm, MD

RELEASE DATE: March 2010

TERMINATION DATE: March 2011

The estimated time to complete this activity is 1 hour.

GOAL

To understand scleromyxedema to better manage patients with the condition

LEARNING OBJECTIVES

Upon completion of this activity, you will be able to:

1. Recognize the clinical and histopathologic features of scleromyxedema.
2. Identify treatment options for scleromyxedema.
3. Assess the prognosis of scleromyxedema.

INTENDED AUDIENCE

This CME activity is designed for dermatologists and general practitioners.

CME Test and Instructions on page 132.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: February 2010.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Albert Einstein College of Medicine and Quadrant HealthCom, Inc. Albert Einstein

College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Albert Einstein College of Medicine designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This activity has been planned and produced in accordance with ACCME Essentials.

Drs. Marshall, Klepeiss, and Helm report no conflict of interest. Dr. Ioffreda is a consultant for Johnson & Johnson. This relationship is not relevant to this article. The authors report no discussion of off-label use. Dr. Fisher reports no conflict of interest. The staff of CCME of Albert Einstein College of Medicine and *Cutis*® have no conflicts of interest with commercial interest related directly or indirectly to this educational activity.

From the Penn State Milton S. Hershey Medical Center and Penn State College of Medicine, Hershey. Dr. Marshall is a plastic surgery resident and Dr. Klepeiss was a resident, the Department of Dermatology. Dr. Ioffreda is Associate Professor and Dr. Helm is Professor, both from the Departments of Dermatology and Pathology. Dr. Klepeiss currently is a dermatologist, Geisinger Health System, State College, Pennsylvania.

Correspondence: Klaus F. Helm, MD, Penn State Milton S. Hershey Medical Center, Department of Pathology, MC H179, 500 University Dr, Hershey, PA 17033 (khelm@hmc.psu.edu).

Scleromyxedema is a rare variant of lichen myxodermatosus. In addition to cutaneous manifestations, scleromyxedema often presents with systemic manifestations, including dysphagia, proximal muscle weakness, central nervous system disturbances, encephalopathy, and restrictive lung disease. It is almost always associated with paraproteinemia, usually IgG with γ light chains. We review the literature on scleromyxedema

associated with neurologic symptoms and present a case of a 49-year-old woman with encephalopathy attributable to scleromyxedema.

Cutis. 2010;85:137-140.

Case Report

A 49-year-old woman presented to the emergency department with confusion and painful swelling of both hands (Figure 1). The patient's speech was broken and she was unable to express her thoughts. A family friend reported a 5-day history of forgetfulness that progressively worsened to difficulty finding words and nearly unintelligible speech. According to family members, the patient's baseline mental status was sharp, intelligent, and quick-witted. Review of systems was remarkable for fatigue, occasional blurred vision, muscle pain, and tingling and numbness in the extremities that resulted in difficulty ambulating. The patient also reported skin changes throughout a year that manifested as a nonpruritic pink rash on her upper lip (Figure 2) and eyebrows as well as small white papules on her ears and arms.

The patient was admitted to the hospital for evaluation of her confusion. Physical examination demonstrated pink plaques on her nose, glabella, and periorbital region bilaterally, as well as tiny white papules on her ears, posterior aspect of the arms, and anterior aspect of the thighs (Figure 3). Her skin was thickened and firm to the touch, with the appearance of an early leonine face. All cranial nerves, except the olfactory nerve, were intact by examination. Initially she was able to follow simple commands; however, by her second day in the hospital, she was unable to respond to verbal commands.

Results from blood work for nutritional or endocrine etiology were normal, ruling out metabolic encephalopathy. Blood cultures, serologic viral

titers for Lyme disease and parvovirus B19-Au, and initial evaluation of her blood and colony-stimulating factors (CSFs) showed no signs of an infectious etiology. Magnetic resonance angiography and magnetic resonance imaging of the neck and head were normal; however, the electroencephalogram showed diffuse slowing of activity consistent with diffuse encephalopathy. Serum immunofixation revealed IgG lambda monoclonal paraprotein representing 25% of the total serum IgG. Further evaluation of CSFs showed normal levels of IgG and oligoclonal bands suggestive of a monoclonal gammopathy. On her third day in the hospital, her serum IL-6 level also was elevated (14.96 pg/mL [reference range, 0.31–5.0 pg/mL]). A punch biopsy from a fine, papular, symmetric eruption on her lateral thigh showed a dermal proliferation of fibroblasts associated with mucin deposition (Figure 4). Clinical, serologic, and pathologic findings were all consistent with a diagnosis of scleromyxedema.

The patient was started on intravenous (IV) methylprednisolone (60 mg IV every 12 hours), which resulted in a marked improvement in her mental status. After a diagnosis of scleromyxedema was confirmed, IV immunoglobulin was added. She was discharged from the hospital on the 17th day with complete resolution of her confusion. Cutaneous manifestations of the disease were still present, albeit improved.

Comment

Scleromyxedema is a rare variant of lichen myxedematosus. The localized form without systemic manifestations is generally called lichen myxedematosus (also known as papular mucinosis), and the more sclerotic diffuse form with systemic manifestations is referred to as scleromyxedema. The localized form does not follow the same disabling or even fatal course as scleromyxedema. In all forms there



Figure 1. Swelling of the right hand.



Figure 2. Fine papules on the upper lip.



Figure 3. Papules on the thigh.

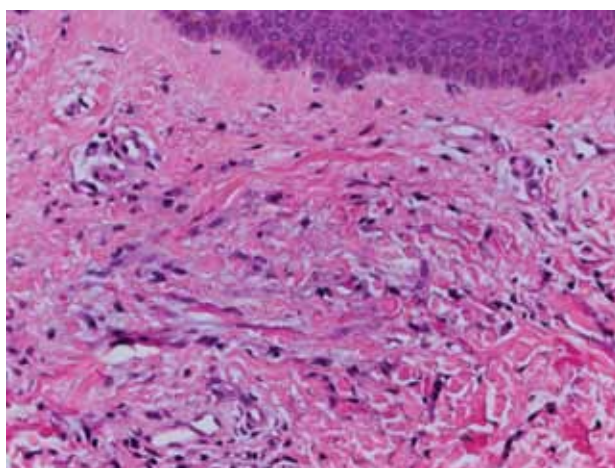


Figure 4. Dermal proliferation of fibroblasts associated with mucin deposition (H&E, original magnification $\times 40$).

is a generalized or acral eruption of papules, but in scleromyxedema there also is a diffuse thickening of the skin associated with erythema.¹ The most common sites of involvement are the head and neck region, upper trunk, forearms, hands, and thighs. Patients with scleromyxedema often present

with skin thickening and decreased joint mobility. Scleromyxedema affects men and women equally, usually between 30 and 80 years of age,² and is characterized by waxy, erythematous or yellowish papules caused by an accumulation of mucin in the dermis.¹ The papules often become confluent and form plaques, giving the skin a thick sclerotic appearance. Although the pathogenesis is unknown, fibroblast proliferation and excessive deposition of acid mucopolysaccharides in the dermis are characteristic of all forms of the disease. It is frequently associated with an IgG-type light chain monoclonal gammopathy; however, the role of paraproteinemia in the pathogenesis of the disease remains uncertain.^{3,4}

Primarily a cutaneous disorder, associated systemic involvement has been described, including cardiovascular, renal, hematologic, rheumatologic, and neurologic abnormalities, as well as restrictive lung disease and esophageal dysmotility.^{5,6} Neurologic impairment associated with scleromyxedema is rare and reports include myopathy, entrapment neuropathy, convulsions, and encephalopathy.^{5,7} Although generally a chronic disease, the prognosis is poor when neurologic dysfunction is involved.⁸ Scleromyxedema associated with encephalopathy rarely is reported in the literature. Several cases have been described in which the triad of fever, convulsions, and coma were associated with a prodromal flulike illness, sometimes with spontaneous resolution and other times resulting in death.⁵ Dysarthria and/or confusion often precede severe neurologic dysfunction and often are associated with a fatal outcome.⁶⁻¹² Our patient remained afebrile while in the hospital, and her neurologic symptoms resolved with high-dose IV steroids.

Our patient's elevated serum IL-6 levels were worthy of further investigation. IL-6 is a cytokine secreted by macrophages that induces acute-phase protein production. It has been suggested that elevated levels of IL-6 in CSFs may play a role in the pathogenesis of encephalopathy in patients with scleromyxedema. Furthermore, IL-6 may regulate the permeability of the blood-brain barrier. In the report by Johkura et al,⁸ a patient's CSF was evaluated during episodes of encephalopathy associated with scleromyxedema. Both CSF and serum IL-6 levels were markedly elevated during episodes of encephalopathy, whereas other markers of inflammation such as tumor necrosis factor α and IL-2 remained within reference range. Furthermore, the elevation of IL-6 was more prominent in the CSF than the serum and seemed to correlate with the level of confusion.⁸

According to a review of the literature using PubMed and the search terms *scleromyxedema* and

IL-6, our patient is the second case in which serum IL-6 levels are mentioned in association with scleromyxedema. The serum IL-6 level was measured on the patient's third day in the hospital, a day after she was started on IV steroids. The correlation of CSF and serum IL-6 levels with episodes of confusion warrants further investigation, as does the administration of high-dose steroids early in the disease course (before confusion progresses).

There is no definitive cure for scleromyxedema. Melphalan, systemic corticosteroids, and plasmapheresis have been suggested as first-line treatments² and are the mainstay of treatment in patients with systemic complications. Second- and third-line treatment modalities include cyclophosphamide, retinoids, thalidomide, topical corticosteroids, extracorporeal photopheresis, autologous stem cell transplant, IV immunoglobulin, interferon alfa-2b, psoralen plus UVA radiation, and radiation and electron-beam therapy.^{2,4} Initial favorable responses to immunosuppressive agents may not be consistently maintained, and despite aggressive treatment, the disease remains fatal in a high percentage of patients.

REFERENCES

1. Elder DE, Johnson B Jr, Elenitsas R, eds. *Lever's Histopathology of the Skin*. 9th ed. Philadelphia, PA: Lippincott; 2005.
2. Heymann WR. Scleromyxedema. *J Am Acad Dermatol*. 2007;57:890-891.
3. Rayson D, Lust JA, Duncan A, et al. Scleromyxedema: a complete response to prednisone. *Mayo Clin Proc*. 1999;75:481-484.
4. Berger JR, Dobbs MR, Terhune MH, et al. The neurologic complications of scleromyxedema. *Medicine (Baltimore)*. 2001;80:313-319.
5. River Y, Levy I, Gilead L, et al. Fever, convulsions and coma in scleromyxedema: a "dermato-neuro syndrome." *Neurology*. 1996;46:1778-1779.
6. 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(2, pt 2):289-294.
7. Rothe MJ, Rivas R, Gould E, et al. Scleromyxedema and severe myositis. *Int J Dermatol*. 1989;28:657-660.
8. Johkura K, Susuki K, Hasegawa O, et al. Encephalopathy in scleromyxedema. *Neurology*. 1999;53:1138-1140.
9. Fudman EJ, Golbus J, Ike RW. Scleromyxedema with systemic involvement mimics rheumatic diseases. *Arthritis Rheum*. 1986;29:913-917.
10. Kantor GR, Bergfeld WF, Katzin WE, et al. Scleromyxedema associated with scleroderma renal disease and acute psychosis. *J Am Acad Dermatol*. 1986;14(5, pt 2): 879-888.
11. 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.
12. Reid TL, Spoto DV, Larrabee GJ, et al. Monoclonal paraproteinemia with subacute encephalopathy, seizures, and scleromyxedema. *Neurology*. 1987;37: 1054-1057.

DISCLAIMER

The opinions expressed herein are those of the authors and do not necessarily represent the views of the sponsor or its publisher. Please review complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings, and adverse effects before administering pharmacologic therapy to patients.

CONFLICT OF INTEREST STATEMENT

The Conflict of Interest Disclosure Policy of Albert Einstein College of Medicine requires that authors participating in any CME activity disclose to the audience any relationship(s) with a pharmaceutical or equipment company. Any author whose disclosed relationships prove to create a conflict of interest, with regard to their contribution to the activity, will not be permitted to present.

The Albert Einstein College of Medicine also requires that faculty participating in any CME activity disclose to the audience when discussing any unlabeled or investigational use of any commercial product, or device, not yet approved for use in the United States.