Skin Changes Help Identify Scleroderma Mimics

BY PATRICE WENDLING

CHICAGO — Few physicians would be fooled nowadays by gadolinium-induced nephrogenic systemic fibrosis, but there are other diseases that can masquerade as scleroderma.

The precise diagnosis of scleroderma-like illnesses is important because even though many of them are called scleroderma, they are different from systemic sclerosis in their treatments and outcomes, Dr. Virginia Steen said at a symposium sponsored by the American College of Rheumatology. The diagnosis is most often based on the distribution and clinical characteristics of skin findings, as biopsies don't always differentiate types of scleroderma. She recommended watching for the following conditions:

► **Lipodermatosclerosis** is one condition that physicians often fail to think of as a scleroderma mimic. Also known as hypodermatitis sclerodermaformis, it refers to localized chronic inflammation and fibrosis of the skin and subcutaneous tissues of the lower leg. In the acute stage, the leg is inflamed and warm, the skin is very tight, and cellulitis may be present. The ankle and toes are not involved.

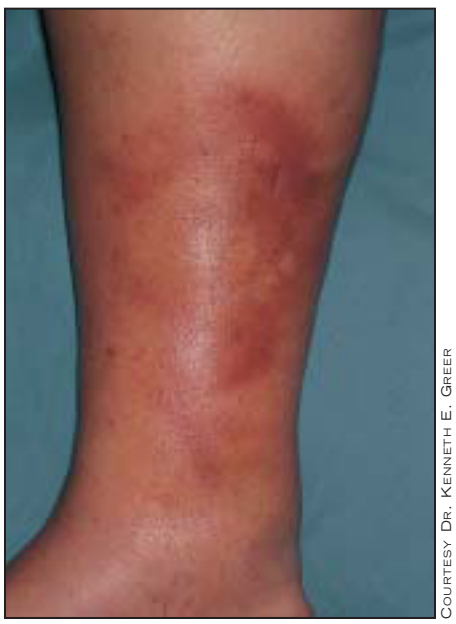
In its chronic stage, there is induration, contraction of the skin and subcutaneous tissues, and irregular depressions that can look almost identical to lower-leg scleroderma, she said. The leg eventually resembles an inverted champagne bottle, in which the upper half remains edematous and has a much greater circumference than does the lower sclerotic portion.

Lipodermatosclerosis is a sign of severe end-stage venous insufficiency, and should be differentiated from scleroderma, cellulitis, superficial thrombophlebitis, and erythema nodosum. The diagnosis is made from clinical observation, but direct immunofluorescence of early and late lesions has been used to show dermal pericapillary fibrin deposits.

If left untreated, lipodermatosclerosis can progress to ulceration, atrophy blanche, or shortening of the Achilles tendon. Treatment involves weight loss, controlling the underlying disease, and emphasis on support stockings that may need to be specially made, said Dr. Steen, professor of medicine and director of the rheumatology fellowship program at Georgetown University in Washington. Topical steroids are useful if the skin is inflamed, and antibiotics are recommended for cellulitis.

► **Scleredema** tends to target the upper body without affecting the lower extremities. The skin on the neck and face thicken and harden; severely affected patients are unable to wrinkle their foreheads or open their mouths. In most patients, the shawl sign is present, with skin involvement over the chest and arms, she said.

Pathological features include swollen collagen with clear spaces and accumulation of hyaluronic acid and glycosaminoglycans. Although scleredema is commonly associated with diabetes, it can also occur after a viral illness. The treatment emphasis is on better diabetes control, but spontaneous resolution of symptoms is possible after infection.



COURTESY DR. KENNETH E. GREER

The sclerotic plaque on this patient's lower leg is lipodermatosclerosis.

► **Eosinophilic fasciitis** is a rare disorder characterized by symmetrical and painful inflammation and swelling of the extremities, leading to induration and the characteristic peau d'orange configuration. The palms may be involved, but typically the fingers and toes are spared. Contractures demonstrating the groove sign commonly evolve as a result of induration.

Eosinophilic fasciitis is slightly more common in middle-aged men, but can occur in women and children. It was initially distinguished from systemic sclerosis by the absence of Raynaud's phenomenon, autoantibodies, and visceral involvement, and it responds to corticosteroids.

Histologically, there are marked eosinophilia and inflammatory infiltrates in the fascia. The extent of the histologic changes depends on the stage of the disease, and thus is not a consistent component of the disease. Aside from marked peripheral eosinophilia, other laboratory features to watch for include an increased erythrocyte sedimentation rate, increased gamma globulin, and an increased aldolase, with a normal creatinine phosphokinase.

Physical therapy is a key component of treatment, because this and most scleroderma mimics discussed here can cause joint contractures. In eosinophilic fasciitis, low- to moderate-dose prednisone—and, if needed, methotrexate—can be given. There is also some evidence to suggest that rituximab, mycophenolate mofetil, or tumor necrosis factor inhibitors may be useful, Dr. Steen said.

► **Diabetic cheiroarthropathy** is a syndrome of limited joint mobility in the hands. It is characterized by thickened, tight, waxy hands with sclerosis of the palmar tendon sheaths that noticeably restricts mobility in the proximal interphalangeal joints and metacarpophalangeal joints. Therapeutic options are focused on improved diabetic control and exercise to improve mobility, said Dr. Steen, who disclosed having no relevant conflicts of interest. ■

Skin Elasticity May Serve as Potential Biomarker for Sclerosis

BY JEFF EVANS

SEATTLE — Reductions in skin elasticity appear to be a possible biomarker for the progression of amyotrophic lateral sclerosis that deserves further study, according to study results.

The change in the potential biomarker was associated with changes in the Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised and other clinical measures of disease progression, including forced vital capacity.

ALS patients are known to have reduced skin elasticity, in which the skin returns slowly to its original shape and dimensions after being stretched. However, this phenomenon has not been quantified and suffers from substantial intra- and interobserver variability.

'Our objective was to test the hypothesis that chronologic, quantitative measurements of skin elasticity could be a useful, noninvasive, biomechanical biomarker.'

Structural and biochemical abnormalities of the skin in ALS also have been identified, including reduced and loosely woven collagen bundles with accumulation of amorphous materials between the bundles, collagen fibrils with irregular diameter, noninflammatory vasculopathy, and deposits of beta-amyloid protein close to blood vessels. One study also found a significant negative correlation between the diameter of collagen fibrils and the duration of ALS (J. Neurol. Sci. 1993;119:74-8), Dr. Harvey Arbesman said at the annual meeting of the American Academy of Neurology.

The skin changes that appear in ALS patients could be analogous to changes that are occurring in the CNS because both the CNS and skin arise from the neural crest in development and many diseases affect both systems, suggested Dr. Arbesman, a dermatologist in Williamsville, N.Y.

"Our objective was to test the hypothesis that chronologic, quantitative measurements of skin elasticity could be a useful, noninvasive, biomechanical biomarker of disease progression in patients with ALS and aid in diagnosis," he said.

Dr. Arbesman and his colleagues measured skin elasticity with a cutometer on the arm and back at baseline in 40 ALS patients and 30 of their family members or caregivers, who served as controls. Most of the control participants were spouses. None of the patients had superoxide dismutase 1 (SOD1) mutations, which are known to cause about 20% of familial ALS cases.

Compared with the controls, skin elasticity in ALS patients was significantly reduced in measurements on the arm with 2-mm and 8-mm Cutometer probes.

The investigators controlled for age at baseline because skin elasticity declines with age. Cutometer measurements with 2-mm probes assessed the elastic properties of the epidermis and papillary dermis, whereas measurements with the 8-mm probe evaluated the elastic properties of the whole skin, he said.

"We took into account if the patient had developed, let's say, right-sided disease first and that was the presenting complaint, then we used the affected side. If it was bilateral involvement when it was presented, then by default we used the right side," Dr. Arbesman said.

Because the hydration status of the skin will affect its elasticity, the investigators instructed patients not to make any changes in their skin care habits on the day of each visit. The air temperature and humidity of the clinic were monitored at each visit to ensure that they were the same.

Skin elasticity on the back was significantly correlated with scores on the ALS Functional Rating Scale–Revised, as well as forced vital capacity, at 3 months. The group has collected 6-month follow-up data that are still being analyzed, he said.

The changes in the Cutometer readings between baseline and follow-up measurements were assessed on a plot of the area under the curve for the ratio between the two curves that are generated during the suction and relaxation phases of the elasticity measurement for each anatomic location. This tends to correct for any edema or changes in subcutaneous fat that might have occurred between measurements, he said.

"Further studies are needed to elucidate the relationship of this biomarker to specific biochemical changes relevant to the pathogenesis of ALS," Dr. Arbesman concluded.

The study was funded by ArbesIdeas Inc., the Muscular Dystrophy Association's Wings Over Wall Street, Prize4Life, and the University of Missouri–Columbia Dermatology Research Fund. Dr. Arbesman, the vice president of ArbesIdeas Inc., was awarded part of a $100,000 prize pool for winning Prize4Life's ALS Biomarker Discovery Prize. ■