JOINT DECISIONS

The progression to systemic lupus in this patient is a "fascinating example of the spectrum of clinical presentation and chronicity in systemic lupus erythematosus," Dr. Sheilagh Maguiness said at a meeting of the Society for Pediatric Dermatology.

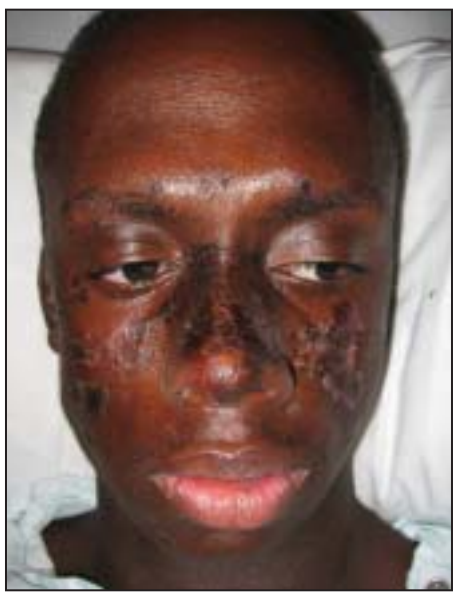
Although neither the boy nor his mother reported his history of disease at birth or infancy—and in fact initially denied any such history or related family history—a chance consultation with Dr. Ilona Frieden of the University of California, San Francisco, who was familiar with the patient and had reported on the case in 1998, shed light on his condition.

He was born to a 22-year-old mother at 35 weeks' gestation with a widespread rash consisting of reticulate atrophic plaques, hyperpigmentation, desquamation, and alopecia.

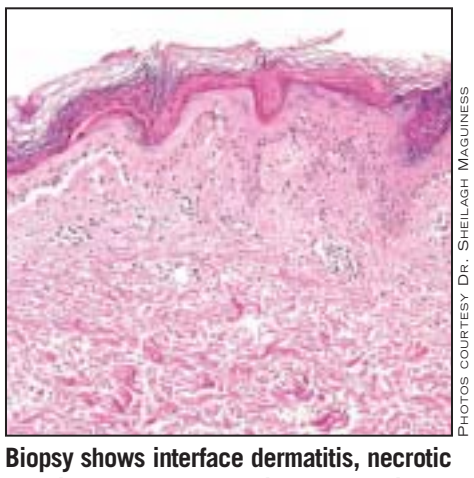
Hematologic abnormalities at that time included pancytopenia; positive antinuclear antibodies (ANA); and negative Ro, La, and anticardiolipin antibody titres. The mother also had positive ANA and was negative for Ro/La, said Dr. Maguiness, also of the university.

A skin biopsy shortly after birth revealed atrophic epidermis with areas of vacuolar interface dermatitis and increased mucin. Direct immunofluorescence showed granular IgG at the dermoepidermal junction, and the diagnosis of congenital lupus erythematosus was made, she said.

The patient's early disease course included three hospitalizations during infancy for inguinal hernia repair, respiratory distress, and exacerbation of cutaneous lesions. During the final hospitalization, the patient's ANA remained positive and double-stranded DNA became positive. He improved gradually after treatment with intravenous immunoglobulin, and had no evidence of recurrent disease at a follow-up visit at age 5 years. He was lost to follow-up until presenting at age 15.



Discoid, hyperkeratotic, and hyperpigmented plaques are seen on teen's face.



PHOTOS COURTESY DR. SHEILAGH MAGUINESS

Biopsy shows interface dermatitis, necrotic keratinocytes, and subepidermal clefting.

At that time, he had an extensive rash and several other symptoms, including arthritis, headaches, and high blood pressure.

"He had widespread, hyperpigmented, annular, atrophic, hyperkeratotic lesions over sun-exposed areas," Dr. Maguiness said, noting he also had diffuse alopecia.

There was an unusual background of hypo- and depigmentation over his trunk, which, according to the patient, had been present since birth but looked like partially treated vitiligo, she said.

Multiple investigations revealed strongly positive ANA, anti–Ro/La antibodies, positive small nuclear ribonucleoproteins, and renal involvement. A biopsy indicated class II lupus nephritis.

A biopsy of the upper outer arm that was taken to confirm the diagnosis showed an acute interface dermatitis with vacuolar changes, necrotic keratinocytes, parakeratosis, and a positive direct immunofluorescence, leading to the diagnosis of SLE with extensive cutaneous involvement.

The patient was hospitalized and treated with pulse Solu-Medrol, hydroxychloroquine, antihypertensives, and topical steroids, Dr. Maguiness noted.

His renal disease has remained stable, but the cutaneous aspect of his disease has been difficult to control despite immunosuppression, she said.

Mainly, the patient has had discoid and subacute cutaneous lupus erythematosus–type lesions. In December, however, he experienced a cutaneous exacerbation with more target lesions, despite having no history of herpes simplex infection. He had violaceous plaques with some desquamation and involvement of the palms and soles. His mucous membranes were clear.

Another biopsy from his trunk at this presentation showed vacuolar interface dermatitis with subdermal clefting and numerous necrotic keratinocytes, which could be consistent with either bullous lupus erythematosus or bullous erythema multiforme.

Direct immunofluorescence in this exacerbation was negative (previously it was positive), suggesting a diagnosis of Rowell's syndrome, which "very basically is erythema multiforme occurring in the setting of systemic lupus," she said.

"Our patient's case … raises interesting questions about this congenital presentation of lupus. It is unusual for patients with typical neonatal lupus to develop SLE later on. This case makes one wonder if maybe that we should be questioning the sole role of maternal autoantibodies in this patient's case of congenital lupus. Perhaps he had some endogenous predisposition to develop lupus. This is the first patient we have observed with the clinical presentation of congenital, neonatal, and infantile lupus progressing to systemic lupus erythematosus as a teenager," Dr. Maguiness said.

—Sharon Worcester

Autoantibody Predicts Cancer Risk in Myositis

BY BRUCE JANCIN
Denver Bureau

SNOWMASS, COLO. — A novel myositis-specific autoantibody shows promise for predicting which patients with idiopathic inflammatory myositis are at increased cancer risk, Dr. Robert L. Wortmann said at a symposium sponsored by the American College of Rheumatology.

"It looks like we may have found a marker that's more predictive of cancer than any marker we've had before," observed Dr. Wortmann, professor of medicine at Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

Case-control and population-based cohort studies show patients with idiopathic inflammatory myositis are at increased risk of cancer. A serologic test to help identify the subgroup warranting intensive cancer surveillance is needed.

Dr. Wortmann credited Dr. Hector Chinoy of the University of Manchester (England) and coworkers at the University of Pittsburgh with demonstrating the new autoantibody's utility in predicting cancer-associated myositis. The antibody is a doublet directed against a 155-kDa protein and a 140-kDa protein.

The investigators tested for this and a comprehensive array of more conventional myositis-specific autoantibodies in a large cohort comprising 109 white adults with polymyositis, 103 with dermatomyositis, and 70 myositis/connective tissue disease overlap patients with primary diagnoses including systemic sclerosis, mixed connective tissue disease, Sjögren's syndrome, and systemic lupus erythematosus.

Sixteen of the 282 patients had cancer-associated myositis, defined as cancer developing within 3 years of diagnosis of the myositis. Fifteen of the 16 had dermatomyositis and 1 had a connective tissue disease overlap syndrome, confirming reports that cancer risk is greater in dermatomyositis than in polymyositis.

Anti–155/140-kDa antibody was found exclusively in dermatomyositis patients, with a prevalence of 18%. The antibody was present in 8 of 16 patients with cancer-associated myositis, but in only 11 of 266 without it. Seven of eight anti–155/140-kDa antibody–positive patients who developed cancer did so within 1 year of dermatomyositis diagnosis.

A positive anti–155/140-kDa antibody test had 96% specificity, 50% sensitivity, a 42% positive predictive value, and a 97% negative predictive value for cancer-associated myositis.

The combination of a positive anti–155/140-kDa antibody test and a negative result on a routine myositis antibody panel testing for anti–Jo-1, anti–U1-RNP, anti–U3-RNP, anti–PM-Scl, and anti-Ku antibodies detected 15 of 16 cases of cancer-associated myositis. The combination had a sensitivity of 94% and a negative predictive value of 99% (Ann. Rheum. Dis. 2007;66:1345-9).

Testing for anti–155/140-kDa antibody isn't commercially available at present. ■

Involvement of Vitamin D, Estrogen In SLE May Point to New Therapies

BY BRUCE JANCIN
Denver Bureau

SNOWMASS, COLO. — Vitamin D and estrogen may provide the basis for a new generation of nonimmunosuppressive therapies for systemic lupus erythematosus, Dr. Betty Diamond predicted at a symposium sponsored by the American College of Rheumatology.

Presenting vitamin D to cultured SLE dendritic cells inhibits expression of interferon-inducible genes, decreasing the pro-immunogenic inflammatory cascade. Vitamin D also promotes expression of regulatory T cells, suppresses interleukin-12, and balances Th1 and Th2 T-cell responses.

Vitamin D deficiency is highly prevalent in patients with SLE, and serum vitamin D levels correlate inversely with SLE Disease Activity Index scores.

Dr. Diamond, head of the Center for Autoimmune Diseases at the Feinstein Institute for Medical Research, Manhassett, N.Y., and her coinvestigators are launching a clinical trial of vitamin D supplementation in patients with mild lupus. "I don't think vitamin D is going to change fulminant disease. It's not going to change fixed damage. It's not going to treat rip-roaring lupus nephritis or vasculitis or clots. But I think it may be able to prevent progression to lupus," she said.

Turning to estrogen as a potential therapeutic target in SLE, Dr. Diamond said her interest was initially piqued by the epidemiology of the disease.

"The greatest risk factor for lupus is being female," she said. And, "Before puberty the ratio of girls to boys who get lupus is about 3:1, after puberty it's 9:1, and after menopause it goes down to 2:1."

In mouse models of lupus, physiologic titers of estradiol alter the B-cell repertoire by promoting rescue of pathogenic high-affinity DNA-reactive B cells while impairing maturation of low-affinity DNA-reactive B cells. This is accomplished through increased expression of B-cell activating factor. The high-affinity DNA-reactive B cells generate antibodies which form proinflammatory immune complexes, suggesting antiestrogenic therapies might reduce the risk of lupus in women in their reproductive years to a level comparable to that of prepubertal girls or postmenopausal women. ■

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