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times. We don't know who is going to [be polyphasic]."

The third course of the disease, chronic continuous, affects mostly teens. "We have a very hard time treating these patients," Dr. Szer said. "These are children who are at very high risk for calcinosis. They require prolonged immune suppression."

Current treatment for severe DMS involves intravenous pulse methylprednisolone with oral steroids and methotrexate. More aggressive treatment options include monthly intravenous IgG, azathioprine, cyclophosphamide, and mycophenolate mofetil.

"As soon as they're feeling better, we work on strength and conditioning and endurance," she said. "We also encourage and advocate normal function and school attendance."

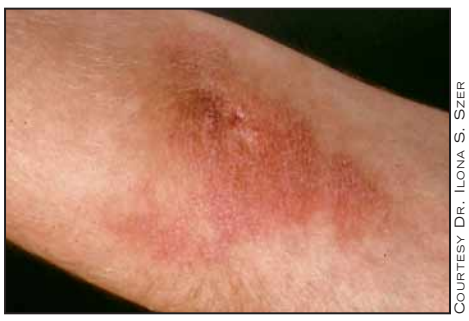
DMS isn't the only rheumatic disease that can stump clinicians. Systemic lupus erythematosus is another. Suspect SLE in a young woman with constitutional symptoms and multiorgan manifestations. "I am forever seeing 4-year-old boys with positive ANAs [antinuclear antibody tests] referred to me who are suspected of having lupus," she said, noting that 90% of cases occur in women (particularly young women).

"I would like everyone to think three times before ordering an ANA because up to 20% of healthy children have positive ANAs," said Dr. Szer, also a professor of pediatrics at the University of California, San Diego. "That's practically everybody."

A common cutaneous sign of SLE is a malar rash that spares the nasolabial folds. Other cutaneous signs include discoid rash, photosensitive rash, and recurrent mouth sores.

"Lupus in children is usually insidious," she added. "It may be acute, but it is always organ- or life-threatening. Delay in diagnosis clearly leads to lupus crisis. There is a point of no return with these patients. There's irreversible renal damage and death."

Erythrocyte sedimentation rate tends to be very high. Corrected sedimentation rate tends to be normal unless your patient has an infection, and renal disease is found in 90% of children. "The disease is very aggressive in children, especially during the first 2 years," she said. "We think of this as cancer medicine. We induce things into remission and then we maintain that remission." ■



COURTESY DR. ILONA S. SZER

This rash over the extensor surface of the elbow is characteristic of DMS.

Gene Linked to Acute Rheumatic Fever Identified

VIENNA — A polymorphism in the gene coding for toll-like receptor 2 appears to constitute a powerful susceptibility gene for acute rheumatic fever, H. Hakan Aydin, M.D., Ph.D., said at the annual European Congress of Rheumatology.

Indeed, 56 of 61 unselected Turkish children who met diagnostic criteria for acute rheumatic fever were heterozygous for the simple polymorphism, in which arginine is replaced by glutamine at position 753 in the toll-like receptor 2 (TLR-2) gene, according to Dr. Aydin of Ege University, Izmir, Turkey.

In contrast, 9 of 91 ethnically matched healthy pediatric controls and 12 of 116 healthy adult controls were heterozygous for TLR-2 *Arg753Gln*. Not one patient or control was homozygous for *Arg753Gln*.

Genetic differences in host susceptibility to acute rheumatic fever as reflected in the TLR-2 polymorphism go a long way toward explaining why only 0.3%-3.0% of patients with acute group A streptococcal pharyngitis go on to develop acute rheumatic fever, he said at the meeting sponsored by the European League Against Rheumatism. TLRs play a key role in host immunity, initiating the full range of both adaptive and innate immune responses against all manner of foreign microbes. Thus, a polymorphism in TLR-2 rendering affected individuals hyporesponsive to bacteria which contain TLR-2 agonists—as do gram-positive group A strep—could have important clinical consequences.

The finding that a TLR-2 polymorphism is strongly associated with increased susceptibility to rheumatic fever should eventually lead to a simple genetic test to risk-stratify patients for a disorder the World Health Organization says is still a major health problem, particularly in developing countries. It also opens the door to pharmacologic manipulation of TLR-2 for therapeutic purposes, Dr. Aydin predicted.

—Bruce Jancin