Refining Treatment of Juvenile Dermatomyositis

Newly created consensus protocols can help clinicians determine the best therapy.

BY AMY ROTHMAN SCHONFELD

FROM A MEETING SPONSORED BY NEW YORK UNIVERSITY

NEW YORK – Because juvenile dermatomyositis is a rare disease and its symptoms often differ from those seen in adult dermatomyositis, pediatricians and family physicians may not recognize it and diagnosis can be delayed, Dr. Brian Feldman said.

He described a recent practice survey that found variability in juvenile dermatomyositis (JDM) treatment and, in the absence of randomized controlled trials, urged clinicians to consult newly created consensus protocols developed by rheumatologists and to gather data that may help to optimize treatment and minimize side effects in the future for those with JDM.

Dr. Feldman described a 15-year-old patient who had progressively deteriorated over a 3-year period despite being seen by pediatricians and dermatologists. His initial symptoms included fatigue and elevated muscle enzymes, including aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), and creatine phosphokinase (CPK).

Within a year, the patient developed a purple skin rash on his hands, elbows, and knees. He later developed Raynaud's syndrome and muscle weakness with decreased range of motion that interfered with participation in sports and other activities of daily living. Upon examination, he was quite thin with a scaly rash over his knuckles (Gottron's papules), healing skin ulcerations on his hands (from severe Raynaud's), periungual erythema, and lipodystrophy and erythema of his forearms. Magnetic resonance imaging showed acute inflammation of his shoulder girdle, said Dr. Feldman, chief of pediatric rheumatology at the Hospital for Sick Children in Toronto.

Dr. Feldman said that one of the best diagnostic clues for JDM comes from microscopic examination of nail folds. In this case, the patient had tortuous, bushy nail folds, dilated or missing capillaries (capillary density of 3 per mm of nailfold length while normal ranges from 7-11 per mm), and cuticular overgrowth indicative of JDM.

For rheumatologists, the different presentation seen with children compared with adults may hinder a correct diagnosis. For instance, calcinosis is seen much more often in children than adults. Children are less likely to have some of the systemic symptoms, such as fever, poor weight gain, and pulmonary effects, and they almost never have cardiac problems. Unlike adults with dermatomyositis or polymyositis who appear to have a fourfold increased risk of malignancy, very few cases of malignancy have been associated with JDM. Children are more likely to experience dysphonia/dysphagia but are as likely to have arthritic symptoms (around 58% of each group). Myositis-specific antibodies do not seem to play as important a diagnostic role for children as adults.

Children who develop JDM appear to have a better prognosis than adults. Although adults with myositis have appreciable mortality (about 10%) and progressive disability, findings from Dr. Feldman's group show that outcomes were often excellent in children. "We have not had a single death from JDM in 30 years," he said.

About two-thirds of children with JDM have a polycyclic, chronic, unremitting disease course, but about one-third follow a monocyclic course and have disease symptoms that last for 2-3 years and then go away, with, or potentially even without, treatment. In a very small proportion of these patients, symptoms may return many years later. It is possible to predict which patients will follow a chronic course and which patients will have early remission. In his experience, the risk of persistent disease falls by half if Gottron's rash disappears within 3 months of diagnosis (odds ratio, 0.5; $P = .0013$) (Arthritis Rheum. 2008;58:3585-92).

The results of a recent practice survey by the Childhood Arthritis and Rheumatology Research Alliance (CARRA) of almost 200 pediatric rheumatologists in North America found both similarities and differences in treatment approaches to JDM (J. Rheumatol. 2010;37:1953-61).

Corticosteroids and methotrexate (MTX) are mainstays of care, but the route and pattern of corticosteroid administration varied: 82% of respondents initially pulsed with high-dose intravenous methylprednisolone (IVMP) while 18% prescribed oral prednisone. MTX was used concurrently with steroids 84% of the time. Sixteen percent reported also using IV immunoglobulin, with or without MTX, for more severe disease, refractory disease, and prominent cutaneous disease. Hydroxychloroquine was given for milder cases, especially for rash, while cyclophosphamide was prescribed for ulcerative disease or for patients with pulmonary symptoms.

While these findings reflect the current prescribing practices of rheumatologists, there are almost no randomized controlled trials of medications for JDM, Dr. Feldman pointed out.

This reflects in part the rare nature of the disease, its complexity, the difficulty of conducting studies in children, and the high cost of randomized controlled trials. There have been studies using advanced analytic techniques to provide strong comparative data in lieu of an randomized controlled trial. One such study by Dr. Feldman and associates (Arthritis Rheum. 2008;59:989-95) showed that more aggressive corticosteroid therapy does not give better 3-year outcomes.

A recent randomized controlled trial presented at the annual meeting of the American College of Rheumatology looked at dermatomyositis in 76 adults and 48 children and found that 80% had a response to rituximab within a year of treatment. Interpretation of the study may have been limited by the design, which allowed patients to receive add-on medications during the trial.

In light of the CARRA study's findings of heterogeneity in the treatment of JDM and the absence of randomized controlled trials, a group of 12 pediatric rheumatologists met to study treatments in JDM using a new approach: by developing consensus treatment protocols (Arthritis Care Res. 2010;62:219-25).

"This is similar to what has been done in pediatric oncology," said Dr. Feldman, who was one of the participants. "We are hoping physicians throughout the world will take these protocols off the shelf, and by using standardized doses, follow-up, and measurements, we will be able to accumulate enough evidence over time to know which is the best therapy."

In brief, the group recommended three protocols for the treatment of patients with moderately severe JDM: pulse IVMP plus MTX; IVMP, MTX, plus IVIG; or oral prednisone plus MTX. The third protocol is the one followed most often at the Hospital for Sick Children. The treatment protocols are not intended as treatment recommendations, although it is hoped that a physician will choose to follow the standardized protocol that most closely reflects his or her preferred practice. It is presented as a "first step to allow comparison of different approaches to the treatment of JDM," he said.

Dr. Feldman has done contracted research with Bayer Healthcare Pharmaceuticals. He has referenced unlabeled/unapproved uses of drugs or products in his presentation. ■

Climate Change May Result in More Lyme Disease

BY SHERRY BOSCHERT

EXPERT ANALYSIS FROM A DERMATOLOGY SEMINAR

LAS VEGAS – Climate change has expanded geographic ranges of tick and parasite vectors, pushing some infectious diseases that cause joint pain in children into unfamiliar territory, Dr. Sigfrid A. Muller said at a dermatology seminar sponsored by Skin Disease Education Foundation (SDEF).

Lyme disease has spread well into Canada, and leishmaniasis is moving north from Mexico into Texas, Arizona, Oklahoma, and Ohio. Reports of Chagas disease are increasing in the United States and Central and South America. Peru and Ecuador are seeing more Carrion's disease, said Dr. Muller, a dermatologist in Las Vegas and chair of the International Society of Dermatology's Climate Change Task Force.

Global warming may be debated in the popular media, but there is little controversy about it in the scientific literature, he said. June 2010 was the warmest month on record (combining global land and ocean average surface temperatures) and the 304th consecutive month with a global temperature above the 20th-century average, according to the National Oceanic and Atmospheric Administration.

Scientists predict changes already underway will warm the planet at least 2 or 3 degrees Centigrade this century, and perhaps double or triple that if humans don't alter the behaviors that contribute to climate change. Current scientific estimates suggest that an increase of 2 degrees Centigrade may be the "tipping point" that triggers irreversible changes (such as methane release from melting permafrost) with unpredictable but severe consequences for the planet and its inhabitants, Dr. Muller said.

Some projected changes already are being seen in the extreme summer heat in western Russia, flooding in Pakistan, intense wildfires in Australia, and drought in regions of the United States and elsewhere. The patterns of resulting changes in joint diseases due to infection from these conditions will vary regionally depending on altitude, latitude, storms, deforestation, desertification, urbanization, land use patterns, energy production, and transportation.

Dr. Muller highlighted changes in several diseases:

► **Lyme disease.** Lyme disease used to be limited to five U.S. geographic regions, but its geographic range has expanded into many areas of Canada as temperatures have become more hospitable to the rodents and deer that act as vectors and reservoirs, spreading into southern and northern Ontario, southern Québec, Manitoba, the Prairie Provinces, the Maritime Provinces, and British Columbia.

► **Carrion's disease.** Children bear the brunt of this reemerging disease that has spread to new areas between the jungle and highlands of Peru and Ecuador. Its symptoms take the form of bone pain, among others. Changes in sea surface temperatures that triggered extreme seasonal rain patterns known as El Niño events in the 1980s and 1990s were associated with a nearly fourfold increase in Carrion's disease in Peru's Ancash region.

SDEF and this news organization are owned by Elsevier. ■