

# Henoch-Schönlein Purpura Is Difficult to Define

BY BARBARA J. RUTLEDGE

Contributing Writer

The diagnosis of Henoch-Schönlein purpura requires a small-vessel biopsy to confirm the presence of IgA, Dr. Thomas G. Cropley said at the 21st World Congress of Dermatology in Buenos Aires.

IgA deposits in vessel walls along with prominent extracutaneous manifestations are the hallmarks of Henoch-Schönlein purpura, a specific type of small-size vessel vasculitis that is the most common vasculitis syndrome in children, often occurring after a respiratory tract infection.

In recent years three different sets of classification criteria have been proposed, the oldest of which does not list IgA deposition among its diagnostic criteria. In 1990, the American College of Rheumatology published its Classification of Henoch-Schönlein purpura (*Arthritis Rheum.* 1990;33:1114-21), which requires four diagnostic criteria:

- ▶ Palpable purpura, defined as raised “palpable” hemorrhagic skin lesions not related to thrombocytopenia;
- ▶ Age less than 20 years at disease onset;
- ▶ Bowel angina, or diffuse abdominal pain, which might include bloody diarrhea;
- ▶ Presence of granulocytes in vessel walls.

“Notice that there is no mention of immunofluorescence or IgA here,” said Dr. Cropley. The ACR definition is based only on histopathology and clinical symptoms. Dermatologists were not involved in developing the classification system, which has since been criticized for the “rather obvious lack of dermatological insight,” said Dr. Cropley, professor of medicine in the division of dermatology at the University of Massachusetts, Worcester.

A group of rheumatologists, nephrologists, and pulmonologists convened in Chapel Hill, N.C., in 1994 and developed consensus guidelines for the diagnosis of various forms of vasculitis, including Henoch-Schönlein purpura (*Arthritis Rheum.* 1994;37:187-92). “The Chapel Hill



Even in the presence of palpable lesions, vessel biopsy is required to diagnose Henoch-Schönlein purpura.

definition of Henoch-Schönlein purpura requires the presence of vasculitis with IgA-dominant immune deposits affecting small vessels, which they defined as capillaries, venules, or arterioles,” said Dr. Cropley. The definition noted the vasculitis typically involves skin, gut, and glomeruli and is associated with arthralgias or arthritis. “IgA is part of the definition, but there are still many other areas of ‘looseness’ in this definition.”

In 2006 the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology Society published Classification Criteria for Henoch-Schönlein purpura (*Ann. Rheum. Dis.* 2006;65:936-41). In their version, palpable purpura is a mandatory criterion and at least one of the following must be present: diffuse abdominal pain; biopsy-proved predominant IgA deposition; acute arthritis in any joint or arthralgia; and renal involvement (hematuria and/or proteinuria).

The epidemiology of Henoch-Schönlein purpura is well described. In the United States, the incidence is about 10 cases per 10,000. The majority of cases (about 75%) begin in childhood, with an equal prevalence in males and

females. The disease is often preceded by a respiratory tract infection, but no typical or unique pathogen has been associated with the disease, said Dr. Cropley. Prevalence is highest in the autumn and winter, when respiratory tract infections are more common.

Adult cases are less likely to be associated with an antecedent infection. The prevalence of adult-onset is higher in men than in women. “There is anecdotal evidence suggesting that there may be an increased association with malignancy in adult cases,” said Dr. Cropley.

Differential diagnosis of Henoch-Schönlein purpura includes other forms of small-size vessel vasculitis causing palpable purpura, such as IgG leukocytoclastic vasculitis, Wegener’s granulomatosis, and microscopic polyangiitis. Other IgA-associated vasculitides should also be considered, including IgA rheumatoid factor-associated small-vessel vasculitis and acute hemorrhagic edema of infancy.

Whether the presence of IgA predicts an increased risk of renal involvement is unknown. An extensive epidemiologic study of Henoch-Schönlein purpura showed renal involvement in one-third of children (*Kidney Int.* 1998;53:1755-9). Significant independent risk factors for chronic renal disease were severe abdominal symptoms, prolonged purpura, and decreased factor XIII activity. The prognostic significance of IgA status was not evaluated, because the study used the 1990 ACR diagnostic criteria.

IgA deposition is a defining criterion of Henoch-Schönlein purpura in the two most recent diagnostic guidelines. Henoch-Schönlein purpura patients may have a poorer renal prognosis than patients with other forms of small-vessel vasculitis. For these reasons, Dr. Cropley recommends a biopsy for immunofluorescence and histopathology, if possible, in patients who appear to have Henoch-Schönlein purpura. Serum IgA levels have been correlated with the risk of IgA nephropathy in adults with Henoch-Schönlein purpura; thus, monitoring serum IgA level over time may help identify patients at risk of chronic renal disease.

Dr. Cropley reported no conflicts of interest. ■

## Methotrexate Therapy May Delay Cataract Surgery in JIA

BY HEIDI SPLETE

Senior Writer

Early initiation of methotrexate can postpone the development of cataracts requiring surgery in juvenile idiopathic arthritis patients who are at high risk due to posterior adhesions at diagnosis with uveitis, said Dr. Karen M. Sijssens.

Cataract surgery in eyes with inflamed uveas is difficult. The presence of posterior adhesions (synechia) at diagnosis and the treatment of uveitis with corticosteroids have been tied to an increased risk of cataracts in children with JIA who develop uveitis.

To evaluate cataract risk factors and determine effective treatments, Dr. Sijssens of the University Medical Center Utrecht (the Netherlands) and colleagues analyzed 53 children diagnosed with JIA before age 16. Fifty-one had JIA-associated uveitis; 2 had antinuclear antibody-positive uveitis (*Am. J. Ophthalmol.* 2007;144:574-9).

Uveitis was the first manifestation of JIA in 12 children, and arthritis was the first manifestation of JIA in 41 children.

Overall, 11 of the 12 children (92%) for whom uveitis was the first presenting symptom of JIA required cataract surgery significantly sooner after diagnosis, versus

the 16 of the 41 children (39%) for whom arthritis was the first sign of JIA (3.5 years vs. 6.6 years).

Posterior synechia were present at uveitis diagnosis in 15 children. Even after controlling for the use of periocular corticosteroids, children with posterior synechia required cataract surgery significantly sooner than the 33 children without adhesions (3.0 years vs. 8.5 years).

But the need for cataract surgery was significantly delayed in the 17 children treated with methotrexate during the first year after uveitis diagnosis, versus the 25 children not treated with methotrexate (7.0 years vs. 3.5 years). The presence of adhesions was approximately the same in both the methotrexate-treated and untreated children.

The delayed development of cataracts requiring surgery in the methotrexate-treated children may be due to better inflammation control, the researchers noted. “Another explanation may be that treatment with methotrexate diminishes the need for treatment with topical or systemic corticosteroids,” they wrote.

Study limitations include its small size and the fact that no patients were studied who had methotrexate and uveitis as the first JIA symptom, the authors noted. ■

## Brain Atrophy in Pediatric SLE May Improve in Remission

BY JEFF EVANS

Senior Writer

BARCELONA — Atrophic brain changes in patients with juvenile systemic lupus erythematosus may improve upon remission and reduction in corticosteroid dose, contrary to what has been seen in magnetic resonance imaging studies of adult patients with the disease.

Using MRI, Dr. Simone Appenzeller and colleagues prospectively compared the voxel-based morphometry of white and gray matter in 10 juvenile SLE patients (mean age 13 years), and 10 healthy age- and sex-matched controls.

SLE duration was 14 months. Patients had active CNS manifestations (primary to SLE) at enrollment. The investigators excluded six patients who were unable to undergo MRI due to a phobia or conditions that could influence cerebral atrophy, Dr. Appenzeller said at the annual European Congress of Rheumatology.

At entry, the juvenile SLE patients had significantly less deep white matter volume in the anterior region of the corpus callosum and significantly less gray matter volume in the hippocampus and amygdala than controls. The decrease in volume of white and gray matter was independently

associated with score on the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology damage index and with disease duration. Total corticosteroid dose was only tied to gray matter atrophy.

After at least 1 year of follow-up, repeat MRI in the SLE patients showed significant increases in white and gray matter.

These improvements could have been due to normal brain growth or a decrease in disease activity and corticosteroid dose. But Dr. Appenzeller said these changes suggest atrophy reduction because the degree of atrophy seen in patients correlated significantly with disease severity at study entry, independent of age. Dr. Appenzeller conducted the study at the State University of Campinas (Brazil), but is now at McGill University, Montreal.

“This finding indicates that children may respond differently to cerebral insults than adults and may even recover from severe involvement,” she concluded.

In a previous study of adult SLE patients, Dr. Appenzeller found significantly reduced gray and white matter volumes on MRI, vs. healthy age- and sex-matched controls; the atrophy continued to progress over 1.5 years of follow-up (*Neuroimage* 2007;34:694-701). ■