Tried and True DMARD Averts Lupus Nephritis

BY BETSY BATES

SAN FRANCISCO — The erstwhile antimalarial drug hydroxychloroquine is gaining new respect, as study results point to its ability to prevent long-term lupus-induced renal damage in patients living longer lives.

The multicenter, multiethnic cohort included 582 patients with systemic lupus erythematatosus (SLE) who were followed for a mean of 5.5 years, according to data presented during the annual meeting of the American College of Rheumatology.

Use of hydroxychloroquine by lupus patients reduced their risk for early renal damage by about 70%.

DR. ALARCÓN

Treatment with hydroxychloroquine, long used as a disease-modifying antirheumatic drug (DMARD), was far less common among the 73 patients who had developed new-onset renal damage (defined as glomerular filtration rate of less than 50%, 24-hour protein of at least 3.5 g, and end-stage renal disease) than among those who did not, reported Dr. Graciela S. Alarcón of the University of Alabama at Birmingham.

Because hydroxychloroquine is often prescribed only to patients with mild, early-stage disease, statistical modeling was used to ensure that demographic and disease severity differences were accounted for between the two patient groups, she explained.

"After making adjustment for all of the [potentially confounding] variables, the protection is on the order of 70%," said Dr. Alarcón.

"Our data strongly suggest that if renal damage is to be prevented, hydroxychloroquine should be prescribed to all lupus patients early in the course of the disease," concluded the report from Dr. Alarcón and associates at the University of Puerto Rico, San Juan, and the University of Texas, Houston.

Hydroxychloroquine, marketed as Plaquenil, has long been known as a relatively safe, inexpensive, disease-modifying drug for rheumatic diseases, having originally proven its muster against malaria during World War II.

In recent years, however, it has taken a back seat to more powerful disease-modifying medications, especially methotrexate and the biologics.

In treatment algorithms, hydroxychloroquine hovers in the "mild disease" column, generally used only for early-stage patients with nonerosive RA.

Over half of lupus patients develop renal involvement, with 10%-30% eventually experiencing renal damage and, often, end-stage renal disease, she said.

A safe, inexpensive drug that could prevent a "very serious complication" in a substantial majority of patients would represent a highly significant improvement in their long-term care, she said.

Dr. Alarcón reported no financial conflicts of interest. ■

Vitamin D Deficiency Seen in 28% With Systemic Sclerosis

BY SHERRY BOSCHERT

SAN FRANCISCO — A study of 156 patients with systemic sclerosis in two European cities found that vitamin D deficiency was present in 28% of them.

Deficient levels of serum 25-hydroxyvitamin D (25[OH]D)—less than 10 ng/mL—were seen in 29 (32%) of 90 patients in Paris and 15 (23%) of 66 in Cagliari in southern Italy, Dr. Alessandra Vacca and her associates reported in a poster presentation at the annual meeting of the American College of Rheumatology.

In addition, 84% of all patients had insufficient vitamin D levels (less than 30 ng/mL), a result seen in 75 (82%) of the Parisians and 57 (86%) of the Italians.

The mean vitamin D value in the two cohorts was 19 ng/mL, said Dr. Vacca of the University of Cagliari.

The rates of vitamin D deficiency did not differ significantly between cities and so were independent of the different UV radiation levels in the northern and southern cities. Rates of vitamin D deficiency also were independent of usual levels of vitamin D supplementation (800 IU/day), which were taken by 30% of Parisian patients and 45% of Italian patients.

Because conventional doses of vitamin D supplementation did not prevent vitamin D deficiency, higher dose supplementation may be needed in patients with systemic sclerosis, especially those with inflammatory activity, she said.

Low vitamin D levels were associated with pulmonary fibrosis ($P = .04$), systolic pulmonary arterial hypertension ($P = .004$), and inflammatory activity indicated by acute phase reactants—erythrocyte sedimentation rate ($P = .004$) and C-reactive protein values ($P = .01$).

There was a significant negative correlation between low vitamin D levels and European disease activity scores ($P = -0.04$). A mild negative association was seen between vitamin D deficiency and anticentromere antibodies.

Low vitamin D levels may be linked to multiple risk factors, Dr. Vacca suggested, including scarce sun exposure due to disability; insufficient intake and malabsorption of vitamin D due to gastroenteric disease involvement; or use of drugs that can alter metabolism of vitamin D, such as steroids.

There was no association between vitamin D deficiency and other markers of impaired malabsorption such as hemoglobin, ferritin, or albuminemia among other.

No associations were found between vitamin D deficiency and acro-osteolysis, calcinosis, or Medsger's disease severity score.

The patients had a mean age of 57 years, and 97% were female.

Vitamin D, which is a steroid hormone, is essential for bone and mineral homeostasis, and is widely thought to play a role in muscles, vasculature, reproduction, cellular growth and differentiation, malignancy, and the immune system.

The investigators reported no conflicts of interest related to this study. ■

Beyond Vasculitis: Behçet's May Cause Aphthous Ulcers

BY NANCY WALSH

LAKE BUENA VISTA, FLA. — The diagnosis of Behçet's disease must be considered in any patient with recurrent oral and vulvar aphthous ulcers, even if the deep, full-thickness ulcers in the mouth and vulva develop at different times.

Behçet's disease is a chronic inflammatory vasculitis most commonly seen along the ancient silk route from Japan and across Korea, Turkey, and Greece, according to Dr. Andrew T. Goldstein. In the West, it occurs most often among young women of Asian or Mediterranean descent.

"This is a bad vasculitis, with complications including dissection of the aorta, blindness, and stroke," he said.

Aside from the aphthous ulcers, patients with Behçet's disease may have acnelike skin lesions or erythema nodosum as well as ocular, central nervous system, and bowel involvement. The ocular manifestations can be varied and severe, and include iritis, uveitis, and retinal vasculitis. Behçet's disease also can be associated with arthritis and meningitis, and any evidence of this disorder should prompt consultations with ophthalmologists, rheumatologists, and gastroenterologists as symptoms dictate.

"One of the easiest ways of diagnosing Behçet's is the pathergy test," said Dr. Goldstein, who practices in Washington.

The pathergy test, in which a 5- to 7-gauge needle is inserted into the forearm, has a very high predictive value, although its negative predictive value is lower. If induration develops 24-48 hours later at the site of needle insertion, the test is positive, he said at the annual meeting of the International Pelvic Pain Society.

Although a positive pathergy test is helpful in the diagnosis of Behçet's disease, only a minority of Behçet's patients demonstrate the pathergy phenomenon, according to the Vasculitis Foundation. Patients from the Mediterranean region are more likely to show a positive response, with only 50% of patients in Middle Eastern countries and Japan showing the reaction. A positive reaction is even less common in the United States, and other conditions can occasionally mimic the results (www.vasculitisfoundation.org/pathergytest).

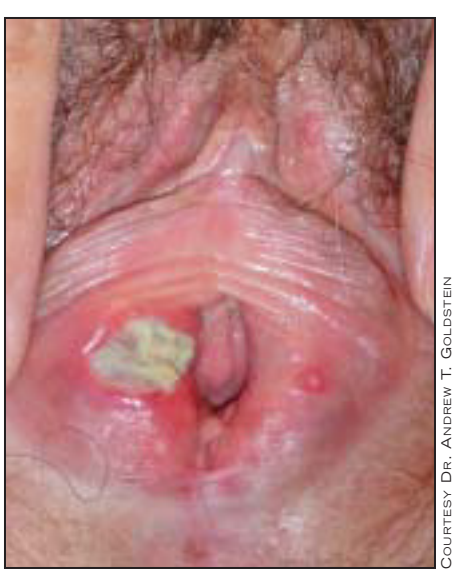
Treatments that have been tried for Behçet's disease include conventional immunosuppressives such as azathioprine and corticosteroids; and anti–tumor necrosis factor therapy, particularly with infliximab, according to Dr. Goldstein, who also practices at George Washington University Hospital, Washington.

A recent international expert panel suggested that anti-TNF therapy might be suitable for patients with severe, organ-threatening disease—patients with two or more relapses of posterior uveitis per year—low visual acuity resulting from chronic cystoid macular edema, or active central nervous system disease (Rheumatology 2007;46:736-41).

Aphthous ulcers not caused by Behçet's disease occasionally can be associated with Epstein-Barr virus or cytomegalovirus, but most commonly they are a manifestation of stress.

"These can be seen in adolescents who are sexually naive and are accused of having herpes and are repeatedly tested and cultured," Dr. Goldstein said.

Treatment for these ulcers involves managing pain with lidocaine and systemic pain medications, intralesional triamcinolone, and amoxicillin-clavulanate and fluconazole for superinfection. ■



COURTESY DR. ANDREW T. GOLDSTEIN

Pain due to vulvar lesions in Behçet's disease may respond to lidocaine.