

# Ten-Year Survival Poor in Antisynthetase Syndrome

BY NANCY WALSH  
New York Bureau

BARCELONA — A review of 30 patients with antisynthetase syndrome found that only half survived 10 years after diagnosis, Dr. Oyvind Palm reported at the annual European Congress of Rheumatology.

This idiopathic inflammatory myopathy is characterized by antibodies directed against tRNA synthetase. The most common is anti-Jo-1, in 80% of cases. Anti-SSA, anti-PL-7, and anti-PL-12 are also sometimes found.

Clinical manifestations include interstitial lung disease (which can be severe), arthritis, Raynaud's phenomenon, and the hyperkeratotic rash known as mechanic's hands, according to Dr. Palm of the department of rheumatology, Rikshospitalet-Radiumhospitalet Medical Center, Oslo.

With the aim of characterizing the disease's clinical and serologic features, researchers reviewed all hospital records of patients diagnosed with an inflammatory myopathy and analyzed the charts of those who had antisynthetase antibodies and pulmonary disease.

The mean age of these 30 patients was 45.5 years. In one-third disease onset was before age 40. Two-thirds

were women. Most patients had histologic evidence of inflammatory myopathy and elevated serum creatine kinase, but only four had elevations of creatine kinase exceeding 3,000 IU/mL. Muscular manifestations rarely caused significant disability and were present at the onset of disease in only six cases.

Anti-Jo-1 antibodies were detected in 90%. Anti-SSA autoantibodies, commonly found in patients with Sjögren's syndrome, were detected in 50% but rarely were tied to dry eyes and mouth, Dr. Palm wrote in a poster.

Pulmonary involvement was classified as follows:

▶ Type I (acute): Found in 24%; rapid onset of dyspnea or cough with development of hypoxemia within 1 month after the onset of disease.

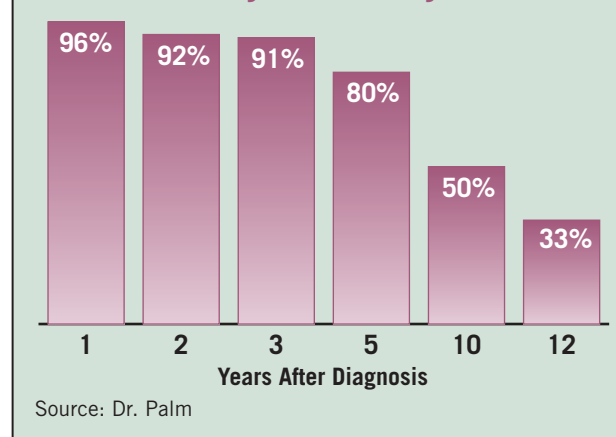
▶ Type II (subacute): Found in 64%; gradual onset of pulmonary symptoms.

▶ Type III (asymptomatic): Found in 12%; coincidentally detected pulmonary abnormalities on x-ray or CT scan with subsequent developing pulmonary symptoms.

Honeycombing with end-stage pulmonary disease was found in 30.4%.

All but one patient had received immunosuppressive drugs including corticosteroids, cyclophosphamide, and

## Survival Rates for 30 Patients With Antisynthetase Syndrome



rituximab. Four patients died. Two had type I pulmonary involvement. "While approximately 90% survive the first 3 years of disease, thereafter the mortality increases sharply, and new treatment strategies are clearly warranted," according to Dr. Palm.

## Baseline Antibodies May Help Predict Response to Rituximab in Lupus

BY NANCY WALSH  
New York Bureau

BARCELONA — B-cell depletion with rituximab showed substantial clinical benefits in a small series of patients with active, refractory lupus, according to Dr. David A. Isenberg, professor of rheumatology, University College London.

Approximately one-third of a series of 45 patients who have undergone treatment with rituximab have remained well without needing further immunosuppressive therapy for a mean of 3 years, Dr. Isenberg reported at the annual European Congress of Rheumatology.

The regimen being used in the Bloomsbury Rheumatology Unit, University College London, involves two rituximab infusions of 500 mg, 2 weeks apart, usually in combination with cyclophosphamide and corticosteroids. Follow-up data are available for 35 patients, all of whom have failed lengthy courses of immunosuppression with cyclophosphamide, mycophenolate mofetil, azathioprine, and corticosteroids.

A total of 14 patients remained well after a single course of rituximab treatment, whereas 12 flared between 6 and 12 months after B-cell depletion, 5 flared earlier than 6 months after depletion, and 4 flared later than 12 months.

The mean time to flare was 10 months after B-cell depletion. The mean duration of depletion was 4 months. Two patients remain depleted, one for 73 months. One patient's B cells did not deplete at all, said Dr. Isenberg.

On the scoring system of the British Isles Lupus Assessment Group (BILAG), mean global scores fell from 13 to 5 at 6 months, representing "substantial benefits" in these patients, he said.

"While not all of the new biologic therapies are active against the whole panoply of lupus systems, it appeared that B-cell depletion was useful for just about every type of lupus feature—skin, renal, musculoskeletal, vascular," he said.

Serologic effects also were pronounced, with anti-double-stranded (ds) DNA antibodies being significantly reduced after 6 months, from me-

dian titers of 203 to 74 IU/mL. Analysis of 12 patients for whom 1 year of follow-up data are available suggested the baseline antibody profile might predict which patients will respond to B-cell depletion.

Patients whose anti-dsDNA antibodies were accompanied by extractable antibodies to DNA (anti-ENA) were more likely to flare at any time after depletion, with an odds ratio of 6.

Also striking was that patients with anti-Sm or anti-La antibodies were more likely to flare, with odds ratios of 9 and 10, respectively. Anti-Sm antibodies vary with ethnicity; they are present in about 10% of Caucasians and 30% of blacks.

A low serum C3 complement level also was associated with a shorter time to flare, with a median time to flare of 12 months in those with low baseline levels. In contrast, the median time to flare among patients with normal C3 levels has not yet been reached.

Thus far, retreatment seems as effective as initial treatment. Among patients who flared, 14 were retreated, 10 for two cycles and 4 for three cycles. "Experience with rheumatoid arthritis suggests that B-cell depletion is safe for three cycles, but after the fourth infusion you do begin to see falls in total immunoglobulin levels," he said.

Treatment was well-tolerated by most. Serious adverse events included one case of pneumococcal sepsis, one severe serum sickness-like reaction, and one case of seizures related to hyponatremia, probably tied to cyclophosphamide, Dr. Isenberg said. In addition, one patient developed fatal pancarditis related to active lupus after B-cell repopulation.

"We regard the safety profile as reasonable, given the fact that these are very active patients, often who have had years of very aggressive immunosuppression," he said. "We found that most patients flare from 6 to 12 months after depletion if they are going to flare, and that baseline autoantibody profiles may be useful in predicting which patients may respond to this treatment."

Dr. Isenberg disclosed no conflicts of interest in this study.

## Coronary Flow May Predict Early Heart Disease in SLE

BY KATE JOHNSON  
Montreal Bureau

New evidence suggests premenopausal women with systemic lupus erythematosus also have impaired coronary microvascular function, supporting "the notion that many of these young patients have subclinical coronary artery disease," wrote Dr. Kumiko Hirata from Columbia University, New York, and colleagues.

"Systemic lupus erythematosus (SLE) patients have a significantly increased risk of coronary heart disease that is not fully explained by the classic risk factors," the study's investigators wrote.

"Measurements of coronary vasomotor function may therefore provide more relevant information with which to predict and assess potential cardiovascular damage related to limited vascular responsiveness," they added.

Because invasive measurements of coronary flow are hard to justify in young patients, the investigators used noninvasive transthoracic Doppler echocardiography (TTDE) to estimate coronary flow velocity reserve (CFVR).

The study looked at 38 premenopausal women, (27 Chinese, 11 American Hispanic) 19 of whom had SLE, and 19 controls. All were assessed following an overnight fast.

In order to avoid confounders that might influence endothelial function, exclusion criteria included a history of smoking, diabetes mellitus, hypercholesterolemia, and cardiovascular disease (Arthritis Rheum. 2007;56:1904-9).

Using TTDE, the investigators recorded the left anterior descending coronary artery flow under both basal and hyperemic conditions in all 38 study participants.

The researchers measured serum levels of lipids, high-sensitivity C-reactive protein (hsCRP), and serum anticardiolipin antibodies, and assessed disease activity with the SLE Disease Activity Index (SLEDAI).

The CFVR in SLE patients was found to be significantly lower than that of controls, after adjustment for body mass index and serum triglyceride levels (the latter being nonsignificantly higher in SLE patients, compared with the control group), reported the authors.

"The CFVR was not significantly correlated with the SLEDAI score, disease duration, level of anticardiolipin antibody, hsCRP, total cholesterol, LDL cholesterol, triglycerides, or HDL cholesterol, ethnicity, or type of immunosuppressive drug used," they added.

Moreover, the significance of a blunted CFVR in SLE "may reflect functional alterations in the endothelium, vascular smooth muscle cells, or both." They added that because the TTDE measurement of CFVR is relatively new, further study is needed.

"Altered microvascular function may provide a study model of factors that contribute to coronary artery disease in SLE. It may help us to define the interplay between autoimmunity and atherogenesis and help us to better understand the pathophysiologic process of atherogenesis in general," the researchers concluded.