Registry: Catastrophic Syndrome Picture Emerges

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ABANO TERME, ITALY — Much has been learned about triggering factors and the range of clinical manifestations in catastrophic antiphospholipid syndrome to describe a constellation of events including multiple organ failure, thrombotic microangiopathy, and tissue necrosis, but the pathogenesis is unclear and mortality remains in excess of 50%, said Dr. Ronald A. Asherson.

The condition, also known eponymously as Asherson's syndrome, is a rapidly progressive variant of the classic antiphospholipid syndrome, differing from the classic syndrome in exhibiting predominantly small-vessel involvement and occlusions of unusual organs such as the bowel, reproductive organs, and adrenals. A catastrophic antiphospholipid syndrome (CAPS) registry established by the European Forum on Antiphospholipid Antibodies now includes nearly 300 cases, said Dr. Asherson, who coined the term CAPS 14 years ago.

The condition is a rapidly progressive variant exhibiting predominantly small-vessel involvement and occlusions of unusual organs, like the bowel.

In a congress on skin, rheumatism, and autoimmunity, Dr. Asherson recalled the first patient in whom the syndrome was identified. "We had a patient who had disseminated intravascular coagulation, antiphospholipid antibodies, and who developed ischemic necrosis of the extremities following the ingestion of two tablets of hydrochlorothiazide," he said. "This is a sulfa-containing drug, and we now know that sulfa drugs are dangerous for patients with lupus and the antiphospholipid syndrome," he said.

Analysis of the patients enrolled in the registry has shown that in 60% of cases a trigger such as this can be identified. The most common is infection, which was reported in 22% of patients and included viral infections, leg ulcers, upper respiratory tract illnesses, and urinary tract infections. There also have been cases associated with typhoid fever, dengue, and malaria, he said.

It also has been reported that three patients developed CAPS following immunizations for yellow fever, Japanese B encephalomyelitis, and influenza, implicating peptides in vaccines as triggers.

Trauma associated with surgery is another common trigger, and was reported in 14% of patients in the registry. This can range from major abdominal surgery to something as minor as a needlestick or biopsy, said Dr. Asherson of the rheumatic disease unit, University of Cape Town, and the Rosebank Clinic, both in Johannesburg, South Africa.

The mechanism by which trauma might initiate CAPS remains uncertain, but may involve cytokine production affecting endothelial cell function and the upregulation of procoagulant molecules (Immunobiology 2005;210:727-33). Complement activation also is thought to contribute to the development of tissue injury in CAPS (Clin. Exp. Rheumatol. 2006; 24:S46-51).

Among patients in the registry, 84.5% have a past history of antiphospholipid syndrome, either primary or secondary to lupus or another connective tissue disease. All have been found to be positive for antiphospholipid antibodies, and 82% are positive for IgG anticardiolipin antibodies.

Clinical manifestations of CAPS among patients in the registry vary widely. Renal involvement has been seen in 73% of patients, pulmonary involvement has been observed in 68%, cerebral involvement in 63%, and cutaneous involvement in 58%. The pulmonary manifestations are both thrombotic and nonthrombotic and can include the adult respiratory distress syndrome and pulmonary hemorrhage.

Among patients who died and for whom necropsy findings are available, the major causes of death were cerebral, cardiac events, and infections. Microthromboses were present in 84.5%, Dr. Asherson said.

The registry is based at the systemic autoimmune diseases unit of the Hospital Clinic in Barcelona and is available at www.med.ub.es/MIMMUN/FORUM/CAPS.HTM. ■