Primary biliary cirrhosis (PBC) is a hepatic disease with a probable autoimmune pathogenesis, which involves intrahepatic bile ductules. It is frequently associated with other diseases such as Sjögren’s syndrome, rheumatoid arthritis, and scleroderma, with symptoms that usually occur before the clinical and/or laboratory onset of PBC. Association of vasculitis and PBC has seldom been reported. We describe a woman with microscopic polyangiitis, with kidney and lung involvement, with biopsy proven PBC.

CASE REPORT

In 1998 a 54-year-old Caucasian woman with chronic polyarthritis and ischemic necrosis of a toe was admitted to our Rheumatology Unit. She did not smoke cigarettes and was not addicted to alcohol.

Past medical history revealed cholecystitis with gallstones and a transient episode of shortness of breath (negative allergy tests, normal immunoglobulin E, normal eosinophil count, and normal cardiac functions). In 1996, she developed an asymmetric polyarthritis, with pain, swelling, and impaired function of the lower limb joints. The erythrocyte sedimentation rate (ESR) was 58 mm/h, C-reactive protein (CRP) was within normal limits. Polyclonal hypergammaglobulinemia (29%, normal 12–20%) and raised gammaglutamyltransferase (γGT: 76, normal 8–35) were also present. However, the polyarthritis failed to respond to intramuscular methotrexate (10 mg/week) and treatment with nonsteroidal antiinflammatory drugs (NSAID) was unsuccessful. In 1997 she developed an asymmetric polyarthritis followed by pulmonary and renal involvement and signs of liver disorder. Detection of pANCA and antimitochondrial antibodies with results of renal and liver biopsies allowed a diagnosis of microscopic polyangiitis and PBC. To our knowledge, this is the first report of an association between the 2 diseases. (J Rheumatol 2003;30:2710–2)

DISCUSSION

In the last few years, microscopic polyangiitis has been recognized as a distinct clinical entity. Its features,
described by Guillevin, et al in 1999 in a large study of 85 patients, include several clinical and laboratory manifestations such as necrotizing glomerulonephritis, livedo, mononeuritis multiplex, digital ischemia, arthralgias/arthritis, and lung involvement (alveolar hemorrhage, pneumonitis, pleuritis, and dyspnea). Gastrointestinal tract involvement includes bowel angina and melena due to mesenteric vasculitis, but also raised levels of aspartate aminotransferase and/or alanine aminotransferase. p-ANCA are frequently but not inevitably positive.

PBC has been recognized since the 19th century; the discovery of AMA allowed an early diagnosis, even prior to clinical liver involvement. In the natural history of the disease, AMA occur first, then later colestasis indices become positive, and finally, clinical manifestations (pruritus, xanthelasmas, etc.) become evident. p-ANCA are present in 25–30% of patients and their pathogenic role is still debated. PBC has been rarely reported in association with systemic vasculitis, including Churg-Strauss vasculitis, Wegener’s granulomatis, giant cell arthritis, and Goodpasture’s syndrome, but this is the first reported case of association between PBC and microscopic polyangiitis.

This case shows how rheumatic diseases can present as syndromes. Specifically in this case chronic polyarthritis evolved within a few years into systemic vasculitis and finally into microscopic polyangiitis associated with PBC. An association between PBC and vasculitis has been rarely described and at present there is no clear explanation for the simultaneous occurrence of the 2 conditions. Regarding Sjögren’s syndrome, the pathogenic link may be the presence of shared antigens, expressed on the membrane of both biliary epithelial cells and salivary ductal epithelial cells, which may induce autoimmune cross-reactivity. E2 antigen, the 74 kDa E2 component of pyruvate dehydrogenase complex, is thought to be the target of AMA, and 66% of patients with PBC express E2 on both salivary and biliary epithelial cells. They also have increased serum levels of soluble intercellular adhesion molecule-1 (sICAM-1), which have also been found in patients with nonspecific hepatitis such as alcoholic liver disease. The findings of increased serum levels of sICAM-1 and over-expression of ICAM-1 on endothelial cells in vasculitis suggest that this molecule may represent a possible pathogenic link for the association of PBC with vasculitis. Further studies will be necessary to clarify the mechanisms underlying the association of PBC with other autoimmune diseases.

REFERENCES
6. Conn DL, Dickson ER, Carpenter HA. The association of


