Inflammatory Arthritis in a Patient with Primary Biliary Cirrhosis: B Cell Mediated Synovitis

To the Editor:

Primary biliary cirrhosis (PBC) is a chronic cholestatic autoimmune liver disease of unknown etiology, associated with the presence of antimitochondrial antibodies in 95% of patients[1-6]. Prevalence of this condition is estimated at between 20 and 240 cases per million population, the most frequent symptoms being fatigue, jaundice, and pruritis. Arthritis is reported in 4%–42% of patients with PBC in several series[1-3]. Some patients develop a symmetrical erosive small-joint arthritis, often in association with a positive rheumatoid factor (RF), that is indistinguishable from rheumatoid arthritis (RA). There is an increased incidence of RA, Sjögren's syndrome, Raynaud's phenomenon, and hypothyroidism in patients with PBC[7]. Up to 31% of patients, however, develop an asymmetric, nondeforming arthritis that seems unique to PBC[7]. However, there have been reports of PBC patients developing a deforming and/or erosive arthritis[3,4,7].

We describe the case of a 62-year-old woman with known PBC, with antimitochondrial antibodies in the serum and a liver biopsy consistent with the diagnosis of PBC. She presented with a 5-year history of an erosive, destructive arthritis involving both wrists (Figures 1 and 2), in the absence of RF or antibodies to cyclic citrullinated peptides in the serum. She did not respond to sulfasalazine, and methotrexate was not used due to concerns about safety in view of her active liver disease and the lack of evidence of its efficacy in PBC[8]. She did respond to both oral and intraarticular corticosteroids, but her wrist arthritis progressed to the stage where she required a synovectomy and arthroplasty, first on the right and then the left wrist joint. At the time of the second wrist surgery, synovial tissue was processed for immunohistochemical labeling. Cryosections 4 μm thick were prepared on APTS (Sigma, St. Louis, MO, USA) treated glass slides and fixed in ice-cold acetone for 4 minutes. Sections were brought to room temperature, washed in phosphate buffered saline (PBS), and underwent immunohistochemical labeling for a range of cell-surface markers [anti-CD68 (EBM11; Dako Australia, Botany Bay, New South Wales, Australia) to detect macrophages, Mab 67 (Serotec, Kidlington, Oxford, UK), which recognizes CD55, to detect fibroblast-like synoviocytes, anti-CD3 (BD Biosciences, San Jose, CA, USA) and anti-CD45Ro to detect T cells and memory T cells, respectively, anti-CD22 (Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands) to detect B cells, anti-CD38 (BD Biosciences) to detect plasma cells]. Cell adhesion molecules [vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1)] and e-selectin and cytokines (interleukin 1ß (IL-1ß), IL-6, and tumor necrosis factor-α (TNF-α) were detected in all tissues using a double-enhancement method as described. To eliminate bias from run-to-run variability, all antibody staining was performed on synovial tissue on the same day. The synovial tissue displayed marked villous hypertrophy, widespread synovial cell hyperplasia, and synoviocyte hypertrophy, although there were areas of relatively normal synovium around the wrist (Figure 3). There was a dense lymphoplasmacytic inflammatory infiltrate, interpreted by the pathologist as being consistent with RA (Figure 3). Immunohistochemical staining, however, showed few macrophages or T cells within the infiltrate, the main inflammatory cells being B cells and plasma cells, a result quite different from that seen in RA (Figure 4). There was little expression of TNF, IL-1, or IL-6 in the synovial tissue (Figure 5).

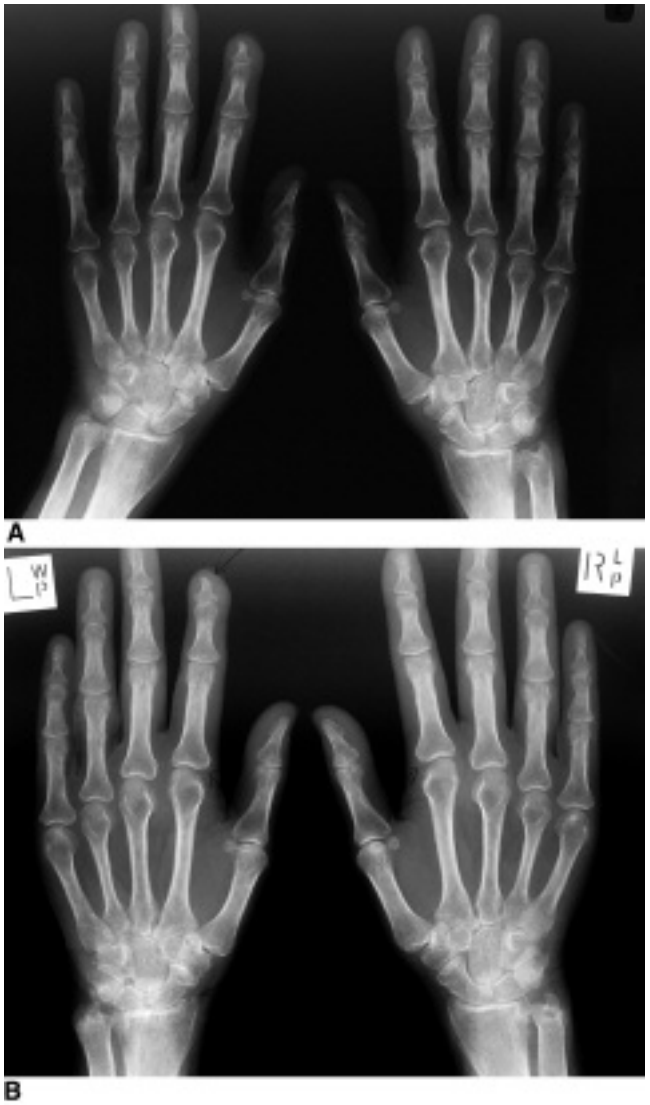

Figure 1. Radiographs of the hands taken in 2002 (A) and 2003 (B), showing progression of left wrist arthritis.

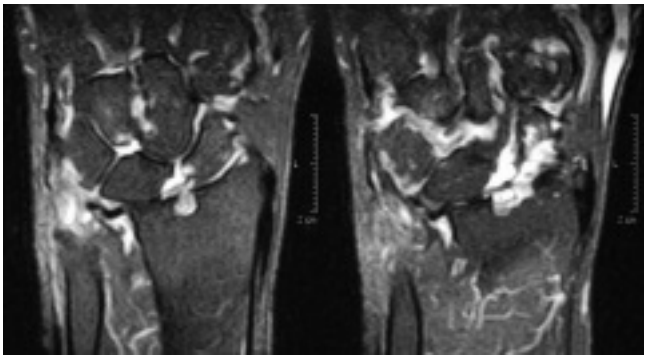

Figure 2. Magnetic resonance imaging scan (with gadolinium) of left wrist.

This patient with PBC had a small-joint erosive arthritis, somewhat distinct from the pattern seen in RA, that was particularly difficult to treat. This is the first time that the synovial tissue pathology in PBC-related arthritis has been reported. Synovial tissue examination demonstrated a somewhat different pathology to that usually seen in RA and suggested a predominant B cell and plasma cell infiltrate. This suggests that it would be logical to treat such patients with anti-B cell therapies, and a trial of rituximab treatment in such patients would be worthy of consideration.

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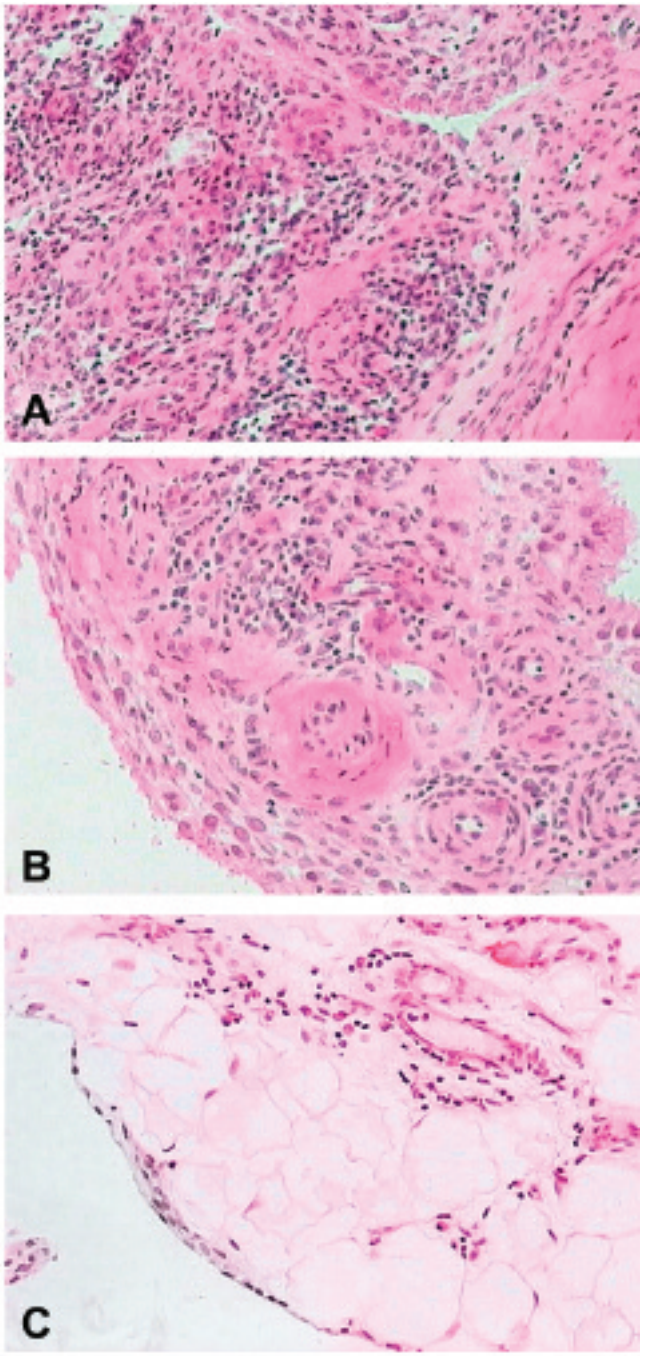

Figure 3. Sections of synovial tissue: (A) midcarpal joint, (B) radiocarpal joint, (C) extensor compartment (H&E stain; original magnification ×200).

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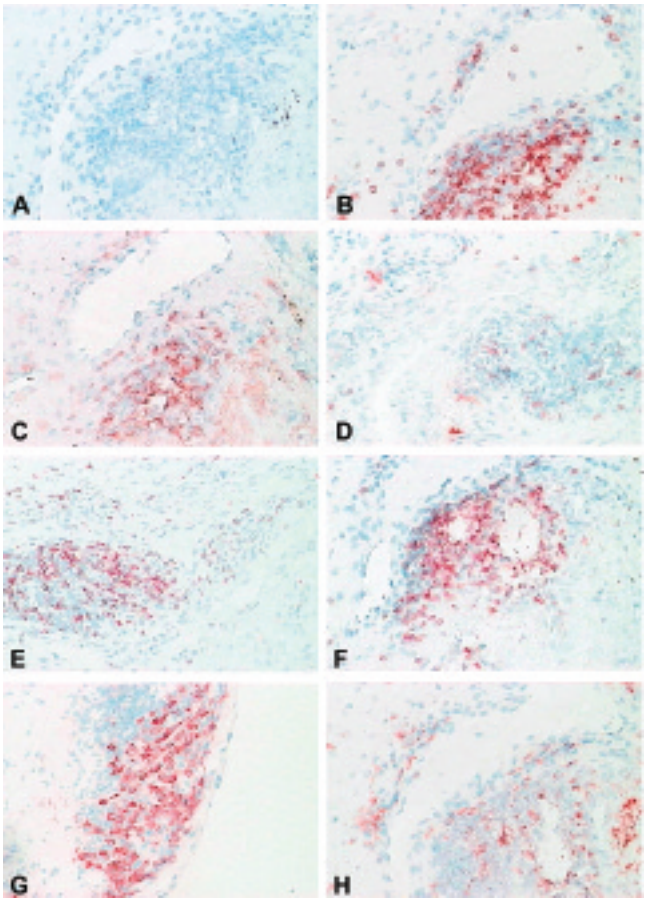

Figure 4. Immunohistochemical labeling of synovial tissue using AEC (red) as chromogen. (A) negative control, (B) CD3, (C) CD4, (D) CD8, (E) CD45Ro, (F) CD22, (G) CD38, (H) CD68 (original magnification ×200).

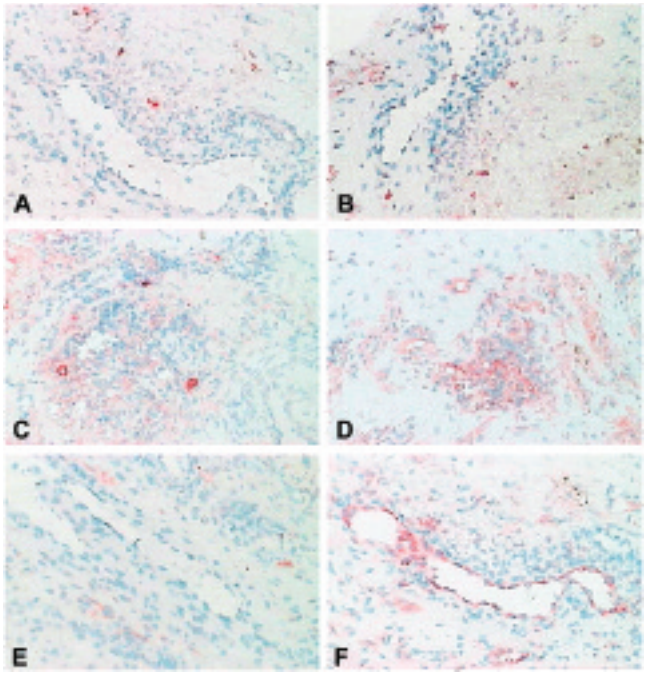

Figure 5. Immunohistochemical labeling of synovial tissue using AEC (red) as chromogen. (A) TNF-α, (B) IL-1ß, (C) IL-6, (D) ICAM-1, (E) VCAM-1, (F) E selectin (original magnification ×200).

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