Lymphoma of the Hands in a Patient With Rheumatoid Arthritis: Case Report

Max J. Gordon, BA, Bruce A. Peterson, MD, Keith M. Skubitz, MD

The correlation of rheumatoid arthritis and lymphoma—and more generally, autoimmune disease and malignancy—has long been observed. Here, we present the case of a woman with rheumatoid arthritis who developed lymphoma limited to her hands. *(J Hand Surg Am. 2014; 39(4):728–731. Copyright © 2014 by the American Society for Surgery of the Hand. All rights reserved.)*

Key words Lymphoma, rheumatoid arthritis.

Rheumatoid arthritis (RA) is a common autoimmune disease causing a systemic inflammatory disorder characterized by chronic inflammation of the synovial lining, which leads to bone and cartilage destruction and ultimately joint deformity. The systemic nature of RA can result in multiple, extra-articular manifestations include immune-mediated anemia, neuropathy, vasculitis, renal and pulmonary disease, and subcutaneous nodules, among others. The pathophysiology of RA is not well understood,[1] but a depletion of B-lymphocytes can result in a dramatic improvement of the disease. In addition to the major disability that occurs from joint inflammation and destruction, patients with RA have an increased risk of non-Hodgkin lymphomas (NHL), which account for about 4% of all new cancer cases in the United States.[2–4] There are many different types of NHL, but the great majority are B-cell malignancies, and their pathogenesis is complex. In the setting of rheumatologic disease, tumorigenesis seems to be triggered by B-cell antigenic stimulation and chronic inflammation, which is further aided by immune dysfunction.[3,5] We present a case of a woman with RA who developed diffuse large B-cell lymphoma in both hands.

From the Department of Medicine, Division of Hematology, Oncology, and Transplant, University of Minnesota Medical School, Minneapolis, MN.

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Corresponding author: Keith M. Skubitz, MD, Department of Medicine, University of Minnesota Medical School, Office Mayo Mail Code 286, 420 Delaware Street SE, Minneapolis, MN 55455; e-mail: skubi001@umn.edu.

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CASE REPORT

A 77-year-old woman with a 20-year history of seropositive RA involving both hands presented to her primary care provider because of an enlarging mass in the left hand. She had been receiving twice-weekly methotrexate for RA for several years. There was no history of trauma, and there were no constitutional symptoms of fever, night sweats, or weight loss. Energy and appetite were normal. She had quit smoking 20 years before and had diabetes with mild neuropathy.

At a visit 4 months later, her examination was notable for an increase in size of the mass, surrounding ecchymosis, and a 2-cm ulceration on the first web of the left hand. The mass extended to the wrist flexion crease and both dorsally and volarly. No lymphadenopathy was present. X-rays showed soft tissue swelling in the thenar regions bilaterally and in the dorsum of the left hand and a diffuse permeative process involving the second left metacarpal (Figs. 1, 2). A magnetic resonance imaging study of the left hand showed a 5.5 × 4.0 × 6.8-cm soft tissue mass in the first web with pathologic fracture of the second metacarpal. A needle biopsy revealed a diffuse large B-cell lymphoma, which was positive for Epstein-Barr virus (EBV)-encoded small RNA (EBER), which indicated that the lymphoma cells were infected by EBV, and for CD20, a marker characteristic of B-cell lymphomas and often a therapeutic target for drugs such as rituximab.

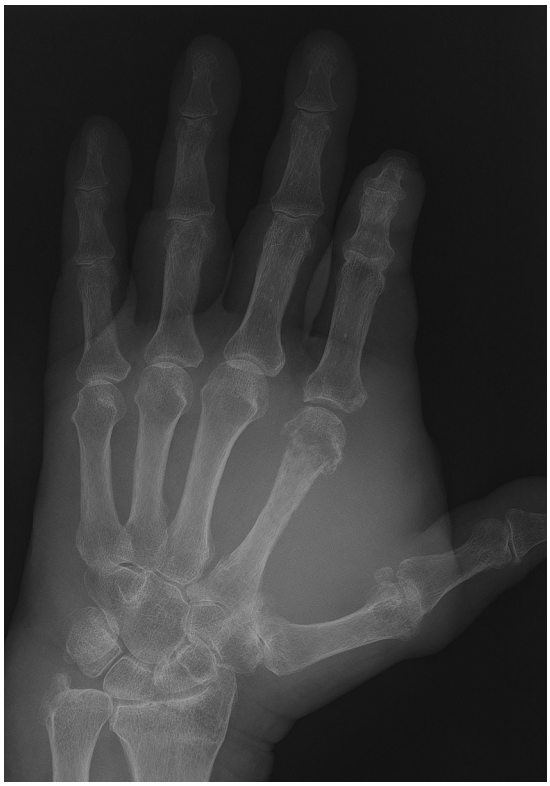

FIGURE 1: Plain radiograph of the left hand showing a soft tissue mass and index metacarpal involvement.

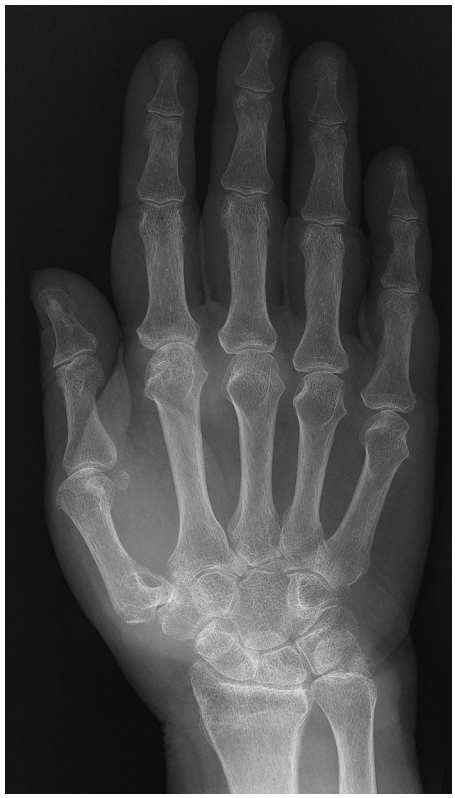

FIGURE 2: Plain radiograph of the right hand showing a soft tissue mass.

Methotrexate was stopped and a positron emission tomography (PET) was obtained (Figs. 3, 4). This showed increased fluorodeoxyglucose uptake associated with the soft tissue mass in the left hand. There was also increased fluorodeoxyglucose uptake associated with a soft tissue mass in the right hand. Standard uptake values for fluorodeoxyglucose were suggestive of malignancy in both hands. The remainder of the examination was normal. A magnetic resonance imaging study of the right hand showed a 5.8 × 3.1 × 2.6-cm enhancing intramuscular mass involving the deep aspect of the thenar eminence. Biopsy showed an EBER-negative diffuse large B-cell lymphoma. Complete staging, including bone marrow biopsies with molecular studies for immunoglobulin gene rearrangement, was negative for lymphoma outside the hands.

The patient was begun on allopurinol and received 3 doses of rituximab, an anti-CD20 monoclonal antibody, followed by standard chemotherapy for diffuse large B-cell lymphoma consisting of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. A follow-up PET scan after 6 cycles of chemotherapy showed no evidence of lymphoma in either hand, but revealed new metabolic activity in the cecum. Plain radiographs were not obtained at the time of follow-up. To complete the lymphoma therapy, she was given external beam radiation, 3,060 cGy to each hand in 17 fractions. An adenocarcinoma of the cecum and ascending colon corresponding to the new abnormality on PET scan was found by colonoscopy. She was treated with hemicolectomy followed by adjuvant chemotherapy for stage IIIB colon cancer.

The patient returned to her baseline hand function before the development of lymphoma. She did not require specific therapy for her hands. Because the RA remained difficult to control, she was restarted on methotrexate 2.5 years after stopping and continues to takes 15 mg weekly. A computed tomography scan of the chest, abdomen, and pelvis at 4.7 years' follow-up was normal, as was the PET scan 1 year after diagnosis. At 5.5 years after the initial treatment, she had no evidence of recurrent lymphoma by physical examination or laboratory studies. She did have persistently active RA involving the hands and knees bilaterally with fluctuating joint swelling, tenderness, and residual weakness. Grip strength was mildly reduced, and there was moderate atrophy of the thenar muscles in the left hand. Functionally, she was able to button shirts.