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Several drugs have been shown to cause necrotizing vasculitis. When occlusion of the digital arteries of the hands occurs, the cause is usually small vessel disease rather than thromboembolic events. We report a patient who developed digital vasculitis after treatment with interferons. We add this form of toxicity to those known to be caused by interferons and emphasize such toxicity may be seen in patients who are receiving long-term interferon therapy. This complication is considered clinically important because long-term interferon therapy is used in the treatment of chronic hepatitis B infection, inflammatory and viral dermatoses, rheumatoid arthritis and with increasing frequency in hematologic malignancies such as CML, myeloma and non-Hodgkin's lymphoma.

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DIGITAL VASCULITIS ASSOCIATED WITH INTERFERON THERAPY

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DIGITAL VASCULITIS ASSOCIATED WITH INTERFERON THERAPY

Several drugs have been shown to cause necrotizing vasculitis [1]. When occlusion of the digital arteries of the hands occurs, the cause is usually small vessel disease rather than thromboembolic events [1,2]. We report a patient who developed digital vasculitis after treatment with interferons. We add this form of toxicity to those known to be caused by interferons and emphasize such toxicity may be seen in patients who are receiving long-term interferon therapy. This complication is considered clinically important because long-term interferon therapy is used in the treatment of chronic hepatitis B infection [3], inflammatory and viral dermatoses [4], rheumatoid arthritis [5], and with increasing frequency in hematologic malignancies such as chronic myelogenous leukemia, myeloma, and non-Hodgkin's lymphoma.

A 42-year-old man was diagnosed with chronic myelogenous leukemia in August 1988. He was a nonsmoker and denied any history of vascular or neurologic disorders. He participated in a Cancer and Leukemia Group B protocol using recombinant α-interferon (Hoffmann-La Roche) and γ-interferon (Genentech). The interferons were alternated weekly, and each was given at a dose of 5×10^6 IU/m^2/d by subcutaneous injection for 7 days.

Interferon-related toxicities were transient and mild and included arthralgia, fever, sweats, and nausea. Fifteen months after beginning interferon therapy, the patient noted paresthesias of the distal fingers bilaterally, more prominent on the right hand. Within 4 weeks, this progressed to numbness in all fingertips. He noted discoloration and diminished temperature of the right index finger that were not precipitated by temperature changes. The patient was taking no other medications. He denied fevers, arthralgias, myalgias, dysphagia, history of frostbite, toxin exposure, or trauma.

Physical examination revealed a cold blue, swollen right index finger with a small necrotic area at the distal tip. The remaining fingers were pale and cool. There was no sclerodactyly. Radial and ulnar pulses and Allen's test were normal bilaterally. There was diminished sensation to pinprick in all fingertips extending to the proximal interphalangeal (PIP) joint in the right index finger. The lower extremities were not involved. Results of the remainder of the physical examination were normal.

The chest radiograph, electrocardiogram, and echocardiogram were normal. A complete blood count showed a leukocyte count of 2.7×10^9/L, hemoglobin level of 11.5 g/dL, and a platelet count of 221×10^9/L. Serum chemistries, prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen, protein C, antithrombin III, protein S, and complement levels were all normal. The sedimentation rate was 26 mm/h. Rheumatoid factor, antinuclear antibody, VDRL, antibody to the two interferons, and hepatitis B serologies were all undetectable. Results of indirect and direct Coombs' tests and blood cultures were negative.

Digital plethysmography showed an absence of waveforms in the right index finger. Arteriography revealed a normal aortic arch and great vessels. Digital subtraction angiography (DSA) of the hands showed that each finger in both hands had at least one digital artery completely occluded (**Figure 1**), and the vascular profile suggested endothelial proliferation. Both digital arteries in the right index finger were occluded. Warfarin therapy was initiated, and the interferons were continued. After 4 weeks the symptoms were unchanged, and a new necrotic lesion developed on the distal aspect of the left second toe. The warfarin and both interferons were discontinued. After 2 weeks, the right index finger remained cool, assumed normal color, and demonstrated healing. The other fingers were warm. The paresthesias, numbness, and sensory loss had resolved. Plethysmography showed partial return of arterial waveforms in the right index finger.

The DSA in our patient showed evidence of a beaded pattern in the digital arteries, consistent with vasculitis [6]. The improvement in his hand

Figure 1. DSA of the right hand. There is occlusion of both arteries in the index finger proximal to the PIP joint. The beaded pattern (**arrow**) observed in the lateral artery of the third finger is suggestive of vasculitis.

after discontinuation of the interferon therapy, including the return of arterial waveforms, is supportive of the fact that vasculitis was induced by one or both of the interferons.

The toxicities seen commonly from interferons include pyrexia, arthralgias, myalgias, and leukopenia. In addition, numbness, paresthesias, and sensory loss have been seen occasionally at high doses of interferon and early in treatment [7]. Sangster *et al* [8] describe a patient who developed digital vasculitis 1 week after initiation of human lymphoblastoid α-interferon therapy at a dose similar to that used in our patient. However, our patient differs from this case in three respects: the vasculitis occurred after 16 months of therapy; our patient received recombinant interferons; and combination interferon therapy was used.

Subacute vasculitis should be considered in the differential diagnosis of patients receiving interferon therapy who present with extremity numbness and paresthesias. As in our patient, these symptoms may be related to vascular injury rather than to a direct interferon effect on peripheral nerves.

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NOTE: The opinions expressed in this article are solely those of the authors and are not necessarily those of any government agency.