MALT Non-Hodgkin's Lymphoma Associated With Hepatitis C Virus Infection Treated by Interferon Alpha

To the Editor: A possible role of hepatitis C virus (HCV) infection in the pathogenesis of non-Hodgkin's lymphoma (NHL) is a recent and exciting subject of debate [1,2]. We wish to add a case of MALT NHL associated with HCV seropositivity treated by interferon (IFN) alpha. Because gastric MALT NHL is known to evolve from antigenic stimulation caused by a microorganism, *Helicobacter pylori,* a pathogenic role for HCV merits discussion in this setting.

A 27-year-old woman consulted us in June 1995 for management of NHL. Her past medical history included a steroid-responsive autoimmune hemolytic anemia discovered in 1992 without evidence of NHL. Since this period she presented with a positive DAT of IgG type. Noticeably, this patient is seropositive for HCV like her grandmother and mother. Her sister, who did not receive maternal milk, is not infected. Only ALAT were slightly increased at 53 iu/l (normal, <33), with an otherwise normal liver biology. PCR for viral RNA was positive in the blood. A liver biopsy performed in March 1993 evidenced criteria of moderate active chronic hepatitis. A low-grade MALT NHL was diagnosed in April 1995 on a biopsy of a mass of the oral cavity. Clinically, this woman exhibited multiple cervical lymphadenopathies with marked time-dependent variations of volume. Unfortunately, investigations were truncated because of the patient's refusal of any invasive procedures including biopsies or endoscopies. Nevertheless, the hemogram and bilirubin, LDH, and CRP, levels were normal. Beta-2-microglobulin was increased at 2.74 μg/l (normal, <2).

HIV serology was negative. Serum protein electrophoreus demonstrated a hypogammaglobulinemia (5.3 g/l). Nasopharynx, orbits, and thorax were normal, but multiple abdominal and pelvic lymphadenopathies were found associated with a splenomegaly using CT scan. IFN alpha (Introna°, Schering-Plough, Levallois-Perret, France) was introduced at 5 million units TIW. This therapy was well-tolerated, and after 3 months of IFN, HCV-RNA PCR became negative. This result is presently confirmed at month 6 of therapy. The abdominal CT scan shows a marked decrease in lymphadenopathies. Nevertheless, cervical adenopathy remained unchanged at clinical examination. The dose of IFN was decreased to 3 million units TIW for a planned duration of 6 additional months.

HCV is now recognized as associated with mixed cryoglobulinemia [3]. Its participation in Waldenström's macroglobulinemia remains hypothetical [4], as in other types of NHL. On the other hand, some viruses, e.g., $HTLV_1$ or EBV, have been implicated in peculiar subtypes of human NHL. HIV-positive patients are well-known high-risk populations for NHL. Furthermore, the antiviral drug zidovudine combined with IFN alpha has shown significant activity in $HTLV_1$ T-NHL [5]. IFN alpha was especially interesting to prescribe in our patient because this molecule represents the main therapy of HCV infection and demonstrates some activity in low-grade NHL. This therapy merits further evaluation in larger clinical studies for patients representing associations in which chemotherapy is not recommended because of liver injury. As described in many papers, NHL are heterogeneous disorders with multifactorial agents. Nevertheless, in gastric MALT NHL, the role of *H. pylori* seems essential. Interestingly, tumoral disappearance has been obtained using antibiotics active against this bacteria. As *H. pylori,* HCV could represent here one of several causative events which enhance lymphoid proliferation. Of course, more extensive biological data should be obtained to confirm this very speculative hypothesis. To our knowledge, this is the first reported case of disseminated MALT NHL associated with HCV infection.

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Halogenoderma of the Forearm Caused by 2-Chlorodeoxyadenosine Treatment

To the Editor: 2-chlorodeoxyadenosine (2-CDA) is a purine analog which is the treatment of choice for hairy-cell leukemia [1]. The most common adverse effects include bone-marrow suppression and fever. There have been no reports of dermatologic toxicity or complications from accidental drug extravasation. Recently, subcutaneous administration of 2-CDA has been described with no adverse dermatologic effects [2]. We report on the development of skin necrosis over the forearm requiring excision and skin grafting in a patient with hairy-cell leukemia who was treated with intravenous infusion of 2-CDA.

R.A., a 41-year-old male, was admitted to our department for treatment with 2-CDA following the diagnosis of hairy-cell leukemia presenting with fatigue, splenomegaly, anemia, and thrombocytopenia. He was treated with 2-CDA, 0.1 mg/kg/day, by continuous intravenous infusion over 7 days. The infusion was administered through peripheral veins, and during the last 3 days of treatment into the left antecubital vein. During the course of treatment the patient developed transient anemia, thrombocytopenia, and fever, and was treated with blood products and antibiotics (amikacin and mezlocilline). One day after completion of treatment, erythema and swelling were noted over the left forearm, in proximity to the site of the last 2-CDA infusion. There was no fever. Presumptive diagnosis of phlebitis was made, and he was treated with cloxacillin. Over the next 3 days there was rapid progression of local swelling, with central skin necrosis. Surgical incision yielded no purulent secretions, and all bacterial cultures were negative. During the next few days there was rapid extension of the necrosis to an area of about 10 cm, requiring excision and skin grafting. Histologic examination of the excised tissue showed pseudoepitheliomatous hyperplasia with inflammatory infiltrate, suggestive of halogenoderma (Fig. 1). The patient made a complete recovery after surgery, and is presently in continued remission from his hairy-cell leukemia.

This is the first report to our knowledge of halogenoderma following the administration of 2-CDA. Halogens, such as iodide, bromide, and fluoride, are known to cause skin damage, both after topical and systemic administration [3]. Numerous reports exist on iododerma following adminis-