

Lichen Planus, Erythema Nodosum, and Erythema Multiforme in a Patient With Chronic Hepatitis C

Donato Calista, MD, Cesena, Italy

Giorgio Landi, MD, Cesena, Italy

After identification of the hepatitis C virus (HCV) in 1989, evidence was established supporting its role in the pathogenesis of a number of cutaneous diseases. This evidence ranges from mere epidemiologic associations, such as lichen planus, to molecular biological investigations that have identified the virus in the pathologic tissues of cutaneous vasculitis, vasculitis with mixed cryoglobulinemia, and porphyria cutanea tarda. We describe a 52-year-old man who was diagnosed with chronic hepatitis C, preceding the appearance of lichen planus, erythema nodosum, and erythema multiforme that coincided with the reactivation of viral replication.

Cutaneous disorders, such as vasculitis and especially mixed cryoglobulin-associated vasculitis, porphyria cutanea tarda, and lichen planus, have been recognized as having a pathogenic correlation with chronic hepatitis C virus (HCV) infection.^{1,2} Anecdotal cases of manifold skin diseases have occasionally been associated with the persistence of HCV infection and the worsening of liver disease.²⁻¹³

Case Report

A 52-year-old man was seen in October 1995 because of the onset of pruritic red-violaceous papules on the volar aspect of his forearms (Figure 1), scalp, axillae, and groin and the appearance of longitudinal striation associated with onychoschizia on the nail plate of his hands (Figure 2). The punch biopsy of a lesion taken from the scalp revealed lichen planus follicularis, so lichen planopilaris was diagnosed. The patient's history was unremarkable until June 1994, when he tested positive for HCV. In December 1995,

the patient experienced weakness and malaise, followed by the onset of 2 distinct dermatoses: bilateral, dermal, painful, tender plaques on both shins and confluent bright red papules on his trunk (Figure 3) and arms. The patient denied any drug use or the onset of infections during the previous 2 months.

Laboratory investigations showed a rise in serum levels of aspartate aminotransferase (AST) (910 U/L) and alanine aminotransferase (ALT) (1130 U/L). Serologic markers for hepatitis B, cytomegalovirus, and Epstein-Barr virus were negative. A qualitative recombinant immunoblot assay on serum showed the presence of HCV messenger RNA. Skin biopsy specimens obtained from the different skin lesions confirmed the clinical diagnosis of erythema nodosum of the legs and erythema multiforme of the trunk (Figure 4).

Treatment with prednisolone, 1 mg/kg, completely cleared both areas of dermatitis in 3 weeks. During the next 3 months, the erythema nodosum relapsed twice, coincidentally with the rise of AST and ALT levels. A liver biopsy showed chronic active hepatitis C without cirrhosis, and therefore, the patient was treated with 6 million units of recombinant interferon alfa-2 every other day for 24 months. The patient's hepatic enzymes normalized, and at a 2-year follow-up examination, he presented with no evidence of cutaneous or hepatic disease.

Comment

Since its discovery in 1989, HCV has become the most frequent etiologic agent of chronic evolutive hepatitis and is an important medical problem because of the high prevalence of HCV in the general population and the high social costs correlated to it.^{1,2} HCV infection is asymptomatic in almost 90% of patients and is usually marked by periodic relapse.¹ In 50% of patients, liver damage can develop into chronic hepatitis in an undetectable manner, and 20% to 50% of cases may evolve into cirrhosis.¹⁻³

Drs. Calista and Landi are from the Department of Dermatology, M. Bufalini Hospital, Cesena, Italy.
Reprints: Donato Calista, MD, Department of Dermatology, M. Bufalini Hospital, Viale Ghirotti 286, 47023 Cesena, Italy (e-mail calista@iol.it).



Figure 1. Pruritic red-violaceous papules on the volar aspect of forearms.



Figure 2. Longitudinal striations and onychoschizia on the nail plate of the hand.



Figure 3. Confluent bright red papules on the back.

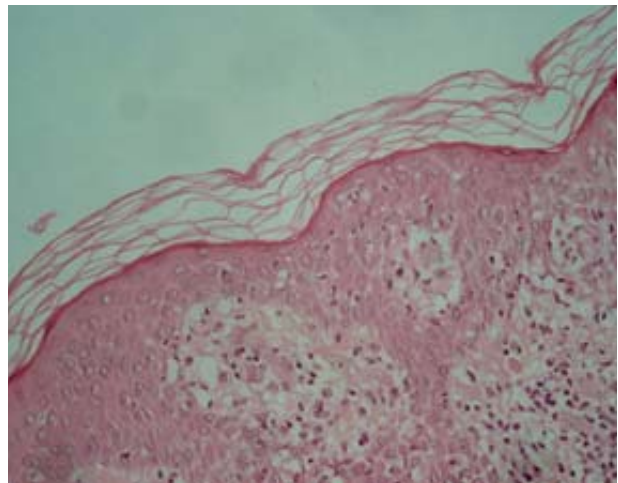


Figure 4. Vacuolar degeneration and isolated necrotic keratinocytes of the epidermis of the trunk. Note the lymphohistiocytic infiltrate around the blood vessels (H&E, original magnification $\times 20$).

Many organs or systems may be involved because of the induction of various immunologic abnormalities.⁴

Mixed cryoglobulinemia is found in 36% to 45% of patients with chronic hepatitis C; however, it only becomes clinically manifested as systemic vasculitis, purpura, neuropathy, Raynaud's syndrome, or glomerulonephritis in less than one third of cases.^{3,5} The possibility that mixed cryoglobulinemia could be the origin of lymphoproliferative hematologic disorders is being evaluated.^{3,5}

Rheumatoid arthritis develops in 20% of patients with chronic hepatitis C.⁴ Some problems relevant to the association of HCV infection with a proportion of autoimmune disorders (including hepatitis with liver/kidney microsomal antibodies, thyroiditis, Sjögren syndrome, hemolytic anemia, and idiopathic thrombocytopenia) are still debatable because their exact prevalence remains undetermined.^{2,4}

The role of HCV in the pathogenesis of leukocytoclastic vasculitis with essential mixed cryoglobulinemia and sporadic porphyria cutanea tarda has been firmly sustained by epidemiologic and immunologic evidence.^{1,5}

The frequency of lichen planus associated with HCV infection varies in literature and clearly reflects several forms of bias that influence the reported seroprevalence of HCV in different populations.^{6,7} The strength of an epidemiologic association between HCV and a number of other skin diseases, such as erythema multiforme, erythema nodosum, polyarteritis nodosa, urticaria, scarlatiniform exanthem, dermatomyositis, and livedo reticularis, differs greatly and deserves further study and documentation.⁸⁻¹³ With the increasing use of HCV antibody testing and the diagnosis of a growing number of infected patients, an ever-greater

spectrum of HCV-associated disease is becoming apparent. The validity of many of these epidemiologic associations depends on further prospective studies and detailed pathophysiologic investigations of representative cases.

To our knowledge, this is the first reported case in which lichen planus, erythema nodosum, and erythema multiforme developed in a patient with chronic hepatitis C. The clinical course of lichen planus appeared to be independent of ongoing viral relapses, whereas the erythema nodosum and erythema multiforme occurred in conjunction with flare-ups of viral activity. When the hepatitis relapsed, the former dermatitis occurred twice over the following months. The concurrent onset and extension of erythema multiforme were probably correlated with higher levels of viremia. These findings, together with the level of HCV viremia, could confirm the role of HCV in the pathogenesis of erythema nodosum and erythema multiforme.

We advise that patients who develop cutaneous diseases (even if the disease is only occasionally associated with HCV infection) should undergo either a diagnostic assessment of the otherwise undetected HCV infections or a check of both the level of activity and severity of the HCV infection.

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