CASE REPORT

Lichenoid eruption occurring during chronic hepatitis C treatment with interferon-alpha 2-b plus ribavirin

İnterferon alfa 2-b ve ribavirin ile tedavi edilen kronik hepatit C'li hastada gelişen likenoid döküntüler

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Approximately half of the chronic hepatitis C virus infection patients might develop at least one extrahepatic manifestation during the course of the disease. Lichen planus is in group B in accordance with its relation with hepatitis C virus infection, meaning that the prevalence of this disorder is higher than in controls. On the other hand, lichenoid eruptions may arise as an adverse reaction of interferon therapy in chronic hepatitis C virus infection. Our patient had hepatitis C virus infection and developed lichenoid eruptions during the 9th month of interferon plus ribavirin treatment.

Key words: *Hepatitis C, lichen planus, extrahepatic manifestations*

Kronik hepatit C'li hastaların yaklaşık yarısında hastalık seyri esnasında en az bir karaciğer dışı bulgu ortaya çıkar. Liken planusun hepatit C ile ilişkisi grup B olarak tanımlanır ki bunun anlamı kontrollere göre daha yüksek sıklıkda görülmekte olduğudur. Bunun yanında likenoid döküntüler kronik hepatit C tedavisine bağlı gelişen bir yan etki olarak da karşımıza çıkabilir. Bizim vakamız interferon 2-b+ribavirin tedavisinin 9. ayında likenoid döküntüleri ortaya çıkan bir hastadır.

Anahtar kelimeler: *Hepatit C, lichen planus, ekstrahepatik bulgular*

INTRODUCTION

Hepatitis C virus (HCV) is associated with a wide spectrum of clinical and biological extrahepatic manifestations (EHM) (1,2). According to different studies, 40-74% of patients infected with HCV might develop at least one EHM during the course of the disease (3). Common EHMs of HCV are mixed cryoglobulinemia, membranoproliferative glomerulonephritis, Sjögren syndrome, autoimmune thyroiditis, malignant lymphoma, porphyria cutanea tarda, and lichen planus (LP) (4).

In this paper, we present a case of lichenoid drug eruption occurring during HCV infection treatment with interferon-alpha (IFN–α) 2-b plus ribavirin and we review the related literature.

CASE REPORT

Our patient was a 42-year-old woman. Her body mass index was 24.8. She was anti-HCV (+), and her serum HCV RNA level was 250,000 copies/ml, genotype Ib. Serum alanine aminotransferase (ALT) levels and complete blood count were all in the normal range. Anti- nuclear antibody was negative. Her physical examination was completely normal. She was started on pegylated IFN–α 2-b 100 mcg/week s.c. plus ribavirin 1000 mg/day treatment. HCV RNA level after four weeks of treatment was still positive. She had flu-like symptoms with slightly decreased levels of leukocytes and platelets. After 12 weeks of treatment, her serum HCV RNA level was 350 copies/ml, without any change in white blood cell (WBC) or platelet levels. At 24 weeks, hemoglobin (Hb), WBC and platelets were 8.5 g/dl, 2500/µL and 100000/µL, respectively, and HCV RNA level was negative. She was hospitalized and given erythrocyte suspensions, and her ribavirin dose was decreased to 800 mg/day. During the follow-up, no further modifications in drug doses were required. At the 9th month of treatment, eroded, papular and itching lesions appeared, scattered on both upper and lower extremities (Figures 1-3). These lesions were compatible with lichenoid eruptions. We did not find any mucosal lesions. During this time, serum HCV RNA and cryoglobulinemia levels were negative. Local corticosteroid ointment plus oral antihistaminic treatment were started. LP lesions had partially regressed after four weeks of treatment. At the end of treatment and 24 weeks after completion of 48 weeks of treatment, HCV RNA levels were negative. LP lesions had completely resolved after completing a 48-week treatment period.

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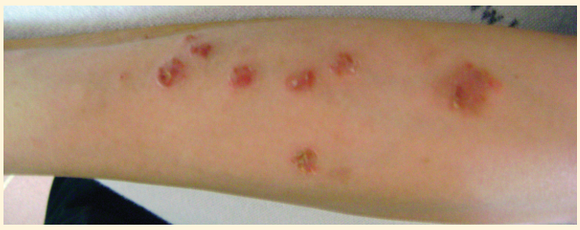

Figure 1. Lichenoid eruption: right forearm.

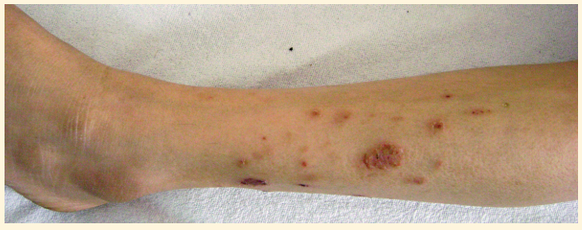

Figure 2. Lichenoid eruption: left leg.

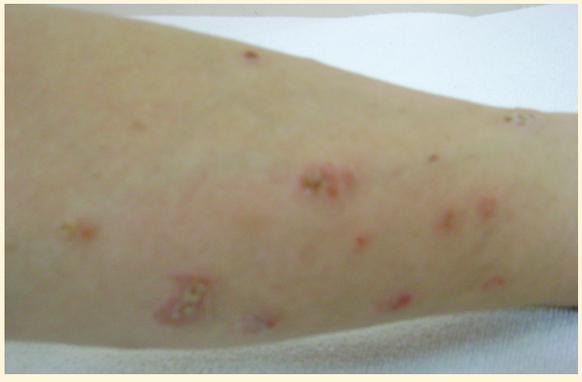

Figure 3. Lichenoid eruption: right leg.

DISCUSSION

Lichen planus (LP) is an inflammatory disease in which chronic keratonosis occurs in the skin or mucous membranes, or both. Skin lesions are generally found in the extremities, genitalia, nails, face, and scalp. Lesions in the mucous membranes are found in the oral cavity, nasal mucous membranes, throat, esophagus, stomach, bladder, vulva, vagina, and glans penis (4). LP may appear in various forms such as linear, atrophic, annular, hypertrophic, erosive, vesicobullous, follicular, and actinic. The biopsy shows a lymphocytic infiltration in the upper dermis, with vacuolar degeneration of basal epithelium and the presence of acidophilic bodies, probably represented by apoptotic keratocytes (5). However, biopsy is not mandatory for diagnosis.

The prevalence of LP is less than 1% of the population (6). The cause of LP is unknown, but immunological and genetic factors, drugs and chronic hepatitic disease have been implicated as causative factors. HCV is thought to contribute to the development of LP, and it has also been estimated that HCV-infected patients have at least twice the risk of developing LP than the general population (7). The association between HCV and LP is unclear. However, one study demonstrated an increased level of tumor necrosis factor (TNF)-α and reduced levels of interleukin (IL)-1, IFN-γ, and IL-8 in HCV-infected patients with LP (8).

Chronic hepatitis C is often treated with IFN. As regards the effects of IFN therapy on LP lesions, there is a report of improvement in LP lesions (9), reports of LP manifestation triggered by IFN (10-14), and a report of aggravation of LP (15). The association of lichenoid drug eruption and hepatitis C is well documented, but the mechanism remains perplexing (16). One possibility is that different HCV genotypes may have different effects. One study found that prevalence of HCV genotype 1b was increased in older patients with LP (17). However, in an Italian study of LP, the prevalence of different HCV genotypes was similar to that in a population with chronic liver disease without LP (18).

Several recent studies in southern Europe and Japan have confirmed that HCV is an important correlate in patients with LP (18-20). However, a much lower percentage of HCV infection has been found in LP patients in England and northern France (21,22).

Some studies have suggested that host genetics may be an important factor in explaining the association between HCV and LP. Indeed, the HLA-DR6 allele can influence infection and could explain the geographical heterogeneity of the association between HCV and LP (17,18).

Damaged keratocytes and HCV share some similar antigens. This similarity may explain the association between HCV infection and LP by cell-mediated cytotoxicity.

The role of IFN-α in the development of LP is controversial. Several authors report that patients treated with IFN-α for hepatitis C do not develop LP. Conversely, reports of IFN-induced LP are found in the literature (23,24). Based on a recent work performed involving patients with hepatitis C associated with LP, an improvement in hepatitis was observed after IFN therapy; however, the LP showed no objective response to this drug (16).

Our patient had chronic hepatitis C infection and developed lichenoid drug eruptions during the 9th month of in-

terferon plus ribavirin treatment. HCV RNA level was negative at the time of drug eruption. We continued antiviral treatment for 48 weeks and added topical corticosteroid ointment plus oral antihistaminic for four weeks.

Although HCV treatment improves most of the extrahepatic manifestations, the effect of antiviral treatment on lichenoid lesions is controversial. Progression, regression or triggering of the new lesions could be seen during the antiviral treatment. We think that treatment should continue with the addition of local and symptomatic drugs for lichen lesions if the response to antiviral treatment is good.

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