Borderline tuberculoid leprosy and type 1 leprosy reaction in a hepatitis C patient during treatment with interferon and ribavirin*

Hanseníase boderline tuberculóide e reação hansênica do tipo 1 em paciente com hepatite C durante tratamento com interferon e ribavirina

Mônica Santos[1]
Paulo Luis da Costa Ferreira[3]
Emily dos Santos Franco[2]
Wornei Silva Miranda Braga[4]

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Abstract: Hepatitis C is an inflammatory disease of the liver caused by a single-stranded RNA virus belonging to the Hepacivirus genus in the Flaviviridae family, called the hepatitis C virus. After initial infection, 70% to 85% of the patients develop chronic hepatitis C with hepatic fibrosis. In addition to specific liver changes, various extrahepatic manifestations have been associated with the hepatitis C virus infection or with medications used to treat the condition. We report the case of a patient with chronic hepatitis C who presented with the signs and symptoms of borderline tuberculoid leprosy and type 1 reaction four months after the start of treatment with a pegylated interferon/ribavirin combination.
Keywords: Hepatitis C; Interferons; Leprosy; Therapeutics

Resumo: A hepatite C é uma doença inflamatória fígado causada por um vírus RNA de fita simples, pertencente ao gênero Hepacivirus e à família Flaviviridae, denominado de vírus da hepatite C. Após infecção inicial 70 a 85% dos pacientes infectados evoluem para hepatite C crônica, com fibrose progressiva. Além das alterações hepáticas específicas, várias manifestações extra-hepáticas têm sido relacionadas à infecção pelo vírus da hepatite C ou às medicações utilizadas no seu tratamento. Nesse trabalho, apresenta-se caso de paciente portador de hepatite C crônica, que manifestou um quadro hanseníase boderline tuberculóide e reação hansênica do tipo I, quatro meses após início do tratamento com interferon peguilado associado à ribavirina.
Palavras-chave: Hanseníase; Hepatite C; Interferons; Terapêutica

INTRODUCTION

Hepatitis C is an inflammatory disease of the liver caused by a single-stranded RNA virus belonging to the *Hepacivirus* genus in the *Flaviviridae* family, called the hepatitis C virus. After initial infection, only 15% to 30% of hepatitis C patients recover spontaneously, while 70% to 85% develop chronic hepatitis C, which is defined as HCV persisting for more than six months after infection.[1] The main consequence of chronic hepatitis C is progressive hepatic fibrosis, which can lead to cirrhosis, liver failure and hepatocellular carcinoma. In addition to specific liver changes, various extrahepatic manifestations have been associated with HCV infection.[2] Dermatologic changes constitute a significant part of the spectrum of extrahepatic manifestations in hepatitis C and can be divided into those associated with the presence of HCV itself and those caused by medications used to treat the condition.[3] Among the manifestations com-

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[1] PhD in tropical medicine. Dermatologist at the Alfredo da Matta Foundation – Manaus (AM), Brazil.
[2] M.D. Pathology resident at the Getúlio Vargas University Hospital - Manaus (AM), Brazil.
[3] M.D. Infectologist at the Tropical Medicine of Amazonas Foundation (FMT-AM) - Manaus (AM), Brazil.
[4] PhD in tropical medicine. Infectologist at the Tropical Medicine of Amazonas Foundation (FMT-AM) - Manaus (AM), Brazil.

monly associated with HCV, the most notable are cryoglobulinemia, porphyria cutanea tarda, leukocytoclastic vasculitis and livedo reticularis. Hepatitis C is normally treated with a pegylated interferon/ribavirin combination to prevent it from progressing to the chronic form.[4] Despite the undeniable benefits of this combination, when used in clinical practice it can lead to a range of adverse effects, including dermatologic complications, many of which are the result of the immunomodulatory effects of interferon. These effects may also include the exacerbation of existing cutaneous diseases.[5]

CASE REPORT

A 57-year-old male with hepatitis C using pegylated interferon and ribavirin for treatment of hepatitis C. Four months after the start of the treatment, disseminated cutaneous lesions appeared, as well as intense pain along the course of the cubital and fibular nerves. Dermatologic examination revealed small and large, highly infiltrated erythematous plaques on his back, arms and legs (Figure 1). Physical examination revealed thickened cubital and fibular nerves that were highly painful to palpation. The patient reported that he had developed a small erythematous plaque on his back two years previously, which had been treated unsuccessfully as dermatophytosis. In light of the clinical history and the results of the dermatological examination, a hypothesis of borderline tuberculoid leprosy with type I reaction was put forward and an incisional biopsy was performed. A histological exam revealed granulomatous inflammatory infiltrate in the upper dermis and around blood vessels and hair follicles, but Wade staining and bacteriological examination were negative (Figure 2). The Mitsuda reaction was positive. As the diagnosis was confirmed, six months of multidrug therapy for paucibacillary (PB) leprosy was started, together with an initial 80 mg/day dose of prednisolone, which was then gradually reduced. After the case was discussed with the hepatology team, the decision was taken to interrupt the interferon and ribavirin treatment until the treatment for PB leprosy was completed. There was a clinical improvement in the patient's leprosy reaction (Figure 3), and he was discharged as cured after completing MDT for PB leprosy (Figure 4). Six months ago, the patient again began treatment for hepatitis C with interferon and ribavirin, but obtained no sustained virological response and awaiting this release for use of pegylated interferon and ribavirin associated with protease inhibitor (telaprevir or boceprevir). At the time of writing, the patient is undergoing follow-up at the dermatology and hepatology services and has not presented with any clinical manifestations of leprosy reaction.

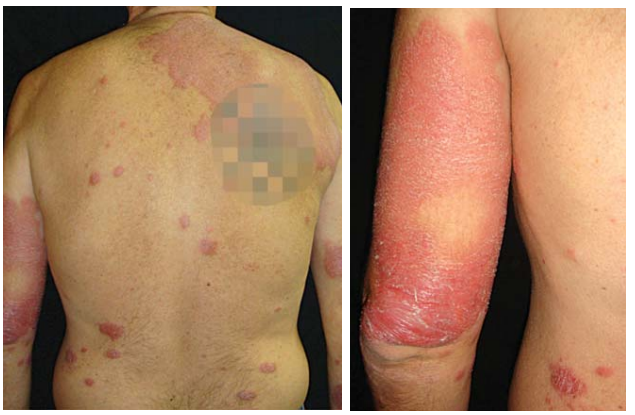

Figure 1: Erythematous plaques with dense infiltrate on the trunk and arms

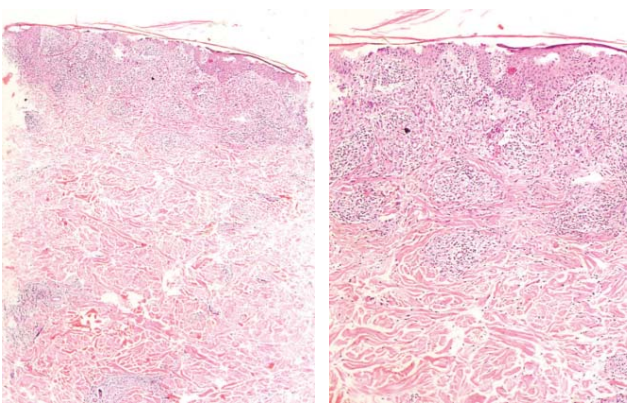

Figure 2: Histological examination revealed granulomatous inflammatory infiltrate in the dermis made up of lymphocytes, epithelioid cells and multinucleated giant cells. The infiltrate touches the epidermis in several places, surrounds vessels and hair follicles and does not have a halo of lymphocytes

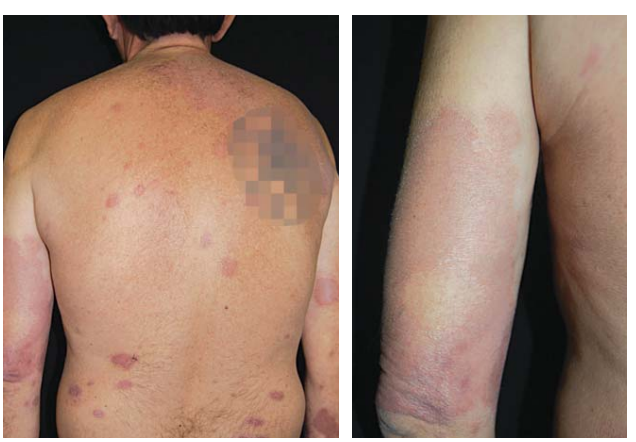

Figure 3: Reduced plaque infiltration after treatment with oral corticosteroids was started

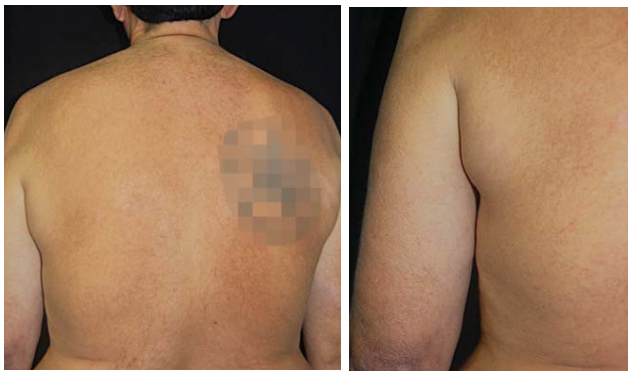

Figure 4: Lesions were clinically cured six months after the end of the multidrug therapy (MDT) for paucibacillary (PB) leprosy

DISCUSSION

Leprosy is a chronic granulomatous condition caused by *Mycobacterium leprae*, which affects the skin, peripheral nervous system and, sometimes, other organs and systems. During the natural course of the disease, manifestations related to exacerbation of cellular immunity or the formation of immunocomplexes (known, respectively, as type 1 and type 2 leprosy reactions) may occur.[6] Type 1 reaction or reversal reaction is an acute inflammatory episode in the skin and peripheral nerves that is found in up to 30% of leprosy patients and commonly causes physical disabilities. Multidrug chemotherapy and viral infections (such as the hepatitis B or C viruses and HIV) are associated risk factors. It generally manifests in borderline forms, with a clinical picture characterized by signs of acute inflammation, such as pain, redness, infiltration and swelling of preexisting lesions. New lesions may also appear. Neural involvement is also common and can lead to deformities if not diagnosed and treated early.[7] The nerves most frequently affected are the cubital, radial, median, tibial and fibular nerves. The whole reversal reaction is associated with a sudden increase in cell-mediated immunity and is an example of a delayed hypersensitivity reaction.[8] In type 1 leprosy reaction, there is participation of T lymphocytes with production of TH1-type cytokines, especially IL-2 and IFN-Y. Although type 1 leprosy reaction can be triggered by the viral infection itself, in the case under discussion, it is more likely that the reaction was caused by the use of interferon, as the patient believed that he had been infected with HCV for at least ten years, but had not had similar episodes previously. In addition, there are reports in the literature of autoimmune events, such as thyroiditis and vitiligo, being precipitated by interferon therapy as a result of the T helper 1 response induced.[9] Interferons are natural proteins modifying immunobiological response, effective antiviral, antiproliferative and immunomodulator. The immunomodulatory effect of the product includes various actions on elements of the immune system, such as stimulation activities lytic natural killer cells, cytotoxic T lymphocytes and macrophages on infected tumor cells, modification of the production of antibodies by B cells, regulation of expression of MHC antigens in the cell membrane and stimulating the production of interferon alpha[10] In the case described here, the patient probably already had undiagnosed leprosy, as he had reported having an erythematous plaque on his back, and the use of pegylated interferon may have triggered the reversal reaction as this is an immune-mediated reaction.

In this paper, we report the case of a patient with chronic hepatitis C who presented with the signs and symptoms of borderline tuberculoid leprosy and type 1 reaction four months after starting treatment with a pegylated interferon/ribavirin combination. Multidisciplinary follow-up allowed reversal reaction to be diagnosed and early treatment to be started, thus avoiding any potential disabilities.❑

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Mailing address:
Mônica Santos
Av. Pedro Texeira, 25 - Dom Pedro
69040-000 - Manaus - AM
Brazil
E-mail: m.n.souza.santos@gmail.com

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