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Case report

Induction of cytoplasmic pattern in the form of "rods and rings" through the treatment of hepatitis C: a case report☆

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ABSTRACT

Female patient, complaining of weakness and pain in hypogastric, was admitted to the emergency department of the University Hospital of the West of Paraná (HUOP). During the interview reported treatment of chronic infection with hepatitis C virus (HCV) with peginterferon and ribavirin. Among the laboratory tests ordered, the search for self-antibodies against cellular antigens, traditionally known as antinuclear factor, showed fluorescence shaped like rods and/or rings in the cytoplasm of cells. This study attempts to clarify the relationship between this pattern not yet completely understood and the clinical picture of the patient. This pattern is characterized by 3–10 μm rods or rings with 2–5 μm in diameter scattered throughout the cytoplasm of the cell. Therefore, this new standard has been designated as "rods and rings" (RR). The antigenic target of this reaction was identified as inosine-5′-monophosphate dehydrogenase type 2 (IMPDH2) which is a key enzyme in the synthesis of purine nucleotides. The IMPDH2 enzyme aggregated or modified shaped RR in those patients treated with ribavirin may become antigenic and induce an autoimmune response. It is possible that interferon alpha stimulates the occurrence of anti-RR reactivity apparently induced by ribavirin. So far it is not known why the standard RR in HEp2 cells occurs only in a fraction of patients with HCV. Previous studies presented in this paper allow affirming that these antibodies associated with the standard RR are strongly related to hepatitis C. Moreover, it can be stated that the occurrence of anti-RR reactivity is promoted by combination therapy with interferon and ribavirin.

☆ Study conducted at Diagnostic and Therapeutic Support Service (SADT), Hospital Universitário do Oeste do Paraná (HUOP-Unioeste).

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Indução do padrão citoplasmático em forma de "bastões e anéis" através do tratamento da hepatite C: relato de caso

Palavras-chave:
Hepatite C
Autoanticorpos
Bastões e anéis
Padrão citoplasmático

RESUMO

Paciente do sexo feminino, queixando-se de astenia e dor em hipogastro, foi admitida no pronto-socorro do Hospital Universitário do Oeste do Paraná (HUOP). Durante a anamnese relatou tratamento de infecção crônica pelo vírus da hepatite C (VHC) com inteferon peguilado e ribavirina. Dentre os exames laboratoriais solicitados, a pesquisa de autoanticorpos contra antígenos celulares (PAAC-HEp-2), conhecido tradicionalmente como fator antinúcleo (FAN), apresentou fluorescência em forma de bastões e/ou anéis no citoplasma das células. Esse padrão é caracterizado por bastões de 3-10 μm e anéis com 2-5 μm de diâmetro espalhados através do citoplasma da célula. Portanto, esse novo padrão tem sido designado como "bastões e anéis" (traduzido do inglês: *Rods and Rings*, RR). O alvo antigênico dessa reação foi identificado como inosina-5′-monofosfato desidrogenase tipo 2 (IMPDH2) que é uma enzima chave na síntese de nucleotídeos púricos. A enzima IMPDH2 agregada ou modificada em forma de RR nos pacientes tratados com ribavirina pode tornar-se antigênica e induzir uma resposta autoimune. É possível que o interferon alfa estimule a ocorrência de reatividade anti-RR aparentemente induzida pela ribavirina. Até o momento não se sabe por que o padrão RR em células HEp-2 ocorrem apenas em uma fração de pacientes portadores do VHC. Os dados apresentados em trabalhos anteriores possibilitam afirmar que esses anticorpos associados ao padrão RR estão fortemente relacionados com o tratamento da hepatite C. Além disso, pode-se afirmar que a ocorrência de reatividade anti-RR é promovida pela terapia combinada com interferon alfa e ribavirina.

Introduction

Hepatitis C virus (HCV) is an RNA virus of the Flaviviridae family, genus *Hepacivirus*, with a high rate of hepatic replication. This is an enveloped virus, with a size between 30 and 40 nm.[1–3] HCV was originally isolated in a serum sample of an individual with non-A, non-B hepatitis in 1989 by Choo et al.[4] Since then, hepatitis C gained special relevance among the causes of chronic liver disease worldwide. In 1992, the first test for identification of the antibody against HCV was developed, providing greater safety in blood transfusions.[1,2]

The HCV transmission occurs through contact with infected blood due to percutaneous exposure, blood and/or blood products transfusion and transplants from infected donors. Although some patients with acute HCV infection have an immune system able of eliminating the virus, 55–58% of patients develop chronic infection, defined as the persistence of infection for no less than six months, with only 10–15% of cases reaching spontaneous healing. The hepatocellular injury, seen in chronic HCV infection, does not seem to be directly related to a viral cytopathic effect, being related to immune mediators, with natural killer cells and CD8 + T lymphocytes playing a central role in the pathogenesis.[1,2]

The treatment of HCV infection aims to control the progression of liver disease by inhibiting viral replication. Furthermore, the reduction in inflammatory activity prevents its progression to cirrhosis and hepatic carcinoma. The recommended therapy for chronic HCV infection is a combination of a formulation of interferon alpha and ribavirin.[3]

Interferon is a cytokine which composes the innate response of the human host. The addition of one polyethylene glycol molecule to the interferon molecule prolongs the action, increases the rate of absorption, extends the half-life and reduces the clearance of interferon. Ribavirin is a nucleoside analog antiviral agent used orally, with a wide spectrum of action against viral pathogens. Ribavirin also has the effect of modulating the immune response.[2,3] Mori et al. recently demonstrated that ribavirin in therapeutic doses inhibits the replication of HCV RNA, and proposed that this anti-HCV activity is mediated through the inhibition of inosine-5′-monophosphate dehydrogenase (IMPDH).[5]

Case report

Female patient complaining of asthenia and pain at hypogastric area, admitted on October 4, 2011 in the emergency room of Hospital Universitário do Oeste do Paraná (HUOP) in the city of Cascavel-PR. During anamnesis, the patient reported treatment of chronic infection with hepatitis C virus with pegylated interferon alpha and ribavirin, starting on December 7, 2010 and concluded on November 1, 2011. During this period the patient developed severe pancytopenia due to the adverse effects of the medication.

On admission, routine laboratory tests were performed and the results showed significant changes in blood count parameters; and a hematocrit of 23%, associated with normal values of MCH (mean corpuscular hemoglobin), together with clinical data obtained at the time of anamnesis, raised the diagnostic hypothesis of autoimmune anemia. In an attempt to confirm