Systemic lupus erythematosus following virological response to peginterferon alfa-2b in a transplanted patient with chronic hepatitis C recurrence

Francesca Lodato, Maria Rosa Tamé, Antonio Colecchia, Chiara Racchini, Francesco Azzaroli, Antonia D’Errico, Silvia Casanova, Antonio Pinna, Enrico Roda, Giuseppe Mazzella

INTRODUCTION
Autoimmune manifestations are common in patients chronically infected by hepatitis C virus (HCV). On the other hand, tissue autoantibodies are common in liver recipients transplanted for non-autoimmune diseases and may be associated with negative graft outcome. The safety and efficacy of interferon (IFNs) and the newest pegylated interferons (Peg-IFNs) for the treatment of recurrent hepatitis C in transplanted patients are still debated. In particular, it is unclear whether IFN may increase the incidence of acute cellular rejection (ACR) and there are no reports on the development of atypical autoimmune manifestations during post-liver transplantation (LT) IFN or Peg-IFN treatment.

We report a case of severe autoimmune disease, different from ACR, during treatment with Peg-IFN alfa-2b in a transplanted patient with recurrence of chronic hepatitis C (CHC).

CASE REPORT
A 55-year-old man, underwent LT in March 2001 for HCV genotype 1 liver related cirrhosis. Acute immunosuppressive (IS) schedule was cyclosporine, azathioprine (AZA) and steroids. According to the Transplantation Unit IS protocol, AZA and steroids were stopped 3 wk and 1 year after LT, respectively. Screening tests for LT revealed the presence of cryoglobulins with a cryocrite of 8% and antinuclear antibodies (ANA) at low titre (1/160) with homogeneous pattern. After LT, clinical outcome was regular until January 2002, when the patient showed a persistent mild increase of transaminases (ALT 115 U/L and AST 103 U/L) with high viral load (17.5 MEq/mL, Versant HCV-RNA 3.0 bDNA, Bayer). Liver histology showed mildly active chronic hepatitis with severe fibrosis, presence of lymphocytes and macrovesicular steatosis, sug-
gestive of HCV recurrence (Figure 1).

In October 2002 the patient started a cycle of Peg-IFN alfa-2b (1.1 mcg/kg per week) and Ribavirin (6.4 mg/kg per day). After 4 wk of treatment transaminases were normal. HCV-RNA showed a 2 log fall (0.01 MEq/mL) at wk 12; became undetectable by branched DNA, but still positive by polymerase chain reaction (TMA test, Versant HCV-RNA, Bayer) at wk 24 and finally negative by PCR at wk 36.

At wk 44 the patient presented migratory arthritis and the following biochemical parameters: normal transaminases, CrT 240 ng/mL, increased gamma-glutamyltransferase (γGT), alkaline phosphatase (ALP) and bilirubin (384 U/L and 1.69 mg/dL, respectively), gamma-globulins 30%, Waaler-Rose 1/1280, ANA 1/640 and anti-DNA positive. No vascular or biliary complications were revealed by ultrasond and computed tomography, nor any signs of infectious diseases were present. Suspicion of an immune mediated manifestation, prednisone 10 mg/d was started. However, despite the presence of signs of autoimmunity we decided to complete the Peg-IFN cycle in consideration of the fact that we were almost at the end of the planned 48 wk of treatment with the patient responding to Peg-IFN.

At wk 48 the patient was asymptomatic, transaminases and bilirubin were normal, HCV-RNA negative by PCR, while ALP and γGT were decreased (ALP 350 U/L and γGT 94 U/L). Peg-IFN was stopped and steroids were maintained.

One month later, the patient developed pleuro-pericardial effusion and ascites. Liver function tests (LFTs) were normal, HCV-RNA was negative (PCR) and CyA within the therapeutic range (100 ng/mL). Liver biopsy revealed the presence of interface hepatitis, numerous rosettes, cholangitis with ductular proliferation and biliocytes regression (Figure 2). Histological findings were not suggestive for HCV recurrence and did not fulfil the standard criteria for acute or chronic rejection. Therefore, International Criteria for Autoimmune Hepatitis (AIH score) were applied, according to which the patient was categorized as positive for “probable AIH” (score + 11). Consequently, steroid treatment was increased and the patient was switched from cyclosporine to tacrolimus. Response to immunosuppressive treatment was slow but progressive until normalization of LFTs.

DISCUSSION

It is well known that treatment with IFN may cause autoimmune diseases or the development of autoantibodies in non transplanted patients while few data are available on transplanted ones. In particular, to the best of our knowledge, it has never been described the development of autoimmune diseases by the up-regulation of MHC both on transplanted and non transplanted patients. In a series of 677 patients treated for HCV infection in immunocompetent patients treated for HCV infection while few data are available on transplanted ones. In particular, to the best of our knowledge, it has never been described the development of autoimmune diseases by the up-regulation of MHC both on transplanted and non transplanted patients.
Moreover, the interaction of IFN activities in a particular pathway, such as in the immunosuppressed host, may lead to severe autoimmune manifestations that can compromise the graft survival. A relation between virological response to severe autoimmune manifestations that can compromise the pathway, such as in the immunosuppressed host, may lead to severe autoimmune manifestations that can compromise the pathway, such as in the immunosuppressed host, may lead to severe autoimmune manifestations that can compromise the pathway, such as in the immunosuppressed host, may lead to severe autoimmune manifestations that can compromise the path.

In conclusion, the clinician should be aware of the possible development of autoimmune disorders, different from ACR, during interferon-based treatment in LT patients, especially if signs of autoimmunity are present before starting IFN.

REFERENCES

7 Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40: 1725
15 Aspinall RJ, Pockros PJ. The management of side-effects during therapy for hepatitis C. Aliment Pharmacol Ther 2004; 20: 917-929

S-Editor: Wang J L-Editor: Zhu LH E-Editor: Bai SH