

• CASE REPORT •

Does *Fasciola hepatica* infection modify the response of acute hepatitis C virus infection to IFN- α treatment?

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Abstract

Immunologic response to acute hepatitis C is mainly a Th1 response, whereas fasciolopsiasis is associated with a diverse T-cell response. Interferon-alpha has immunomodulatory effects and enhances Th1 immune response. *Fasciola* infection could theoretically interfere with the Th1 immune response, even when acquired after an initial response to interferon-alpha treatment for acute hepatitis C virus (HCV) infection. We report here the case of a male patient who acquired *Fasciola hepatica* infection after an initial response to IFN-alpha therapy with a favorable outcome

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INTRODUCTION

Hepatitis C virus (HCV) infection is a common cause of hepatocellular injury associated with complex immunologic mechanisms including both humoral and cell-mediated responses. Acute hepatitis C infection especially produces a Th1 response^[1]. Fasciolopsiasis, like other helminth infections, is associated with the induction of T-cell responses particularly the Th2 subtype^[2]. Enhanced induction of Th2 cytokines and downregulation of Th1

responses during infection with *Fasciola hepatica* could be expected to interfere with the natural course of and the response to the treatment of acute viral hepatitis C. The concurrence of HCV and *F. hepatica* infection is uncommon and whether *F. hepatica* infection acquired during IFN- α therapy has any effect on HCV replication is unknown.

CASE REPORT

A 50-year-old male patient, with chronic renal failure began hemodialysis 3 mo ago. Prior to initiation of hemodialysis, liver function tests were normal and serological tests for hepatitis B and C were negative. During the 3rd mo of hemodialysis, laboratory evaluation showed elevations of 183 IU/L AST (normal, 5-45 IU/L), 394 IU/L ALT (normal, 5-45 IU/L), 141 IU/L GGT (normal, 0-50 IU/L), and 90 IU/L ALP (normal, 53-128 IU/L). Physical examination was normal. Abdominal ultrasonography showed normal liver size with grade II heterogeneity, normal portal vein size and no ascites. Anti-HCV antibody and HCV RNA were positive. Anti-HAV IgM, HBs Ag, and anti HIV were negative.

The patient was diagnosed with acute viral hepatitis C. IFN- α 2b (Intron A; Schering Plough Corporation, Kenilworth, NJ, USA) was started 3 MU thrice weekly subcutaneously for 12 mo. ALT levels normalized during the 4th wk of the therapy. HCV RNA was negative after 6 mo.

After 6 mo of treatment with IFN- α , the patient reported marked malaise and right upper quadrant abdominal pain. Physical examination revealed right hypochondrium tenderness. Repeated liver function tests showed elevations of ALT (51 IU/L), ALP (196 IU/L), and GGT (272 IU/L). WBC were 6 800/mm³ with marked eosinophilia (20%). Abdominal ultrasonography showed hepatomegaly and a well-defined 9-mm hyperechoic round mass in the anterior-superior segment of the right hepatic lobe which raised the suspicion of hemangioma and the possibility of *F. hepatica*. The causes of eosinophilia were investigated in the 9th mo of IFN- α therapy. Serology for fasciolopsiasis revealed positivity by enzyme-linked immunosorbent assay (ELISA) prepared against a secretory antigen according to Carnevale *et al*^[3]. The assay was reported to have 100% sensitivity and 100% specificity. ELISA absorbance value of the patient's sera was 2 900 units, while the cut-off value was 380. Stool specimens were negative for ova and parasites of *F. hepatica*. Oral triclabendazole (10 mg/kg), twice daily

doses was initiated for fasciolopsiasis. One week after the initiation of triclabendazole (10th mo of IFN therapy), the patient reported to have right upper abdominal pain and was hospitalized. Physical examination showed abdominal tenderness on the upper right quadrant and a positive Murphy's sign. Laboratory tests showed elevations of serum total and direct bilirubin which were 2.28 mg/L (normal, 0.2-1 mg/L) and 2.24 mg/L (normal, 0.1-0.5 mg/L), respectively in addition to elevations of ALT (58 IU/L), AST (53 IU/L), GGT (333 IU/L), and ALP (399 IU/L). WBC were 11 700/mm³ with 10% eosinophilia. Abdominal ultrasonography revealed no intraparenchymal lesion in the liver, thickening of gallbladder wall and a hyperechoic round mass measured 10 mm in the gallbladder. Intra and extrahepatic bile ducts were normal. The patient's condition improved after 48 h of intravenous fluids and antibiotics.

Twenty-four months after the initiation of IFN- α treatment, liver function tests and complete blood count were normal with 2% eosinophilia. Stool specimen for fasciola was negative. HCV RNA was negative. The patient continued his regular hemodialysis schedule.

DISCUSSION

An effective host response against a viral infection requires coordinated efforts by both nonspecific and antigen-specific immune responses. Cytokines play a key role in the cell-to-cell communication necessary for this process. Immediately after viral infection, several antigen nonspecific effector mechanisms are activated^[4].

Among the individuals who recover from acute HCV infection, Th1 subtype responses predominate and are necessary for complete recovery in acute HCV infection^[5,6]. Lechmann *et al*^[7] found that cellular immune responses against a panel of HCV core-derived peptides are stronger than humoral immune responses in individuals who have recovered from acute HCV infection. Also, experimental models reveal that rats with resolved acute hepatitis C have a higher proportion of cells producing Th1 subtype cytokines. Parasitic infections are frequently accompanied with a downregulation of cell-mediated immunity. Parasitic infections can exert bystander suppression of protective Th1 responses to infection and liver flukes may secrete molecules that down-regulate Th1 responses^[2]. In an experimental model, Miriam *et al*^[8] showed that Th1 response to *Bordetella pertussis* antigens is markedly suppressed following infection with *F. hepatica*. Kamal *et al*^[9] showed that patients with acute hepatitis C and schistosomiasis coinfection cannot clear viremia and show rapid progression once chronic infection is established. In contrast, in the present case, the clinical and serological response marked by the clearance of HCV-RNA was maintained though the acquisition of *F. Hepatica*. This

favorable outcome may be related to immunomodulatory effects of IFN- α therapy. IFN- α induces the production of certain cytokines and has been recognized as a cytokine promoting Th1 differentiation^[10,11]. In addition, it increases cytotoxic activity of natural killer cells, cytotoxic T lymphocytes and macrophages^[12]. Recent data suggest that early treatment of acute HCV infection with IFN- α may be highly effective in preventing chronic hepatitis C infection^[13].

In conclusion, the present case illustrates that acute hepatitis C is responsive to the treatment even in the coexistence of fasciolopsiasis.

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