Netherlands
The Journal of Medicine

LETTER TO THE EDITOR

Autoimmune haemolytic anaemia due to chronic hepatitis C virus infection treated with prednisone, pegylated interferon and ribavirin

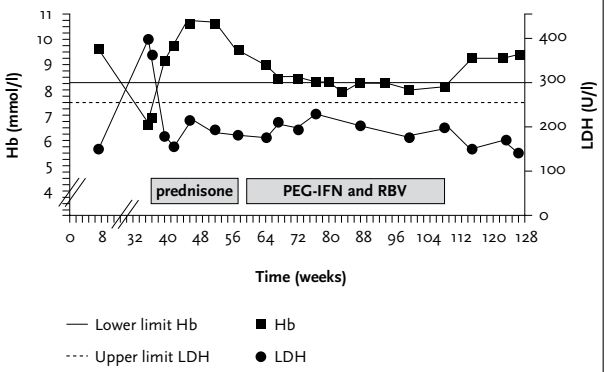
Dear Editor,

Chronic hepatitis C virus (HCV) infection has been associated with various extrahepatic manifestations, including autoimmune cytopenias.[1] Primary autoimmune haemolytic anaemia (AIHA) has been reported as an unusual extrahepatic manifestation.[2]
Combination therapy with pegylated interferon (PEG-IFN) and ribavirin (RBV) is the current treatment of choice for chronic HCV infection.[3] However, this therapeutic regimen can exacerbate underlying autoimmune disorders and may result in a significant anaemia.[4] Though extrahepatic manifestations usually necessitate HCV treatment, the patient with AIHA as an extrahepatic manifestation of HCV infection represents a therapeutic dilemma.

We saw a 29-year-old man of Afghanistan origin with chronic HCV infection, with HCV RNA of 1.3 x 10^6 copies/ml, genotype 1b. Laboratory evaluation revealed moderately increased transaminases (ASAT 63 U/l, ALAT 155 U/l). Test results for HIV and hepatitis B were negative. A percutaneous liver biopsy showed mild chronic inflammation, without signs of fibrosis.
A few months after initial assessment, the patient developed jaundice. Blood tests showed a marked drop in haemoglobin level (from 9.6 to 6.6 mmol/l), macrocytosis (MCV 99 fL) and reticulocytosis (398 x 10^9/l), associated with an elevated indirect bilirubin (34 µmol/l) and lactate dehydrogenase (393 U/l) and a low haptoglobin (<0.20 g/l). A direct Coombs test was positive for IgG. Based on these findings, a diagnosis of Coombs-positive AIHA was made.
The patient received folic acid and prednisone (60 mg/day), which was gradually tapered over a period of five months. Within three weeks his anaemia improved (Hb 9.2 mmol/l) and there was no recurrence of AIHA after discontinuation of prednisone.

Directly after prednisone therapy, the patient started HCV treatment with PEG-IFN alfa-2a (180 µg/week) plus RBV (1000 mg/day) for 48 weeks. During this period the patient's lowest haemoglobin level was 7.9 mmol/l and dose reduction was not required. The patient successfully achieved a sustained virological response. When last seen, the patient was well and had neither signs of HCV infection, nor of AIHA.

Figure 1. *Chronological changes in haemoglobin levels (Hb) and lactate dehydrogenase (LDH) in relation to treatment with prednisone ans pegylated interferon (PEG-IFN) plus ribavirin (RBV)*



HCV infection is a common cause of progressive liver disease. In addition, chronic HCV infection has been associated with a variety of extrahepatic manifestations, including autoimmune disorders. During the past decade, several authors have described the relationship between chronic HCV infection and autoimmune cytopenias.[1] Primary AIHA has been reported as an unusual, but recognised extrahepatic manifestation.[2]
The current best treatment of choice for chronic HCV infection is PEG-IFN plus RBV. However, this treatment combination has a high incidence of haematological side effects. RBV causes a dose-dependent reversible haemolytic anaemia. PEG-IFN may contribute to anaemia by suppressing haematopoiesis.[4] Recently, a few case reports have described the occurrence of severe AIHA induced by PEG-IFN-RBV combination therapy.[5,6] In addition, PEG-IFN can exacerbate pre-existing autoimmune disorders. As a consequence cytopenias and autoimmune diseases are relative contraindications to HCV therapy.

We considered the AIHA in our patient to be an extrahepatic manifestation of chronic HCV infection. We first initiated prednisone therapy, which led to complete remission of AIHA. Subsequent antiviral therapy led to sustained virological response, without recurrence of AIHA. In conclusion, AIHA due to chronic HCV infection can successfully be treated with prednisone therapy and does not form a contraindication to antiviral treatment.

M.H.P. Dietvorst[1], P. van Wijngaarden[1*], R.A. de Man[2]
[1]Department of Internal Medicine, Amphia Hospital, Breda, the Netherlands, [2]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands, [*]corresponding author: tel.: +31 (0)76-595 24 04, fax: +31 (0)76-595 33 27, e-mail: PvanWijngaarden@amphia.nl

REFERENCES

1. Ramos-Casals M, García-Carrasco M, López-Medrano F, et al. Severe autoimmune cytopenias in treatment-naive hepatitis C virus infection. Clinical description of 35 cases. Medicine. 2003;82:87-96.
2. Elhajj II, Sharara AI, Taher AT. Chronic hepatitis C associated with Coombs-positive hemolytic anemia. Hematol J. 2004;5:364-6.
3. De Bruijne J, Buster EH, Gelderblom HC, et al. Netherlands Association of Gastroenterologists and Hepatologists. Treatment of chronic hepatitis C virus infection - Dutch national guidelines. Neth J Med. 2008;66:311-22.
4. McHutchison JG, Manns MP, Longo DL. Definition and management of anemia in patients infected with hepatitis C virus. Liver Int. 2006;26:389-98.
5. Cauli C, Serra G, Chessa L, et al. Severe autoimmune hemolytic anemia in a patient with chronic hepatitis C during treatment with peginterferon alfa-2a and ribavirin. Haematologica. 2006;91:76-77.
6. Gentile I, Viola C, Reynaud L, et al. Hemolytic anemia during pegylated IFN-α2b plus ribavirin treatment for chronic hepatitis C: ribavirin is not always the culprit. J Interferon Cytokine Res. 2005;25:283-5.

MONTHLY NJM ONLINE HITLIST

The table lists online hits for all articles published in the December issue of *the Netherlands Journal of Medicine* 2008 (available online on PubMed since 15 December 2008).

Article	Hits
EDITORIALS	
The *Netherlands Journal of Medicine*: seven years editorial office in Nijmegen, entering a new era	76
Blood pressure measurement in the year 2008: revival of oscillometry?	111
REVIEWS	
Hodgkin's lymphoma: news from an old disease	93
Cardiovascular risk is more related to drinking pattern than to the type of alcoholic drinks	87
ORIGINAL ARTICLES	
Oscillometric blood pressure measurements: differences between measured and calculated mean arterial pressure	127
Reintroduction of Riva-Rocci measurements to determine systolic blood pressure?	94
Thyroid function in patients with proteinuria	98
CASE REPORTS	
Intestinal ischaemia caused by mesenteric inflammatory veno-occlusive disease	111
Anakinra suppresses familial Mediterranean fever crises in a colchicine-resistant patient	76
PHOTO QUIZZES	
Endoscopy for obstructive jaundice	80
An adult with lower abdominal pain	109
MONTHLY NJM ONLINE HITLIST	
For all articles published in September 2008	43
Total	**1105**