Case Report

Treatment of Autoimmune Haemolytic Anaemia with Hepatitis C Virus

A Real Challenge

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Sri Lankan Journal of Infectious Diseases 2016 Vol.6 (2):130-133

DOI: http://dx.doi.org/10.4038/sljid.v6i2.8115

Abstract

Hepatitis C virus (HCV) infection is a potentially curable disease. The first line of treatment is pegylated interferon and ribavirin, both of which cause haemolysis. HCV itself causes autoimmune haemolytic anaemia (AIHA). Treatment of AIHA with steroid is contraindicated in patients on interferon. We report the successful treatment of a patient with AIHA infected with HCV whose treatment was a real challenge due to the risk of exacerbation of haemolysis by antiviral treatment. We describe the successful treatment of this patient initially with corticosteroids followed by pegylated interferon and gradual increase of the dose of ribavirin.

Keywords: Hepatitis C, autoimmune haemolytic anaemia, ribavirin, interferon.

Introduction

Pegylated interferon in combination with ribavirin represents the gold standard treatment for chronic HCV infection but is associated with various side effects, especially haematological abnormalities.[1-3] Haematological abnormalities are the most frequent causes of dose reduction or drug discontinuation.[4] Here we report a case of autoimmune haemolytic anemia in a 46 years old male patient who was treated with corticosteroids for AIHA and subsequently infected with HCV and successfully treated and cured with pegylated interferon and gradually increasing dose of ribavirin.

Case Report

In 1999, a 46yr old male patient presented to our outpatients department with weakness and yellowish discolouration of eyes and urine. On examination, he was pale and icteric. There was no organomegaly or lymphadenopathy. There was history of transfusion of 4 units of blood. On investigation, his haemoglobin (Hb) was 7gm/dL, reticulocyte count 12% and Direct Coombs Test was strongly positive (4+). Total bilirubin was 3.2, unconjugated 2.1 but liver enzymes level were normal. HBsAg and anti HCV and Integrated Confidential Testing and Counselling (ICTC)* at that time were nonreactive. A diagnosis of AIHA was made and treatment with prednisolone 50mg daily commenced. Patient was on and off steroids subsequently. In 2011, he

___* surrogate for HIV testing in India__

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Received 11 June 2016 and revised version accepted 14 October 2016

was re-admitted with pallor and jaundice. He gave a history of receiving one unit of blood 3 months ago. His Hb was 6.2 gm/dl, Direct Coombs test positive (3+), Reticulocyte count 22% and other blood components and Hb indices were normal. His Lactate dehydrogenase (LDH) was 890 U/L (normal values 240 – 480U/L). Liver function tests showed a total bilirubin of 2.3 (unconjugated 1.7, conjugated 0.6) and raised transaminases (SGOT 105, SGPT 121). Urine examination showed presence of urobilinogen. AntiHCV was found to be reactive. HBsAg and ICTC were nonreactive. The viral load was 740,050 copies of RNA/ml of blood and genotype 3A.

Thyroid per oxidase (TPO) value was 196.5 and TSH was 15.96. ANA was negative. Ultrasound scanning (USG) showed mild splenomegaly and upper gastrointestinal tract endoscopy was normal. Prednisolone 50 mg daily was begun with subsequent tapering and he was given 4 units of blood. After a few months, treatment of HCV was started with injected pegylated interferon alpha-2b- 80 microgram (as his weight was 54 kg) weekly for 9 weeks. After two months i.e. after the 9th dose of interferon, ribavirin was added with an initial dose of 200mg (1 tablet) twice daily in the first week which was gradually increased to 1 tablet three times daily in the following 3 weeks. The dose was further increased to 400 mg/day twice daily (2 tablets bid) for another 6 months.

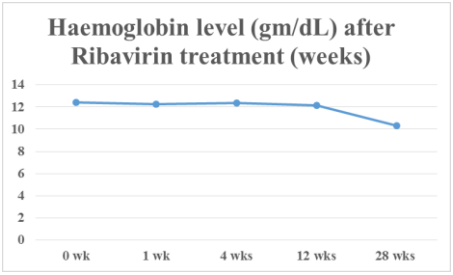

Figure 1 : Haemoglobin level on Ribavarin treatment

After 4 injections of interferon, the viral load decreased to 22,900 and after 8 injections, it came down to 200. After 4 months of interferon treatment, HCV RNA was not detected. . At the start of ribavirin treatment, his Hb was 12.42 gm/dl, 1 week after treatment Hb was 12.27, after 1 and 3 months Hb was 12.38 and 12.17 gm/dl respectively. After completion of 7 months treatment, his Hb was 10.3 gm/dl (Figure 1) with normal bilirubin, AST 66 U/L, ALT 84 U/L and a negative Direct Coombs Test.

The patient was followed up and no HCV RNA was detected up to June 2015

Discussion

Chronic hepatitis C virus (HCV) infection has been associated with various extra hepatic manifestations including autoimmune cytopenias.[5] Elhajj II et al.(2004) reported severe Coombs positive autoimmune haemolytic anaemia as an unusual extra hepatic manifestation of HCV infection.[6] Combination therapy with pegylated interferon (PEG-IFN) and ribavirin (RBV) is the current treatment of choice for chronic HCV infection[3] but this can exacerbate underlying autoimmune disorders and may result in a significant anaemia.[7] RBV causes a dose-dependent reversible haemolytic anaemia with decrease of Hb levels to 1 to 3g/dl over the first eight weeks of treatment.[8] RBV dosages therefore frequently need to be modified during the first eight weeks of treatment.[9] PEG-IFN may also contribute to anaemia by suppressing haematopoiesis.[7] In addition, PEG-IFN can itself exacerbate pre-existing autoimmune disorders or can de novo induce autoimmune complications.[10] Recently, a few case reports have described the occurrence of severe AIHA induced by PEG-IFN and RBV combination therapy.[10,11]. As a result, cytopenias and autoimmune diseases are relative contraindications to HCV therapy by PEG-IFN and RBV.

Although our patient was suffering from AIHA, he was treated successfully with ribavirin and interferon and steroids. Dietvorst et al [12] described a similar case where treatment was initiated with prednisone, leading to complete remission of AIHA. Subsequent antiviral therapy resulted in a sustained virological response, without recurrence of AIHA. However, they did note a drop in haemoglobin during treatment which was not seen in our case, probably due to the gradual incremental increase in the dose of ribavirin.

Directly acting antivirals (DAAs) are now the first line treatment for HCV infection because of shorter treatment course, higher remission rates, being oral agents and having less adverse events with better tolerability (including less haematological events). However, the cost of DAAs still limit universal availability of these agents for treatment of HCV in middle income countries such as ours where therefore the combination of Peg-INF/ribavirin still remains the only treatment option for most patients with HCV infection.

Conclusion

Successful management of our patient offers clinicians the message that patients with autoimmune haemolytic anaemia co-infected with HCV can be successfully treated without exacerbation of haemolysis by using prednisolone for treatment of the AIHA with timely incremental and rational dose selection of PEG-IFN and RBV.

References

1. NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consens State Sci Statements* 2002; 19:1-46.
2. Manns MP, McHutchison JG, Gordon SC, *et al*. Peg interferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *Lancet* 2001; 358:958-65. *doi : http://dx.doi.org/10.1016/S0140-6736(01)06102-5*
3. Fried MW, Shiffman ML, Reddy KR, *et al*. Peg interferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* 2002; 347:975-82. *doi : http://dx.doi.org/10.1056/NEJMoa020047*
4. Fried MW. Side effects of therapy of hepatitis C and their management. *Hepatology* 2002; 36 (Suppl 1):237-44. *doi : http://dx.doi.org/10.1002/hep.1840360730*
5. Ramos-Casals M, García-Carrasco M, López-1. *et al.* Severe autoimmune cytopenias in treatment-naive hepatitis C virus infection. Clinical description of 35 cases. *Medicine.* 2003; 82:87-96. *doi: 10.1097/00005792-200303000-00003*
6. Elhajj II, Sharara AI, Taher AT. Chronic hepatitis C associated with Coombs-positive hemolytic anemia. *Hematol J.* 2004; 5(4):364-6. *doi : http://dx.doi.org/10.1038/sj.thj.6200400*
7. McHutchison JG, Manns MP, Longo DL. Definition and management of anemia in patients infected with hepatitis C virus. *Liver Int.* 2006; 26:389-98. *doi : http://dx.doi.org/10.1111/j.1478-3231.2006.01228.x*
8. Kowdley KV. Hematologic side effects of interferon and ribavirin therapy. *Journal of Clinical Gastroenterology* 39 (suppl I):S3-S8, 2005. *doi : http://dx.doi.org/10.1097/01.mcg.0000145494.76305.11*

9. Fernando Crivelenti Vilar, Gleusa de Castro, *et al*. Autoimmune hemolytic anemia in HCV/HIV coinfected patients during treatment with pegylated alpha-2a interferon plus ribavirin *Revista da Sociedade Brasileira de Medicina Tropical.* 2007; 40(6):678-680. *doi : http://dx.doi.org/10.1590/S0037-86822007000600016*
10. 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. *No doi :*
11. Gentile I, Viola C, Reynaud L, et al. Hemolytic anemia during pegylated IFN-alpha2b plus ribavirin treatment for chronic hepatitis C: ribavirin is not always the culprit. *J Interferon Cytokine Res.* 2005; 25:283-5. doi : *https://dx.doi.org/10.1089/jir.2005.25.283*
12. M.H.P. Dietvorst, P. van Wijngaarden, R.A. de Man. Autoimmune haemolytic anaemia due to chronic hepatitis C virus infection treated with prednisone, pegylated interferon and ribavirin. *Netherlands Journal of Medicine.* 2009; 67(3):109-110 *No doi*