Case report

Management of Dually Active Chronic Hepatitis B (HBV) and Hepatitis C Virus (HCV) Co-Infection: Case Report

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ABSTRACT
We report the case of a 60 year old gentleman referred for management of dually active chronic hepatitis B (HBV) and C (HCV) co-infection. Initial treatment with Pegylated Interferon and Ribavirin was marked by early virological response for HCV as from week 12 with sustained high virological response to the end of treatment at week 48. There was however a non-response of the HBV to this peg interferon and Ribavirin and the introduction of a nucleoside analogue (Tenofovir) at the end of Peg interferon Ribavirin treatment at week 48 resulted in remarkable HBV suppression to undetectable HBV-DNA levels. While this case report demonstrates that HBV/HCV co-infection can be satisfactorily treated in our setting, the high prevalence of both viral infections in Cameroon, the high cost of management and the unavailability of appropriate drugs warrants the Ministry of Public Health to take the lead in implementing adequate preventive and therapeutic strategies so as to reduce morbidity and mortality of liver diseases associated with these infections.
Key Words: Hepatitis B, Hepatitis C, Co-infection, Interferon, Ribavirin, Tenofovir.

RÉSUMÉ
Nous rapportons le cas d'un homme de 60ans référé dans nos services à l'Hôpital Général de Douala pour prise en charge d'une coinfection chronique à hépatite C (VHB) et C (VHC), les deux étant actives. Cette coinfection a été découverte de façon fortuite lors d'un bilan systématique à son lieu de service. Le traitement initial à base d'interféron pegylé et la ribavirine a été marqué à 12 semaines par une réponse virologique précoce et soutenue du VHC jusqu'à la fin du traitement à la 48eme semaine. Néanmoins, une absence de réponse thérapeutique par le VHB à ce traitement a motivé l'introduction de Tenofovir à la 48eme semaine avec une suppression du VHB jusqu'à charge virale indétectable. Malgré le fait qu'à travers ce cas, nous avons démontré que la coinfection VHB/VHC peut être soignée de façon satisfaisante dans notre contexte, la prévalence élevée d'infections par ces virus au Cameroun, le cout élevé de la prise en charge et la non-disponibilité des médicaments appropriés demandent que le ministère de la santé publique prenne des mesures préventives et thérapeutiques stratégiques afin de diminuer la morbi-mortalité associée aux hépatopathies liées a ces infections.
Mots clés : Hépatite B, Hépatite C, Coinfection, Interféron, Ribavirine, Tenofovir.

INTRODUCTION

Hepatitis B (HBV) and C viruses (HCV) are the most common causes of chronic liver disease worldwide [1]. Co-infection is not uncommon especially in areas with high prevalence of both infections, as they share similar risk factors and transmission modes [1]. Patients with dual HBV/HCV infection have more severe liver disease and are at an increased risk for progression to HCC. The use of new cell culture models to examine the interaction between both viruses, has concluded that HBV and HCV may replicate in the same hepatocyte without interference as they have different biological properties, genomic structures and replicative mechanisms [2]. However, dual infections may thus result in additive damage to the hepatocyte, reciprocal or alternating inhibition of both viruses or selective inhibition of one virus which then appears dominant in the infection [2-4]. To date, no standard of care has been able to determine the true prevalence of HBV/HCV co-infection even though some data suggest that 2-10% of anti HCV positive patients are HBV surface antigen (HBsAg) positive and 2.7 – 22% of chronic hepatitis B patients are anti HCV positive [5]. In Cameroon an area of high endemicity to both viruses (7% for HCV and 10% for HBV [6]) no standard of care for dual infection has been established and most cases are managed based on clinician experience with the challenge of choice of optimal antiviral therapy. It was in the light of documenting our experience that we decided to present the case of a sixty year old gentleman with dually active HBV/HCV coinfection who responded favourably to treatment.

CASE HISTORY

A 60 year old gentleman referred to the Douala General Hospital, Cameroon, for specialist opinion three years ago following a positive serology for hepatitis B surface antigen (HBsAg) and HCV antibodies discovered fortuitously during a viral hepatitis awareness campaign in his company. Initial clinical evaluation found intermittent bouts of fatigue that has been occurring for many years as his main complaint which attributed to periodic intense office work. His medical history shows that he comes from a family of diabetics: his mother and three siblings are on insulin likewise him who was recently placed on insulin by a diabetologist with fairly satisfactory diabetic control. In 2008 he was diagnosed of sputum positive pulmonary tuberculosis (TB), treated according to guidelines of the Ministry of Public Health [7] and declared well. He has no previous history of blood transfusion, jaundice, surgery or an intervention with risk of transmission of hepatitis viruses. He does not smoke and drank alcohol sparingly less than 1 unit a week. On physical examination, he was not unwell, his weight was 75kg, vital signs were normal and there were no visible stigmata of chronic liver disease. Examination of other organ systems was unremarkable. At the end of the initial visit, he was briefed on the findings and laboratory tests were requested in order to evaluate the indication for treatment.

Initial baseline work-up showed haemoglobin level of 13g/dl, 4300white blood cells/mm^3 with 2494 polynuclear cells/mm^3 and 218.000platelets/mm^3on complete blood count (CBC), an erythrocyte sedimentation rate (ESR) at 48mm in the first hour, serum glutamate-oxalate transaminase (SGOT) at 82IU/l (Normal <40), serum glutamate-pyruvate transaminase (SGPT) at 61IU/l (Normal <40), Gamma glutamate transaminase (γGT) at 32, normal alpha fetoprotein level (αFP) 2.18ng/ml and Prothrombin time (PT) at 97.3%. Blood urea nitrogen (BUN), creatinine level, lipid profile, tetraiodothyronine (T4), and thyroid stimulating hormone (TSH) were all within normal limits. HIV serostatus was negative.

Further evaluation of hepatitis showed that Hepatitis B e antigen (HBeAg) was positive and Hepatitis D virus (HDV) antibodies were negative (ruling out HDV coexistence with HBV). Molecular characterisation and quantification showed that he harboured HCV genotype 1 with serum RNA levels at 7.37Log and serum HBV DNA levels of more than 9.0Log, signifying very high viral loads for both virus. Morphological studies of the liver by ultrasonography showed normal liver size and structure. Assessment of hepaitic fibrosis was done by a non-invasive marker of liver fibrosis: the fibrotest and staged metavirF4A2. No variceswere found on gastroscopy.

The above findings of HBV and HCV coexistence with very high viral loads, raised transaminases and high fibrosis markers were indication for antiviral chemotherapy. Without being able to distinguish which viral infection was dominant, we assumed co-dominance in which case a pegylated Interferon (PEG-IFN) based therapy could be beneficial in both infections. Treatment was thus commenced with PEG-IFN 180μg subcutaneously per week and Ribavirin 600mg per os twice daily according to guidelines for HCV treatment [8]. The patient was sensitised on the possible adverse effects of the treatment and reviewed on regular basis with the most common adverse effects being fatigue, headaches, joint pains which were managed symptomatically with no repercussions on his normal daily activities.

At week 12, patient review showed that serum transaminases (SGPT, SGOT) had normalised, there was early virological response (EVR)with HCV-RNA less than 1.2 Log. On review at week 24 and 48, it was found that the decrease in HCV-RNA that was seen at week 12 was sustained throughout this period. However, HBV-DNA remained very high throughout the course of Interferon/Ribavirin treatment at 24, 48 weeks respectively as seen in Table 1. A conclusion that there was HBV non-response to treatment was made and Tenofovir300mg orally per daywas added to the treatment regimen. With this treatment, there remained a sustained

virological response (SVR) for HCV and the viral load of HBV sustainably dropped through weeks 72 and 96 to 2Log by weeks 144 (Table 1)

Duration in Weeks / Viral load And Treatment	0	12	24	48	72	96	144
HBV-DNA (Log)	> 9	> 9	> 9	> 9	4.3	3.7	<1.3
HCV-RNA (Log)	> 7.37	< 1.2	< 1.2	< 1.2	< 1.2	< 1.2	< 1.2
Peginterferon	No	Yes	Yes	Yes	No	No	No
Ribavirin	No	Yes	Yes	Yes	No	No	No
Tenofovir	No	No	No	Yes	Yes	Yes	Yes

DISCUSSION

One of the main challenges faced in the management of patients co-infected with HBV and HCV is to determine which of the viruses is dominant. In the case of our patient, we assumed that both were dominant and therefore the treatment chosen was one that could be active against both viruses, hence beneficial for the patient. Another challenge is that of pre-treatment work up and viral load monitoring during treatment. These tests which require skilled laboratory technicians and expensive equipment are very costly for patients and cannot be afforded by most patients in Cameroon [9]. More so with the absence of subvention on this very expensive treatment many patients are left untreated because of low affordability. Therefore there is a bias in the selection of patients to be treated because gastrointestinal specialists in Cameroon who treat chronic HCV patients treat mainly those with health insurance policies as was the case of our patients whose treatment was subsidised by his company. However, with the high burden of Hepatitis in Cameroon and relatively low treatment rates, the Ministry of Health is reviewing strategies to put in place a treatment scheme for those who are infected with HBV and/or HCV and for a few years now, HBV vaccination has become part of the expanded programme of immunisation for children. Nevertheless, to the best of our knowledge, this is the first reported case of treatment of coinfection in our milieu.

Though we assumed that both viruses were dominant in our patient, treatment decisions should generally be made based on the dominant virus: if HCV is found to be dominant, treatment should be as per HCV (PEG-IFN and ribavirin) with achieved results comparable to those of HCV mono-infection. If HBV is dominant patient should be treated as chronic HBV infection. Concerning dual activity very few data are available. Looking at the evolution of viral load in our patient, one is tempted to believe that HBV was the most dominant given that response was poor up till weeks 48. On the other hand HCV could have been the most dominant and both viruses were being exposed to PEG-INF and Ribavirin which perhaps was inadequate for HBV and the addition of a nucleoside analogue appeared to be a feasible option though the best treatment regimen remains to be determined [5]. However, the drop in HCV viral load at week 12 was associated with the normalisation of transaminases and even though HBV viral load remained high, there was no evidence of a flare of HBV activity (as SGPT levels remained normal and fibrosis markers were unchanged) as was reported by other authors [2]. Our timing for the introduction of a nucleoside analogue following persistence of HBV-DNA could have been done at weeks 24 when persistently high viral load of HBV was first noticed but this late start was due more to the unavailability of Tenofovir which could have been commenced before the end of treatment with Peg interferon and Ribavirin. In Cameroon, Tenofovir is readily available in combination therapy for the management of HIV and patients with HIV/HBV coinfection get it for free, whereas, the Tenofovirmonotherapy is not even available for those who could buy and has to be ordered from overseas. Our patient was however lucky to receive Tenofovir with sustained HBV suppression. However, HBsAg and HBeAg remained positive.

CONCLUSION

With the above case, we have shown that in the absence of standardised guidelines for dually active chronic HBV/HCV co-infection, treatment with satisfactory results could still be done in our setting on condition that the treatment is tailored according to the case at hand with strict and close periodic monitoring of both viruses and their response to treatment. Given the high prevalence of both viral infections in Cameroon, the high costs of management, and the unavailability of appropriate drugs involvement of the ministry of health in mana¡ Health Sci. Dis: Vol 13 (2) (June 2012)*Luma et al*. indispensable for in decreasing the morbidity associated with chronic hepatitis.

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