A PATIENT WITH TUBERCULOUS LYMPHADENITIS COMPLICATING INTERFERON BASED HEPATITIS C THERAPY

ALAGAMMAI PALANIAPPAN
Department of Medical Gastroenterology,
CHRISTIAN MEDICAL COLLEGE

Abstract:
Interferon therapy, which remains a backbone of Hepatitis C treatment, is potentially immunosuppressive (1) and can predispose to infections (2). The association between Interferon and tuberculosis is not well described. We herein report a case of tuberculous lymphadenitis complicating Interferon therapy given for chronic Hepatitis C infection.

Keyword: Hepatitis C, Tuberculosis, Interferon, Ribavirin

CASE:
A 22 years old gentle man incidentally detected to be reactive for anti hepatitis C antibody, presented to us for further evaluation and management. He was asymptomatic and had no co-morbidities. Physical examination and basic laboratory parameters, including liver function tests, complete blood count, thyroid function tests and chest x-ray were normal. Serum HBSAg and HIV ELISA were negative. He was infected by HCV genotype 3 with a viral load in serum of 33000 IU/ml (done by real time PCR, Abbott, Germany). On ultrasonography, liver size and echotexture were normal and there was no evidence of portal hypertension. He was administered on Interferon 2b (3 Million units thrice weekly) along with Ribavirin (800 mg per day) for a duration of 24 weeks. During these 24 weeks, he was monitored optimally with regular clinical and laboratory assessments. His blood counts remained normal and he tolerated the treatment with only fatigue/feverishness as the major side-effects.

At the end of treatment at 6 months, though he achieved a complete virologic response, i.e. his viral load was not-detectable (lower limit of detection 12 IU/ml); he had enlarged cervical nodes on examination. Ultrasound neck showed multiple enlarged cervical nodes (of upto 2.2 cms) with necrotic center. Ultrasonography of the abdomen revealed mild ascites with enlarged peri-portal and peri-pancreatic nodes. Excision biopsy of the cervical node demonstrated caseous granulomatous inflammation, highly suggestive of tuberculosis (figure 1). Ziehl Neilsen stain did not reveal any acid fast bacilli.
Full dose routine anti-tuberculosis treatment, ATT (Isoniazid and Rifampicin for 6 months, supplemented by Pyrazinamide and Ethambutol for the initial 2 months) was given to this patient. Liver function tests were monitored regularly and he tolerated the medications with no side-effects. He showed good response to ATT with disappearance of nodes on clinical examination. Repeat ultrasonography of the neck revealed only <5 mm cervical nodes, which on biopsy showed reactive hyperplasia. Repeat ultrasonography of the abdomen was normal. The patient also developed hypothyroidism at the end of interferon therapy and was on thyroxine replacement. The patient remains to be well 6 months after the anti-tuberculous drugs. On testing, the HCV viral load remained persistently negative even at 6 months after stopping anti-viral medications (sustained virologic response).

**DISCUSSION:** Interferon plus Ribavirin therapy in chronic hepatitis C patients is reported to be associated with high rates of infections (2, 3) which is independent from the development of leucopenia (2). Despite the high infection rate, tuberculosis as a complication of Interferon therapy is rarely reported. Killingley et al reported one patient with TB after Interferon therapy in a HIV/ HCV coinfected Haemophilia patient (4). Development of tuberculosis during Interferon therapy in HIV/HCV coinfected patients is invariably found to be associated with a fall in CD4 count (5). There is scarcity on the information about the TB and interferon association among HCV monoinfected population. There are few case reports of TB infection/ reactivation during Interferon therapy either involving the lungs (6-9), lymph nodes or genitourinary tract (10). This may be secondary to reactivation of latent infection (4,6,10). However the interaction process between interferon and TB remains unclear. Thymic dysfunction due to Interferon and consequent lymphocytopenia and alteration in T cell compartments and cytokines is one of the hypothesis explaining infections during interferon therapy (1).

In our case, there was no lymphocytopenia during therapy. We did not measure the various compartments of lymphocytes, including CD4 cells during therapy, but CD4 count done at the completion of Interferon therapy was within normal range. There may be an alternative mechanism involved in the occurrence of TB in patients on Interferon therapy. In our case, we did not do a mantoux/ quantiferon gold prior to initiation of Interferon therapy, if a positive test was available, it would support the hypothesis of TB reactivation with Interferon therapy.

Initial TB symptoms, e.g. fatigue and fever, can be easily confused with the Interferon side effects and result in delay of diagnosis (5). This may have been the case with our patient. A knowledge about the possible reactivation of tuberculosis with interferon can keep the clinicians alert while encountering patients with suspicious symptoms. This may be of particular importance in TB endemic area like India.
Reference:


