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Case report

Regression of a case of Multiple Myeloma with antiviral treatment in a patient with chronic HCV infection ☆

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ABSTRACT

We report a case of a 54 year old patient with Multiple Myeloma (MM) and chronic HCV infection. In 2005 MM was diagnosed and a chemotherapy was prescribed. Before starting treatment a chronic HCV infection was found. When she came to our Institution for a second opinion, chemotherapy treatment was not considered immediately necessary so the patient was treated for the HCV chronic infection (Pegilated alpha-Interferon 180 μg/week and Ribavirin 1000 mg p.o./day). After one month of treatment she presented a reduction of Bence Jones protein (BJ) that further decreased in the following three months. The antiviral treatment was suspended after six months and a re-evaluation showed a complete viral response and a regression of MM. Sixty-eight months after the end of antiviral treatment the patient is asymptomatic and presents a condition compatible with an M-GUS. While the association between HCV infection and non-Hodgkin's lymphoma is consolidated and it is clearly demonstrated that antiviral treatment in these patients can induce a high proportion of partial and complete remission, a similar effect was never described in MM. The response obtained in our patient may suggest a possible a role of HCV in the pathogenesis of MM.

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It is well demonstrated that chronic Hepatitis C Virus (HCV) infection can be associated to non-Hodgkin's lymphoma (NHL)[1] and that antiviral treatment can produce NHL regression in HCV-related forms.[2,3] We observed a case of Smoldering Multiple Myeloma (SMM) and hepatitis C in which a clear regression of SMM followed successful antiviral treatment.

In a 54 year old woman routine blood tests revealed, in January 2005, a monoclonal IgG-k (1.87 g/dl). Bence Jones protein (BJ) was positive, with free k light chains 1.20 g/24 h. No bone lesions were found and the bone marrow biopsy showed 20% plasma cell infiltration, restricted for kappa light chains. Renal function was normal while alanine transaminase (ALT) and aspartate transaminase (AST) were elevated. An increased level of AST, ALT and gamma-glutamyl transpeptidase (GGT) was indeed present since 1985, but further investigations were not previously performed.

The patient was considered stage IA Multiple Myeloma (MM), according to Durie and Salomon criteria, so no therapeutic approach was chosen.

In the following months BJ progressively increased, reaching, in September 2005, 5.7 g/24 h, confirmed in multiple controls. The bone marrow needle biopsy and aspirate confirmed a plasma cell infiltration of 20%, in absence of anemia, renal impairment, bone lesions. The Fish (fluorescence in situ hybridization) analysis revealed deletion 13q14 in 49% of plasma cells. The patient was considered as having MM stage IIA, and a treatment consisting of vincristine, adriblastine and dexamethasone (VAD) was prescribed. Before starting treatment a chronic HCV infection was demonstrated, with b1 genotype and $> 5 \times 10^5$ UI/ml viremia. Liver biopsy found focal periportal low grade lymphoid infiltration with peacemeal necrosis, low portal fibrosis, concluding for chronic hepatitis with a slight degree of activity (1st degree 1st phase). Liver echography showed a diffuse hyper-reflecting structure.

At this point the patient came for a second opinion to our Institution; she was asymptomatic, so the anti-myeloma chemotherapy was not considered immediately necessary and an antiviral treatment with pegilated alpha-interferon (IFN) 180 μg/week and ribavirin 1000 mg p.o./day, was started.

One month after the start of antiviral treatment, a marked reduction of the BJ (586 mg/24 h) was already observed. Two months later, further BJ decrease was registered. The antiviral treatment was discontinued after 6 months (July 2006). The end of treatment re-evaluation documented a complete viral response (HCV-RNA: neg, AST, ALT, GGT in the normal range), while a significant regression of myeloma was also observed: 24 h proteinuria fell into the normal range, although free k light chains

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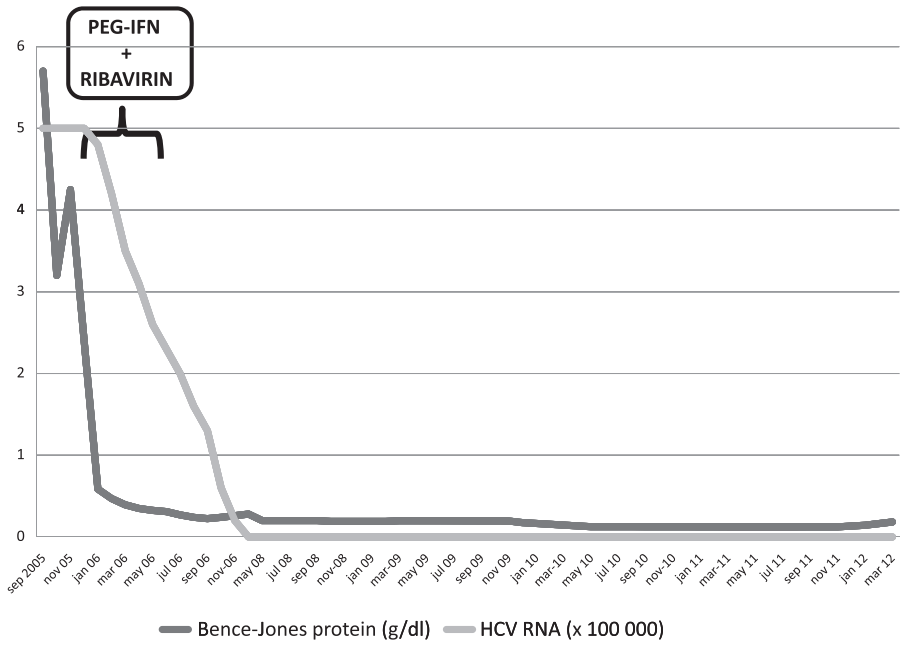

Fig. 1. Simultaneous decrease of HCV-RNA copy number and Bence-Jones protein after treatment with Peg-Interferon and Ribavirin in a patient with HCV positive micromolecular Multiple Myeloma.

were still identifiable by immunofixation. Serum monoclonal IgG-k component was also still present although reduced to 1.5 g/dl, while all the other hematochemical parameters were normal.

Sixty-eight months after discontinuation of antiviral treatment, the laboratory picture of the patient is unchanged, being compatible with an M-GUS without any bone lesion nor any clinical symptom; HCV-RNA is also negative, with normal liver function and serology (Fig. 1).

Although an epidemiological association between HCV and NHL is demonstrated,[1] a similar association is not clearly evident in the case of myeloma: indeed, in a case-control study, Bianco et al. described a similar proportion of HCV positivity in myeloma cases and controls.[5]

In HCV related NHL an antiviral treatment demonstrated a high proportion of complete or partial response of lymphoma: in 2002 Hermine et al. documented lymphoma regression in 9 patients with HCV-related splenic lymphoma with villous lymphocytes (SLVL) [3]; in 2005 Vallisa et al.[2] reported respectively 58% and 16% of complete and partial hematological response after the antiviral treatment with IFN and ribavirin.

Recently, a case control study revealed that HCV chronic infection is also a risk factor in acute myeloid leukemia, but no mention about regression of leukemia after antiviral treatment is reported in literature at the present time.[7] Although a not significantly higher prevalence of HCV correlation was described in hematological disease other than NHL,[5] no other reports about disease regression after antiviral treatment were described.

Finally Arcaini et al.[4] reported in 2011 the effect of antiviral treatment in a large cohort of indolent HCV-related lymphomas confirming response in 77% of patients.

No experience on the effect of antiviral treatment in HCV positive MM is reported to date. The clear response obtained in our case suggests a possible role of chronic HCV infection also in MM, and a possible relationship between viral response and regression of a SMM to a condition of M-GUS. IFN exerts a documented intrinsic anti-myeloma effect, as well as an anti-lymphoma effect: it is impossible to exclude, therefore, a direct effect of the drug against SMM. Limited improvement in terms of overall survival (7 months) and relapse free survival (4.4 months)[6] was demonstrated in a meta-analysis by Fritz et al. about IFN as single agent in maintenance therapy, while the efficacy as mono-therapy in induction is limited.[8] Moreover, in SLVL Hermine[3] evidenced no response in patients treated with IFN without HCV infection; in other experiences the hematological response was correlated to the viral response, but not to the interferon treatment. In conclusion, to our knowledge, this is the first case of regression of MM in an HCV positive patient following antiviral treatment; nevertheless, further studies are needed to confirm this evidence.

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