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Relationship between the pathogenesis of sarcoidosis and hepatitis C

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TO THE EDITOR

I read the article by Kim *et al*[1]with great interest. This is a rare case of systemic sarcoidosis in a patient with chronic hepatitis C without treatment for neither sarcoidosis nor hepatitis C. In this case, spontaneous resolution of sarcoidosis was noted while hepatitis activities were aggravating[1]. The authors suggest that this relationship mentioned above was not a fortuitous coincidence and these two diseases share a common pathogenesis due to the fact that interferon-induced immune activation is an important mechanism of viral replication suppression in chronic hepatitis C, hepatitis activities may be suppressed when chronic hepatitis C is combined with active sarcoidosis[1].

Before a conclusion like this, we consider that some points must be further clarified. Firstly, if there had been no spontaneous regression of sarcoidosis in the related case, one might have easily suggested that hepatic granulomas and cutaneous lesions were not associated with sarcoidosis in a patient who had no lung involvement confirmed by transbronchial biopsy. Hepatic granulomas have been described in up to 9.5% of liver biopsies from HCV-infected patients[2]. Additionally, in another series with hepatitis C, the prevelance of hepatic granulomas was found to be 1.3% before the initition of interferon therapy[3]. Furthermore, a study investigating the dermatopathologic manifestations of hepatitis C virus infection showed that palisading granulomatous inflammation may also present[4]. By contrast, a prospective controlled study recently reported that anti-HCV antibodies were not found in any patients of sarcoidosis[5].

In another aspect, the main controversy about sarcoidosis is its unkown pathogenesis. T-helper-1 (Th1) mediated cytokines, especially IFN-γ have a crucial role in the pathogenesis of the disease but IL-1, TNF-α and IL-2 are also contributory cytokines in inducing and maintaining of granuloma formation. This exaggerated Th-1 immune response is thought to be secondary to stimulation by either exogenous antigens (infectious or environmental) or autoantigens[6]. Although the potential role of IFN-α in the immunopathogenesis of sarcoidosis is not clear, the observations of coincidence of manifestation of sarcoidosis with IFN-α therapy for hepatitis C may support the concept of the cytokine network in pathogenesis of sarcoidosis[7,8]. Reported cases with spontaneous resolving sarcoidois after cessation of IFN-α treatment for hepatitis C may also support this hypothesis[9]. But it is important to remember that a considerable amount of IFN-α is being used in treatment of hepatitis C which may probably modulate an immune response resulting in an expression of a Th-1 mediated granulomatous reaction. Otherwise it is not known whether the amount of IFN-γ releasing during the natural course of sarcoidosis is sufficient to supress viral replication in hepatitis C. As known well in the early phase of hepatitis C, HCV continues to replicate in spite of high level IFN-α expression in the liver[10]. Additionally, plasma cytoid dentritic cells (PDC) predominantly release a considerable amount of IFN-α simultaneously[10]. On the other hand, not only non-cytolytic mechanism (IFN-γ) but also cytolytic mechanisms (Fas ligand, perforin, granzyme, TNF-α) mediated by cytotoxic T lymphocytes play an important role in clearance of HCV from the liver in chronic hepatitis C[10].

Moreover, in this case the duration of sarcoidosis was shorter (20 mo) than that of hepatitis C (20 years). In this regard, the absence of convincing evidence for the interaction of these two diseases has led us to consider a fortutious coincidence.

Certainly, this is a single case and it is obvious that genetic polymorphisms may contribute to individual difference=s in the regulation of cytokine release in sarcoidosis.

Further large and prospective clinical and basic studies are necessary to clarify the relationship between chronic hepatitis C and sarcoidosis.

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