Hepatitis C Virus with Normal Transaminase Levels

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Abstract
Approximately 30% of patients with chronic HCV infection show persistently normal alanine aminotransferase (PNALT) levels. The majority of these patients have some degree of histological liver damage. Controversies still exist regarding the definition of ‘persistent’ alanine aminotransferase (ALT) normality, and the natural history and optimal management of chronic hepatitis C with normal ALT. Although patients with HCV infection and normal ALT have been historically excluded from antiviral treatment, with the advent of the new treatment with PEG-interferon plus ribavirin, it has been suggested that the issue of whether or not to treat subjects with PNALT should be re-evaluated, and that antiviral treatment should be useful at least in selected subsets of patients.

During the course of HCV infection, alanine aminotransferase (ALT) levels could fluctuate, with long periods of biochemical remission [1–4]. It has been suggested that at least two different subsets of HCV carriers exist: patients with wide temporal ALT fluctuations, that could be within the normal range for several months, and true ‘biochemically silent’ carriers, showing persistently normal ALT (PNALT) values. The observation period should not be shorter than 12–18 months, and ALT determinations should be performed every 2–3 months.

The majority of HCV carriers with PNALT have some degree of liver damage on liver biopsy [5–13]. Liver disease is usually minimal/mild and fibrosis is generally absent or minimal [4–6, 8]. However, the natural history of HCV carriers with PNALT is probably not always so benign, and the possibility of a more severe evolution of liver disease among patients with PNALT cannot be ruled out. Several studies [7, 10, 13–15] reported a significant progression of fibrosis in approximately 20–30% of the patients with well-defined ALT normality, and the development of HCC in some cases has been described, despite persistent ALT normality [7, 16]. Sudden worsening of disease with ALT increase and histological deterioration has been described after up to 15 years of follow-up [17].

Historically, patients with PNALT have not been offered antiviral treatment on the belief that carriers with PNALT have milder disease than those with abnormal ALT levels and that IFN might worsen the course of the disease in many patients showing ALT flares during treatment. Given these data, the 1997 NIH Consensus Conference [1] and the EASL Consensus Conference [18] stated that IFN treatment should not be recommended in these subjects.

The introduction of the new combination therapy of PEG-IFN plus ribavirin allowed response rates higher than 50%, with a favorable risk-benefit ratio also in patients with benign or slow progressive disease [19].
Given the efficacy of the new treatments, which soon became the standard of care for CHC, the 2002 NIH Consensus Development Conference suggested that the issue of whether or not to treat subjects with PNALT should be re-evaluated, and that the issue at hand should be whether or not patients with mild disease should be treated [19]. ALT levels may have less importance in deciding who should be treated [19]. Many other factors might influence the decision to treat, such as the age of the patient, HCV genotype, liver histology, patient’s motivation, symptoms, extrahepatic manifestations, comorbid illness.

References


