

THE ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND HEPATITIS C VIRUS INFECTION

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ABSTRACT

Aim: *To study the association between rheumatoid arthritis and HCV infection.*

Subject and Methods: *The study included 40 RA patients diagnosed according to the ACR criteria (group I). It also included 20 inflammatory arthritis patients with RF positive but not fulfilling the criteria for diagnosis of RA (group II). Ten age and sex matched subjects were taken as controls. Anti HCV antibodies were detected in the sera of these patients.*

Results: *0.5% of the patients of group I had anti HCV antibodies while 20% of patients of group II had anti HCV antibodies. As regards the control group, none was anti HCV antibody positive.*

Conclusion and Recommendations: *There is a strong association between the presence of anti HCV antibodies and rheumatoid factor that is stronger than the association between anti HCV antibodies and rheumatoid arthritis. Patients with anti HCV antibodies may have rheumatoid factor positive in their serum, but the picture may not fulfill the criteria of RA. Thus in any case of inflammatory arthritis, hepatitis C virus must be put in consideration.*

INTRODUCTION

Despite major advances in our understanding of the pathogenesis of rheumatoid arthritis (RA), the etiology remains unknown. Current thinking favours the theory that the disease develops in genetically susceptible

individuals in response to one or more environmental triggers, with infection being considered the most likely (*Harris, 1990*).

Hepatitis C infection (HCV) has been associated with RA (*Hirohata et al., 1992*). It is critical to know if the reported associations with HCV infection result from the chance association of these disorders or if HCV predisposes to or causes specific rheumatic disease (*Wenner, 1996*). This allows some judgement about the importance of viral infection in the development of autoimmune disease, which may be related to a significant depression of the suppressor function of T-lymphocytes by viral infection (*Handzha et al., 1997*).

Another explanation for this association is related to the infection risk inherent in a number of medical procedures performed in RA patients (*Cimmino et al., 1996*). On the other hand, *Itoh et al. (1994)* stated that it is of importance in the HCV infected population is that the presence of these autoantibodies is not necessarily linked to rheumatic symptomatology. Thus, interpreting autoimmune serologies in patients with chronic HCV can be problematic. Nevertheless, circulating immune complexes may have biological effects even in asymptomatic individuals as supported by the finding of hypo-complementemia in volunteer blood donors infected with HCV.

Aim of Study:

In this study we aimed at clarifying the association between HCV infection and the presence of rheumatoid factor in patients diagnosed as rheumatoid arthritis and in patients complaining of inflammatory arthritis.

SUBJECTS AND METHODS

This study included 40 RA patients diagnosed according to the proposed 1987 revised American College of Rheumatology criteria for RA (*Arnett et al., 1987*). It also included 20 patients complaining of arthralgia with positive rheumatoid factor but not fulfilling the criteria for diagnosing RA. Ten healthy age and sex-matched subjects were taken as controls.

Any of the subjects with a history showing risk factors for development of HCV as intravenous drug intake or blood transfusion were excluded.

All subjects were subjected to the following:

- Full history taking and thorough medical examination.

- Investigations necessary for diagnosis of RA were done as ESR, RF, etc.
- Detection of antibodies to HCV with ortho HCV ELISA test system (second generation).

RESULTS

This study included 40 female RA patients (group I) whose ages ranged from 28 to 52 years. It also included 20 patients with inflammatory arthritis with positive RF but not fulfilling the criteria for diagnosis of RA (group II). Their ages ranged from 35 to 61 years. Ten healthy age and sex matched subjects were taken as controls. Their ages ranged from 30 to 58 years old.

The presence of rheumatoid factor and anti HCV antibodies were detected in both groups of patients and the controls and the results are shown in table (1).

Table (1): RF and anti HCV antibodies in groups I and II and control subjects.

Group	Number of subjects	RF +ve (%)	HCV Ab (%)
Group I	40	22 (55%)	2 (0.5%)
Group II	20	20 (100%)	4 (20%)
Control	10	-	- (0%)

The results show a strong association between the presence of anti HCV antibody and RF rather than RA disease itself.

DISCUSSION

Arthritis has been described in patients with liver disease. Inflammatory polyarthritis resembling mild non-progressive non-erosive RA was described in 13 patients with Laennec's cirrhosis in 1967 (*Pachas & Pinals, 1967*). The presence of rheumatoid factor in viral diseases and hepatitis has also been well established (*Bartfield, 1969*). More recently hepatitis B virus infection has been associated with polyarthralgia and polyarthritis preceding clinical hepatitis, which resolves after jaundice appears (*Ytterberg, 1993*). In 1989, the existence of HCV was established (*Choo et al., 1989*).

In our study, 2 out of 40 patients (0.5%) with inflammatory arthritis similar to RA were anti HCV test positive while 4 out of 20 patients (20%) with positive rheumatoid factor showed positive anti HCV test in their serum. As regards the control subjects, none of them was anti HCV test positive.

Thalmann et al. (1990) studied 13 male and 28 female RA patients who were all RF positive. The anti HCV was positive in 25 patients (61%). Also, *Tanaka et al. (1990)* studied the presence of anti HCV antibodies in the sera from patients with rheumatic diseases, 2 of 30 RA patients without a history of hepatitis were positive for anti HCV antibodies but they did not correlate the presence of anti HCV antibodies with the presence of rheumatoid factor. In the study of *Sprovieri & Ferri (1993)*, 16% of patients with positive RF were also positive for anti HCV antibody. They found no correlation between RF titer and HCV positivity. They took into consideration the known association between viral infection and the production of anti IgG antibodies and proposed that the selection of subjects with positive RF identifies a group with a higher prevalence of HCV infection.

Lovy et al. (1996) studied 19 patients with inflammatory arthritis who proved to be seropositive inflammatory arthritis. All patients were PCR positive for hepatitis C RNA except one patient. They concluded that HCV infection should be considered in any patient with a history of polyarthritis or unexplained positive RF as RA may be triggered or aggravated by HCV infection in a genetically susceptible host.

This can explain that some cases of hepatic injury attributed to drugs as methotrexate and non-steroidal anti-inflammatory drugs may be due to undiagnosed HCV infection.

Further studies are needed to clarify the validity of this study as HCV is suspected to exacerbate arthralgia, RF production and other signs of inflammation as there is a strong association between the presence of RF (not RA) and HCV positivity.

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التلازم بين مرض الرثيان المفصلي و الإصابة بالفيروس سى

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أجري هذا البحث لدراسة التلازم بين مرض الرثيان المفصلي و الإصابة بالفيروس سى. تمت هذه الدراسة على 40 مريضا مصابون بمرض الرثيان المفصلي و 20 مريضا مصابون بالتهاب المفاصل و لكن لم يشخصوا كرثيان مفصلي و عندهم عامل الروماتويد في المصل. و قد أخذ 10 أصحاء للمقارنة.

و عند تحليل الأجسام المضادة لفيروس سى في المرضى و الأصحاء وجدنا أن نسبة الإصابة بالفيروس أعلى في المرضى الذين عندهم عامل الروماتويد في المصل و أن ارتباط وجود الأجسام المضادة للفيروس بوجود عامل الروماتويد و ليس بوجود المرض نفسه و لذلك نوصى بان يوضع في الاعتبار الإصابة بـفيروس سى عند المرضى الذين يعانون من التهاب المفاصل حتى إذا لم يشخصوا كرثيان مفصلي.