Tocilizumab treatment in a patient suffering from rheumatoid arthritis and concomitant chronic hepatitis C infection

Sir, Immunosuppressive therapy with biologics in patients with RA and concomitant infection with HCV is a challenge in clinical practice. Tocilizumab (TCZ) is a humanized mAb directed towards the IL-6 receptor that has become a novel treatment option for RA. Here we report on an RA patient with chronic HCV infection who received TCZ during an 12-month follow-up period.

A 47-year-old man had suffered from RA since August 2004. RFs and anti-CCP antibodies tested positive [18 U/ml and >500 U/ml (normal <14 U/ml), respectively], and his radiological grade progressed sequentially to a Larsen score of III. Between August 2004 and July 2006, treatment with MTX and LEF also in combination with the TNF inhibitor adalimumab was discontinued due to inadequate response and development of a psoriasis pustulosa palmoplantaris. In July 2006, the patient was found incidentally to be infected with HCV (genotype 1b, viral load $5.7 \times 10^5$U/ml), with the route of transmission remaining unknown. When chronic HCV infection was diagnosed, the liver function tests (transaminases, bilirubin) were within the normal range, and the hepatic ultrasonography demonstrated normal liver parenchyma with no evidence of fibrosis or cirrhosis, therefore a liver biopsy was not warranted. Due to insufficient control of RA with conventional DMARD therapy, subsequent immunosuppression with three different biologic agents (adalimumab, etanercept, abatacept) failed to adequately control the high disease activity. The periodic liver function tests and hepatic ultrasonography were unremarkable.

Due to the high inflammatory state of the RA despite treatment with abatacept (DAS-28-ESR: 4.5), therapy with TCZ was initiated in September 2010. TCZ was accompanied by oral glucocorticosteroid (GS) therapy (prednisolone 12.5-20 mg daily). Due to the lack of data on TCZ treatment in RA patients with concomitant HCV infection, we have started TCZ therapy at a low dosage of 480 mg (4 mg/kg) and we subsequently increased the dosage to 640 mg and finally to the maximal dosage of 800 mg (8 mg/kg) monthly. For the first year during treatment the monthly testing of liver function as well as white cell counts were normal and the viral load remained stable (Fig. 1). During this period, the patient reported substantial improvement, which was in part reflected by a slight decline of the DAS-28-ESR scores (baseline: 4.5; 12 months: 3.5) and in normalization of his inflammatory markers [baseline: ESR 8 mm/h (normal <15 mm/h), CRP 22.3 mg/l (normal <5 mg/l), 12 months: ESR 2 mm/h, CRP 0.06 mg/l].

**Fig. 1** HCV-RNA levels and liver function enzymes [aspartate transaminase (AST), ALP and alkaline phosphatase (AP)] during the TCZ treatment did not reveal relevant changes.
Very recently, similar results with unchanged serum viral load and liver function during TCZ treatment of a multimorbid patient with RA and HCV were reported; however, the TCZ treatment was discontinued after only six doses due to foot cellulitis [1]. In the present case, an IFN-α/ribavirin therapy was not given to eradicate HCV, first due to the risk of further deterioration of the already active RA [2], and secondly due to unremarkable liver enzymes. Moreover, the presence of typical erosions and immunological findings established the diagnosis of RA, which could be clearly distinguished from HCV-related arthritis [3]. Thus, no benefit in the arthritis disease activity from HCV eradication was expected.

In a recent literature review, the safety profile of anti-TNF agents in the setting of HCV infection seems to be acceptable, even if differences in the hepatotoxic profile are apparent between different agents [4]. Furthermore, in cases of concomitant HCV infections, the most currently used traditional DMARD are associated with an increased hepatic toxicity [5]. An exception seems to be with CSA, as data demonstrated its safety in the treatment of autoimmune disorders with concomitant HCV infection [6]. In addition, findings from HCV-infected liver transplant recipients support the hypothesis that immunosuppression with low-dose GC may induce a favourable balance between the control of HCV replication and the minimization of liver damage [7] as opposed to high-dose GC on HCV infection in vivo, which were found to increase HCV dissemination [8]. The role of IL-6 and anti-IL-6 receptor therapy on the liver remains controversial. IL-6 seemed to have an elementary function in liver regeneration and induction of protective pathways during liver damage [9]. However, so far, clinical studies have not confirmed a potential inhibitory effect of anti-IL-6 agents on liver regeneration in humans [10].

In summary, we present the case of an RA patient suffering from concomitant chronic HCV infection, which has been safely treated over a period of 12 months with TCZ in combination with oral GS. However, TCZ should only be considered in these patients with extreme caution. Close monitoring of liver function and HCV-RNA levels is warranted in order to detect potential adverse effects early after TCZ initiation.

**Rheumatology key message**

- TCZ might be utilized in RA patients with HCV infection.

**Disclosure statement**. The authors have declared no conflicts of interest.

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References


