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Anti TNF α for Inflammatory Bowel Diseases in Cirrhotic Patients: A Feasible Option

Desideri Federico*, Pagnini Cristiano, Begini Paola, Menasci Francesca and Marignani Massimo

Digestive and Liver Disease Unit, Faculty of Medicine and Psychology, Sapienza University of Rome, S. Andrea Hospital, Rome, Italy

***Corresponding author:** Desideri Federico, via di Grottarossa 1035, 00189, Rome, Italy, Tel: +390633775615; E-mail: federico.desideri@gmail.com

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Anti TNFα for IBD in Cirrhotic Patients

In Inflammatory Bowel Disease (IBD), the pro-inflammatory cytokine TNFα plays a pivotal pathogenetic role, and the use of anti-TNFα biologic agents is an effective therapeutical option in such patients [1]. Despite the overall good safety profile, these drugs may produce unfavorable adverse events in particular, since TNFα in HBV patients may suppress viral replication, and then its inactivation might theoretically lead to viral reactivation and/or enhanced viral replication, with potential worsening of liver disease [2]. However, the effects of anti-TNFα on liver function in cirrhosis are largely unknown. Anti-TNFα drugs have been reported to cause acute drug induced liver injury or fulminant hepatitis per se, as described in a few cases [3]. The mechanism by which the anti-TNFα can produce such severe side effects is unknown, but dose dependent toxicity is unlikely, since the injury can occur even after the first administration [4]. Very few data are available on the utilization of TNFα agents in chronic hepatitis and to date, no trials are available on IBD patients treated with these drugs in cirrhosis set. In rheumatology, treatment with anti TNF alfa in a cirrhotic has been only described in one case report, a patient with alfa1antitripsin deficiency-related disease successfully treated with adalimumab for severe psoriasis, after infliximab discontinuation due to thrombocytopenia [5]. In patients with serological signs of current or past HBV infection, reports of viral reactivation and development of liver-related morbidity and mortality have been described because of anti TNF treatment [6]. Overt or occult HBV infection does affect the management of patients undergoing immunosuppression for therapeutic purposes [7]. These patients, including those receiving anti TNF treatment or even prolonged, high dose glucocorticoids, should undergo HBV screening, since it is possible to plan effective management when this condition is detected [8]. Several studies evaluated HBV reactivation rate during anti TNFα treatment and lack of antiviral prophylaxis/treatment was one of the factors associated with this event [9,10]. The American College of Rheumatology guidelines state [11] that TNFα blocking agents are contraindicated in the presence of significant liver injury (Child B/C stage), without clear indication for compensated cirrhosis (Child A) and coexistence of chronic HBV infection, and the European League Against Rheumatism (EULAR) indicates that these drugs should be generally avoided in patients with HBV. However, the European Crohn's and Colitis Organization (ECCO) guidelines state that immunomodulators are not contraindicated in HBV-infected patients. The guidelines recommend that HBsAg-positive patients should be treated with specific anti-viral agent before, during, and for at least 12 months after immunomodulation treatment has ceased [12]. In IBD patients, the available literature provided only a case [13] of a patient with compensated, HBV-related cirrhosis that underwent safely two lines of anti-TNFα (infliximab and adalimumab) for ulcerative colitis, without any liver or drug related side-effects suggesting that infliximab and adalimumab could represent a safe option in patients with compensated, HBV-related cirrhosis when adequate anti-viral management is applied. Thus, even if to date there are no randomized controlled trials evaluating the effectiveness of prophylaxis/treatment of HBV reactivation in anti-TNFα treated patients, the available literature [8,14] supports the notion that the appropriate management of chronic active HBV infection (antiviral treatment) might allow the patient to receive the best treatment of his underlying disease, improving its quality of life and minimizing the risks potentially severe effects due to viral reactivation.

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