

Entecavir and Intermittent Etanercept Therapy in a Patient with Concurrent Hepatitis B Virus Infection and Psoriasis

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Traditional systemic therapies are generally contraindicated in psoriatic patients affected by hepatitis B virus (HBV) infection due to the risk of immunosuppression related to the use of cyclosporine and methotrexate and/or the risk of liver toxicity resulting from the use of methotrexate and acitretin (1). Moreover, many authors suggest that anti-tumour necrosis factor (TNF)- α agents are associated with an increased risk of viral reactivation in patients with chronic inactive HBV infection (2). Although increased levels of TNF- α and TNF- α receptor are found in both the serum and hepatocytes of patients with chronic HBV infection (3), it appears that TNF- α , secreted by HBV specific cytotoxic lymphocytes, plays a pivotal role in the downregulation of HBV replication, by promoting "clearance" of the virus from the hepatocytic cells (3, 4). This would explain the reappearance of the HBV surface antigen (HBsAg) and the subsequent development of hepatitis in patients on long-term therapies with immunosuppressants and/or cancer chemotherapeutic agents (2, 5). We present here a case of a psoriatic patient affected by active HBV infection, who was treated with entecavir as first-line antiviral therapy during intermittent etanercept treatment.

CASE REPORT

A 41-year-old man presented with a moderate-to-severe psoriasis vulgaris present since the age of 34 years, characterized

by a recent rapid worsening and poor treatment response. He was treated with narrow-band ultraviolet B (UVB) (6 months) and cyclosporine 3.5 mg/kg/day (6 weeks) experiencing an unsatisfactory disease control and side-effects, respectively. Subsequently, he partially responded to acitretin 0.5 mg/kg/day and, after 9 months of treatment, laboratory tests revealed a consistent increase of liver function tests, aspartate-aminotransferase (AST) and alanine-aminotransferase (ALT), and the presence of active HBV infection, with positive envelope antigen (HBeAg+) screening test, consequently acitretin was interrupted and the patient was treated with entecavir 0.5 mg/day, leading to a gradual worsening of psoriasis. One year later clinical examination revealed a moderate-to-severe plaque-type psoriasis (Psoriasis Area and Severity Index (PASI) score: 17) associated with intense itching and severe impairment of quality of life (Dermatology Life Quality Index (DLQI): 22) (Fig. 1A).

We performed a complete blood cell count, liver and renal function tests, urine analysis, protein electrophoresis, tests for anti-nuclear antibodies, and anti-extractable nuclear antigen antibodies, tests for hepatitis B, hepatitis C and human-immunodeficiency-virus, a QuantiFERON-TB Gold test, an echocardiogram and a chest X-ray. All the aforementioned instrumental and laboratory tests revealed normal results, with the exception of liver function tests, AST (42 IU/l, n.v. 10–38) and ALT (82 IU/l, n.v. 10–41). With regard to tests for hepatitis B, HBV surface antigen and antibody were positive (HBsAg+; HBsAb+) as well as the HBV envelope antigen (HBeAg+), while the envelope antibody was negative (HBeAb-). The level of HBV-DNA was 0.2×10^3 IU/ml based on PCR assay (COBAS® Ampli Prep/COBAS® TaqMan® HBV Test, Roche, Branchbyrg; NJ, USA) that had a detection limit of 20 copies/ml. Liver ultrasonography showed normal liver cell structure. Hence, etanercept 50 mg once weekly was administered, in combination with entecavir, the



Fig. 1. (A) Patient condition before etanercept treatment characterized by a moderate-to-severe plaque-type psoriasis (Psoriasis Area and Severity Index (PASI) score: 17) associated with intense itching and severe impairment of quality of life (Dermatology Life Quality Index: 22). (B) Consistent clinical improvement in psoriasis following 24 weeks of etanercept treatment (PASI score: 1).

antiviral drug never interrupted after the HBV infection diagnosis. After 12 weeks we observed an almost complete improvement of PASI score (PASI 3.2), with concomitant reduction of AST (29 IU/l) and ALT (45 IU/l), HBV-DNA viral load values under the detection limit (0.1×10^3 IU/ml), without variation in other HBV infection markers (HBsAg+, HBsAb+, HBeAg+, HBeAb-). Treatment was continued without side-effects until week 24, obtaining clinical remission (PASI 1), thus etanercept was discontinued (Fig. 1B). Six months after treatment interruption, the patient relapsed (PASI 8). Routine laboratory investigations and liver function tests to screen for liver injury were normal. HBV infection markers resulted unchanged, while HBV-DNA was undetectable. Liver ecography showed mild steatosis. Hence, the patient was re-treated with etanercept 50 mg once weekly and obtained an excellent disease control after 12 weeks (PASI 2) and a further improvement until week 24 (PASI 1.2), when etanercept was discontinued again. No side-effects were observed during the re-treatment period. Liver function tests were ameliorated and there was no evidence of viral replication or variations in infection markers, both during treatment and the follow-up period (8 months).

DISCUSSION

In selected clinical cases, such as in presence of severe and unstable psoriasis, quality of life impairment, multiple treatment failures, the use of anti-TNF- α agents in patients with HBV infection, might be taken into consideration (6–9). In these particular cases, a multidisciplinary collaboration with a hepatologist is mandatory for the definition of a therapeutic or prophylactic regimen with an antiviral treatment (lamivudine, adefovir, tenofovir, telbivudine, entecavir), as shown by several reports in the literature (2, 6, 7, 10). In our case, due to the severity of psoriasis and the particular psychological patient profile, the risk/benefit ratio led to the decision to start an anti-TNF- α treatment. Among anti-TNF- α agents etanercept was preferred due to its efficacy and safety profile bound to its biochemical and pharmacological characteristics (soluble TNF- α receptor fusion protein) and for the option to use the drug with intermittent regimens (1, 6–9). Etanercept was administered in combination with entecavir, an oral deoxyguanosine nucleoside analogue with potent activity against HBV and a high genetic barrier to resistance (10, 11), recommended as first-line monotherapy and indicated for long-term use in chronic hepatitis B. Entecavir is administered orally at a dosage of 0.5 or 1 mg/day for a variable period of time depending primarily on HBe or HBs seroconversion. Follow-up visits are usually performed every 3–6 months (10, 11). In our patient entecavir was used as a continuous antiviral

treatment for approximately one year before etanercept therapy. In conclusion, our clinical experience suggests that the use of etanercept in a patient with psoriasis and hepatitis B could be successful and safe under concomitant entecavir administration and intensive monitoring of liver function tests and viral load.

Conflict of interests: GB has no conflicts of interest to declare. ME, AM, SC and AG served as consultants and speakers for Pfizer.

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