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CASE REPORT

Efficacy and Safety of Tildrakizumab in a Patient with Chronic HBV Infection

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Abstract: The introduction of biologic drugs revolutionized the management of moderate-to-severe forms of psoriasis. However, safety concerns still remain, particularly on patient affected by opportunistic infections. In this scenario, the safety of biologic drugs in patient with HBV infection is debated. Globally, screening for hepatitis before starting biological treatment is mandatory as well as a referral to an infectivologist and eventual prophylactic management should be evaluated case by case, also considering risk factors. On the one hand, the use of anti-Tumor Necrosis Factor seems to increase the risk of HBV reactivation, conversely, the use of recently approved classes of biologics [anti-interleukin (IL) 17 and anti-IL23] seems to have a lower risk of HBV reactivation. However, the evidence on the safety of anti-IL23 drugs in patients affected by HBV is scant, particularly for patients undergoing treatment with tildrakizumab. Herein, we report the first case of a female patient affected by moderate-to-severe psoriasis and with chronic HBV infection undergoing prophylaxis, successfully treated with tildrakizumab without reporting hepatitis reactivation. Even if limited, our case seems to confirm available evidence about the safety of anti-IL23, particularly tildrakizumab, on patients with chronic HBV infection undergoing prophylaxis.

Keywords: psoriasis, HBV infection, biologic therapy, anti-IL23, tildrakizumab

Introduction

Psoriasis is a chronic inflammatory skin condition affecting up to 3% of the worldwide population.[1] Despite the major knowledge on psoriasis pathogenesis led to the development of new effective and safe drugs, such as biologics and small molecules, the management of this condition may be still challenging.[2] Even if the introduction of biologics showed promising results in terms of effectiveness and safety, particularly for the most recently approved drug classes [anti-interleukins (IL) 17 and 23],[3–5] several safety concerns still remain, particularly on the use of biologics in patients affected by chronic bacterial or viral infections.[6]

Hepatitis B is a type of viral hepatitis caused by the Hepatitis B virus (HBV).[7] It can cause both acute and chronic infection and about 30% of worldwide population shows serological evidence of current or past infection.[7]

In this scenario, the immunomodulant nature of biologics makes patients with chronic infections a therapeutic challenge.[8] Even if limited, data on the use of biologic drugs in patients affected by HBV are conflicting.[8] On the one hand, the use of anti-"Tumor Necrosis Factor" α (anti-TNFα) seems to increase the risk of HBV reactivation,[6,9] conversely, the use of recently approved classes of biologics anti-IL-17 and anti-IL-23 seems to have a lower risk of HBV reactivation.[10–19]

The screening for hepatitis B is a routine measure before starting a treatment with biologics is recommended by current guidelines.[20] Patient with HBsAg positivity always require antiviral prophylaxis. A multidisciplinary approach, involving the infectivologist and/or hepatologist, in order to evaluate case by case an eventual prophylactic treatment is mandatory.[21,22]

Tildrakizumab, a humanized monoclonal antibody specifically targeting the p19 subunit of IL-23, is the latest available anti-IL-23 on the Italian market.[23] Even if its effectiveness and safety have been widely reported in both clinical trials and real-life experiences,[24–26] the safety of this drug in patients affected by HBV infection is lacking.

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Case Report

Herein, we report the case of a 45-year-old female patient referring to our Clinic in August 2021 for a worsening of its psoriasis disease. Clinical examination showed the presence of erythematous-desquamative plaques on the trunk, upper and lower limbs. Globally, the patient had a Psoriasis Area Severity Index (PASI) of 15.6, a Body Surface Area (BSA) of 18%, and a Dermatology Life Quality Index (DLQI) of 22. We considered that she was suffering from plaque psoriasis for 10 years. Previous psoriasis treatment included topical therapies (corticosteroids, calcipotriol/betamethasone) and narrow-band ultraviolet B. Screening for comorbidities was negative, except for mild hypertension, not requiring oral medications.

Screening for biologic drug was performed due to psoriasis severity, the impact on the patient's quality of life as well as patient's refusal to conventional therapies for safety concerns. However, blood examination showed positive results for HBsAg and HBcAb while HBsAb was negative. Moreover, the patient revealed that she did not receive HBV vaccination. Thus, HBV-DNA quantitative test was performed showing a negative result. A diagnosis of chronic HBV infection was carried out. The patient denied having carried out transfusions as well as the use of injection drugs and the familiarity for HBV infection. Thus, the cause of HBV exposure remained unknown. Subsequently, the patient was referred to the infectivologist, who prescribed prophylaxis with entecavir 0.5 mg once daily for at least two weeks before starting biologic treatment, with anti-IL-17 or anti-IL-23 classes as preferred ones. Tildrakizumab was chosen, due to the lowest number of administrations required among biologics (1 s.c. injection every 12 weeks after the induction phase), according to the patient's requests and started at labeled dosage (100 mg at weeks 0, 4, and every 12 weeks thereafter). At 4-week follow-up, PASI100 (reduction of PASI of 100%) response was rapidly reached, with a complete skin clearance (Figure 1). Hepatitis B markers and transaminases were evaluated at week 4, 16, and 28, without showing signs of HBV reactivation.

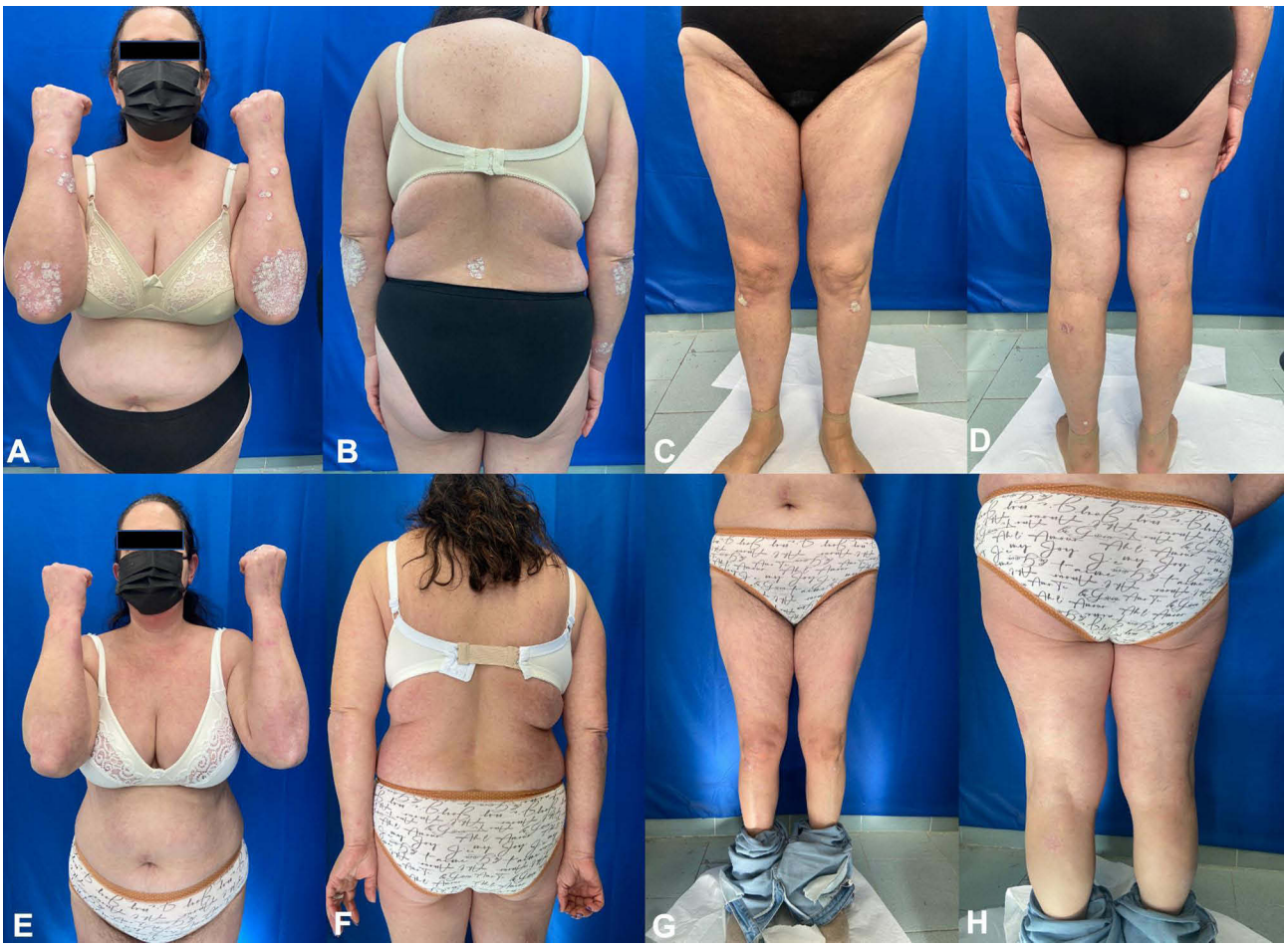

Figure 1 Patient at baseline (**A**–**D**) and after 4 weeks (**E**–**H**) of treatment with tildrakizumab.

Discussion

The introduction of biologic drugs revolutionized the management of psoriasis.[27–29] However, safety concerns may still remain, particularly on patient affected by chronic infections. In this scenario, the safety of biologic drugs in patient with HBV infection is debated. In particular, the use of anti-TNFα seems to increase the risk of HBV reactivation,[6,9] while the use of recently anti-IL-17 and anti-IL-23 seems to have a lower risk of HBV reactivation.[10–19]

Globally, screening for hepatitis before starting biological treatment is mandatory as well as a referral to an infectivologist and eventual prophylactic management should be evaluated case by case, also considering risk factors.[20,21] Patients with a resolved HBV infection do not require specialist follow-up while prophylactic treatment is necessary in patient with HBsAg positivity.[20,21] Of note, patients with HBcAb positivity and HBsAg negativity requires personalized management.[20,21] In these patients, monitoring of transaminases and viral markers with or without antiviral prophylaxis can be chosen following negativity or positivity of HBV-DNA, also considering patient's risk factors and after referral to the infectivologist and/or hepatologist.[20,21] HBV prophylaxis should be started at least 2 weeks before the introduction biological therapy and continued up to 6 months after biologic discontinuation.[20,21]

Currently, the evidence on the safety of anti-IL-23 drugs in patients affected by HBV is scant. In particular, in literature, there are only three cases of a patient with HBV history treated with tildrakizumab.[18,19] Gargiulo et al reported two male patients with HBV history (patient 1: HBcAb positive, HBsAb negative, HBsAg negative, HBV-DNA undetectable; patient 2: HBcAb positive, HBsAb positive, HBsAg negative, HBV-DNA undetectable) successfully treated with tildrakizumab without receiving prophylaxis for HBV infection and monitoring HBV reactivation up to 52 weeks.[18] Similarly, Ch'en et al reported the case of a man with HBcAb positive, HBsAb negative, HBsAg positive and HBV-DNA undetectable successfully treated with tildrakizumab and with a follow-up of 42 weeks.[19]

To the best of our knowledge, our case is the first reporting a female patient affected by moderate-to-severe psoriasis and with chronic HBV infection undergoing prophylaxis, successfully treated with tildrakizumab without reporting hepatitis reactivation. Even if limited, our case seems to confirm available evidence about the safety of anti-IL-23, particularly tildrakizumab, on patients with chronic HBV infection undergoing prophylaxis.

Conclusion

Psoriasis management is moving towards a personalized approach.[30] In this context, the treatment of patients with a positive hepatitis B screening should be evaluated case by case. Even if limited, our case suggests the safety of tildrakizumab also in patients with chronic HBV infection undergoing prophylaxis, suggesting this drug as a valuable option in these subjects. Certainly, further studies are needed to point out a tailored-tail approach in this class of patients.

Ethics Statement

The patient signed a written consent form for the publication of medical data. The consent for the publication of images was included with the patient's consent. Institutional approval was not required.

Consent Statement

Informed consent was provided by the patient for publication of the case.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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