Title
Dupilumab in patients with chronic hepatitis B on concomitant entecavir

Journal
JAAD Case Reports, 5(7)

ISSN
2352-5126

Authors
Ly, Karen
Smith, Mary Patricia
Thibodeaux, Quinn
et al.

Publication Date
2019-07-01

DOI
10.1016/j.jdcr.2019.05.007

Peer reviewed

Dupilumab in patients with chronic hepatitis B on concomitant entecavir

Karen Ly, BA, Mary Patricia Smith, BS, Quinn Thibodeaux, MD, Kristen Beck, MD, Tina Bhutani, MD, and Wilson Liao, MD
San Francisco, California

Key words: atopic dermatitis; biologic; dupilumab; Dupixent; hepatitis B virus.

INTRODUCTION

Biologics such as dupilumab are a highly efficacious and relatively safe treatment option for patients with recalcitrant immune-mediated disease; however, because of their modulation of the immune system, biologics have been associated with severe infections, including reactivation of latent hepatitis B virus (HBV).[1-3] As a result of the increased morbidity and mortality associated with active HBV, physicians are often reluctant to prescribe biologics in patients with chronic HBV infection. Dupilumab is the first biologic therapy approved for the treatment of moderate-to-severe atopic dermatitis (AD).[4] We present 2 cases of patients with AD and chronic HBV treated with dupilumab while receiving concomitant therapy for HBV.

Abbreviations used:

AD: Atopic Dermatitis
HBV: Hepatitis B Virus
IL: interleukin

CASE 1

The patient is 40-year-old man with a lifelong history of severe, generalized AD and chronic HBV via vertical transmission. He presented to our clinic in March 2015 with worsening pruritus and ill-defined erythematous, scaly plaques of the head, neck, trunk, and extremities. The patient was treated with clobetasol, triamcinolone, and mometasone creams with poor response. Because of his concomitant HBV infection, the patient was evaluated by a hepatologist before initiation of a systemic immunosuppressant. His HBV evaluation found normal liver enzyme levels and liver function tests and an HBV viral load of 19,120 IU/mL (alanine aminotransferase, 30 IU/L; aspartate aminotransferase, 34 IU/L; alkaline phosphatase, 55 IU/L; total bilirubin, 0.4 mg/dL; albumin, 4.1 g/dL). An abdominal computed tomography scan found no evidence of advanced liver disease or liver lesions, and a FibroScan showed no evidence of liver fibrosis.

The patient was simultaneously started on entecavir and cyclosporine. He had excellent virologic response to entecavir, and subsequent viral loads were undetectable. Laboratory monitoring occurred every 3 months and was reduced to every 6 months after viral loads became undetectable. After inadequate treatment with cyclosporine for 1 year, dupilumab was initiated, and the patient continued on cyclosporine and topical therapies as needed. His lesions improved significantly within 12 weeks, and cyclosporine was tapered. After 20 months of treatment, his disease remains well controlled on dupilumab monotherapy, he experienced no adverse events, and he maintained normal liver function levels with an undetectable HBV viral load.

CASE 2

The patient is a 73-year-old man with a longstanding history of severe, refractory AD, a 15-year history of prurigo nodularis, and chronic HBV well controlled on entecavir with an undetectable viral load. He first presented to our clinic in May 2011 with diffuse, erythematous plaques with lichenification of

From the Department of Dermatology, University of California, San Francisco.

Funding sources: None.

Conflicts of interest: Dr Liao has a research grant with Sanofi/Regeneron, which manufactures dupilumab. Dr Bhutani has a pending research grant with Sanofi/Regeneron. The rest of the authors have no conflicts to disclose.

Correspondence to: Karen Ly, BA, Department of Dermatology, UCSF, 515 Spruce Street, San Francisco, CA, 94118. E-mail: karen.ly@ucsf.edu.

JAAD Case Reports 2019;5:624-6.
2352-5126

https://doi.org/10.1016/j.jdcr.2019.05.007

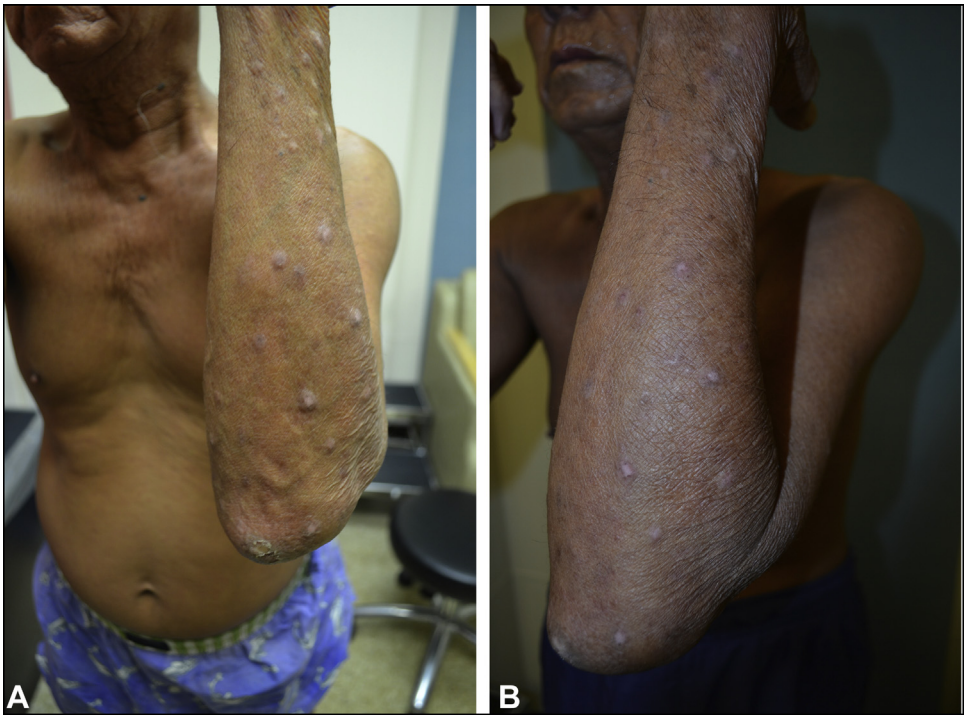

Fig 1. Clinical response of atopic dermatitis to dupilumab therapy. **A**, Week 4 of dupilumab treatment. **B**, Week 12 of dupilumab treatment.

the torso and extremities. On examination, he was also found to have prurigo nodules that were erythematous with excoriations and hemorrhagic crusts of the upper and lower extremities. His AD and prurigo nodularis were poorly controlled with topical treatments, phototherapy, and Goeckerman therapy. The patient was evaluated by the hepatology department and found to have no impairment of liver function (aspartate aminotransferase, 48; alanine aminotransferase, 26; alkaline phosphatase, 78; total bilirubin, 0.8) and an undetectable viral load. Abdominal computed tomography scan and FibroScan found no evidence of advanced liver disease. He was started on dupilumab with concurrent Goeckerman therapy and topical treatments. The hepatology department monitored the patient monthly, which was reduced to every 3 months when viral loads remained undetectable. The patient achieved excellent results within 12 weeks with a significant reduction in lesions and pruritus. He was treated with dupilumab monotherapy for 12 months with no adverse events. His liver function tests remained within normal limits, and his viral load was undetectable throughout his treatment (Fig 1).

DISCUSSION

HBV affects 847,000 to 2.2 million people in the United States and more than 400 million people worldwide.[1] It can cause complications of fulminant hepatitis, cirrhosis, hepatocellular carcinoma, and even death.[3,5] Because of the increased morbidity and mortality associated with HBV reactivation and the increasing prevalence of biologics, it is of utmost importance to define their safety profile in patients with positive HBV serology.[6] Dupilumab, the first biologic therapy for AD, is a fully human monoclonal antibody directed against the α subunit of the interleukin (IL)-4 receptor. It blocks the downstream effects of IL-4 and IL-13, key drivers of type 2-helper T-cell–mediated inflammation.[4] Its safety in patients with chronic HBV is not known, and, to our knowledge, this is the first report describing the use of dupilumab in patients with concomitant HBV.

IL-4 is a pleiotropic anti-inflammatory cytokine that is known to play an important role in the in the modulation of the hepatic immune system. The α subunit of the IL-4 receptor has been reported to promote liver regeneration through hepatocyte proliferation[7] and regulate both the progression and reversal of liver fibrosis,[8] and specific IL-4 genotypes have been associated with the development of chronic HBV after initial HBV infection.[9,10] Additionally, IL-4 has also been implicated in the progression to cirrhosis in patients with HBV.[10] Because of this involvement in the pathogenesis of chronic HBV and its associated complications and

the potential lower immunocompetence of patients on biologics, the decision to initiate dupilumab should be made with careful consideration and in collaboration with a hepatologist. Additionally, prophylaxis with antivirals should be considered to prevent a catastrophic hepatitis flare, liver failure, or HBV reactivation in the setting of immunomodulation therapy for AD.

We presented 2 cases of patients with concomitant HBV on entecavir, treated with dupilumab. Initiation of dupilumab was made after consultation and evaluation by a hepatologist with close surveillance of liver function and HBV status before and during treatment. The patients achieved significant improvement of their recalcitrant symptoms with no evidence of hepatitis or HBV reactivation, as determined by normal laboratory values and an undetectable viral load. Our patients had a positive response to dupilumab, and the treatment was well tolerated when combined with concomitant entecavir therapy and close monitoring of liver function and HBV status.

REFERENCES

1. Abramson A, Menter A, Perrillo R. Psoriasis, hepatitis B, and the tumor necrosis factor-alpha inhibitory agents: a review and recommendations for management. *J Am Acad Dermatol*. 2012;67(6):1349-1361.
2. Mastroianni CM, Lichtner M, Citton R, et al. Current trends in management of hepatitis B virus reactivation in the biologic therapy era. *World J Gastroenterol*. 2011;17(34):3881-3887.
3. Snast I, Atzmony L, Braun M, Hodak E, Pavlovsky L. Risk for hepatitis B and C virus reactivation in patients with psoriasis on biologic therapies: a retrospective cohort study and systematic review of the literature. *J Am Acad Dermatol*. 2017;77(1):88-97.e85.
4. Beck LA, Thaci D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med*. 2014;371(2):130-139.
5. Motaparthi K, Stanisic V, Van Voorhees AS, Lebwohl MG, Hsu S. From the Medical Board of the National Psoriasis Foundation: recommendations for screening for hepatitis B infection prior to initiating anti-tumor necrosis factor-alfa inhibitors or other immunosuppressive agents in patients with psoriasis. *J Am Acad Dermatol*. 2014;70(1):178-186.
6. Chiu HY, Chen CH, Wu MS, Cheng YP, Tsai TF. The safety profile of ustekinumab in the treatment of patients with psoriasis and concurrent hepatitis B or C. *Br J Dermatol*. 2013;169(6):1295-1303.
7. Goh YP, Henderson NC, Heredia JE, et al. Eosinophils secrete IL-4 to facilitate liver regeneration. *Proc Natl Acad Sci U S A*. 2013;110(24):9914-9919.
8. Weng SY, Wang X, Vijayan S, et al. IL-4 Receptor Alpha signaling through macrophages differentially regulates liver fibrosis progression and reversal. *EBioMedicine*. 2018;29:92-103.
9. Wu Z, Qin W, Zeng J, Huang C, Lu Y, Li S. Association between IL-4 polymorphisms and risk of liver disease: an updated meta-analysis. *Medicine (Baltimore)*. 2015;94(35):e1435.
10. Saxena R, Chawla YK, Verma I, Kaur J. Effect of IL-12B, IL-2, TGF-beta1, and IL-4 polymorphism and expression on hepatitis B progression. *J Interferon Cytokine Res*. 2014;34(2):117-128.