中文題目：以 ustekinumab 治療乾癬、乾癬關節炎病患之 B 型肝炎再活化情形: 一跨科別、多中心臨床研究

英文題目：Reactivation of hepatitis B virus infection in patients with psoriatic arthritis and psoriasis treated with ustekinumab: a cross-specialty, multicenter, real-world study

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Background:

More than 350 million people have been infected by hepatitis B virus (HBV) in the world. In high endemic area like Taiwan and Asia, HBV reactivation is a critical issue for psoriasis and psoriatic arthritis patients receiving biological disease modifying anti-rheumatic drugs. However, HBV carrier will almost impossible to be enrolled in clinical trials for psoriasis or psoriatic arthritis. Therefore, data of real-world practice becomes the only way to know the real risk of HBV reactivation during biologic treatment. Ustekinumab, a monoclonal antibody to the p40 subunit of interleukin-12 and interleukin-23, was widely used for psoriasis, psoriatic arthritis. Ustekinumab also revealed efficacy for patients with Crohn's disease or systemic lupus erymatosum.

Method:

We retrospectively collected the clinical and serological data about HBV reactivation under mandatory risk management program, of patients with active psoriasis or psoriatic arthritis with treatment of ustekinumab, by rheumatologists and dermatologists in two tertiary referral centers of central Taiwan. Totally 139 patients were enrolled during January 2013 to September 2019, with mean followed up period of 3.18 years. In our registry, 7.2% (10/139) with positive hepatitis B surface antigen (HBsAg) categorized as HBV carrier. And 57.6% (80/139) of them are with prior HBV infection by positive hepatitis B core antibody (antiHBc) in serological test, but with normal liver function and negative HBV DNA at baseline. Baseline disease activities, co-treatment (especially for systemic corticosteroids), and co-mobidities (diabetes, chronic lung diseases, cardiovascular diseases) were recorded.

Results:

Only in HBV carrier group, 6 events of HBV viral replication breakthrough (defined by increase of viral load for more than 1 log, in compared with baseline data) were detected. There is no viral, biochemical, or clinical breakthrough events in prior-HBV infection group (positive antiHBc but negative baseline HBV DNA), even without any antiviral pre-emptive treatment. In 10 patients of HBV carrier group, only 6 of them were with detectable HBV DNA at baseline. Only 3 of them received pre-emptive antiviral treatment, and there is no viral breakthrough. In the other 3 patients without pre-emptive antiviral treatment, events of viral breakthrough were detected in 8, 11 and 14 months after start of ustekinumab treatment, respectively. All of them received on-demanded antiviral treatment and then became stabilized. No one had to discontinue ustekinumab treatment. No other factor except detectable baseline HBV DNA and no pre-emptive antiviral treatment, were found to be correlated to HBV reactivation.

Conclusion:

Baseline HBV DNA, rather than positive HBs Ag only, is crucial for predicting HBV reactivation in Asian psoriatic arthritis and psoriasis patients treated with ustekinumab. Pre-emptive antiviral treatment is justified for HBV carrier with positive baseline HBV DNA.