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Key words: *5-fluorouracil, Darier disease, treatment*

Conflicts of interest: none declared.

Chronic hepatitis B reactivation and systemic glucocorticosteroid therapy

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SIR, We read with interest the article by Yang *et al.*[1] in a recent issue of the Journal in which they retrospectively reviewed patients with pemphigus vulgaris and dermatomyositis treated with immunosuppressive therapies including systemic glucocorticosteroid (GC). In the article, the authors suggested that four of 98 patients had developed hepatitis because of GC-induced hepatitis B virus (HBV) reactivation. The observation is quite informative and is particularly important to those patients in HBV-endemic areas requiring long-term GC therapy. However, the findings should be interpreted cautiously before concluding that the use of GC has led to HBV reactivation directly in these patients.

HBV reactivation is characterized by a temporal relationship between the rise in viral load of HBV, biochemical hepatitis and medication use. The occurrence of hepatitis during or immediately after cytotoxic chemotherapy is accompanied either by a 10-fold increase in HBV DNA levels or by an absolute increase that exceeds 9 $\log_{10}$ copies mL^{-1}, in the absence of other systemic infections.[2] Therefore, the baseline characteristics of HBV infection are essential to establish a definite diagnosis of HBV reactivation.

The overt biochemical flares or hepatitis in the article may have alternative explanations. The diagnosis of HBV reactivation would not be definite without comparison with the baseline HBV DNA level, as the possibility of silent viraemia before treatment cannot be ruled out. Further, a single elevation of HBV DNA level alone does not guarantee an increment of the level. Besides, it is not uncommon for HBV carriers to develop spontaneous flares – the incidence may be up to 32%[3] – and the use of GC in this setting could possibly be coincidental.

Based on the observation of this case series, Yang *et al.* recommended concurrent use of antiviral agents in chronic HBV carriers receiving long-term immunosuppressive therapy. Current practices are mostly derived from the experience of cancer patients receiving chemotherapy. In a study of Chinese patients with lymphoma, 27% were found to be seropositive for hepatitis B surface antigen. Of these patients, 47% developed reactivation of HBV during chemotherapy and this resulted in 5% mortality.[4] A study by Nakamura *et al.* of Japanese patients with lymphoma reported that only 3·3% of the patients had chronic HBV infection, but the incidence of severe hepatitis was found to be 53%, which was associated with a mortality rate of 24%.[5] Thus, preventing HBV reactivation in HBV carriers with lamivudine has been advocated in patients with haematological malignancies treated with chemotherapy.[6] However, little is known whether universal use of antiviral agents pre-emptively is indicated in noncancer patients under immunosuppressive or GC treatment because the antiviral agents are not panaceas. Prolonged use of lamivudine can decrease hepatitis flares. However, drug-resistant strains of HBV are an emerging problem (15% per year with lamivudine use).[7] Therefore, identification of high-risk groups for HBV reactivation is important before starting immunosuppressive therapy. The risk factors identified in cancer patients receiving chemotherapy include male gender, young age, diagnosis of lymphoma or breast cancer, seropositive hepatitis B envelope antigen, high pretreatment HBV DNA level, use of GC and high cumulative dose of GC.[8–10] In the article by Yang *et al.*, the proportion of HBV-infected patients in the study group was lacking.

We congratulate Yang *et al.* for this first report of possible HBV reactivation in dermatological patients on long-term GC. However, more studies are needed to draw a clear picture on this issue, such as the incidence, rate of severe complications and specific risk factors for HBV reactivation in this group of patients. At this moment, we cannot advocate the pre-emptive use of antiviral agents in these patients. For early detection of possible complications, we can screen the baseline HBV status and regularly monitor the liver function of these patients. When necessary, it is best for us to work in conjuction with gastroenterologists on this emerging problem.

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Key words: *glucocorticosteroid, hepatitis B*

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Chronic hepatitis B reactivation and systemic glucocorticosteroid therapy: reply from authors

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SIR, We thank Dr Wang and colleagues for their comments on our paper on reactivation of chronic hepatitis B virus (HBV) following systemic glucocorticosteroid therapy that was published in the September 2007 issue of this Journal.[1] The authors raise two issues. Firstly, they question whether the hepatitis in four patients described in this article does not represent 'reactivation' because they do not have a baseline HBV DNA viral titre for reference, and thus cannot fit the definition of HBV reactivation. Secondly, Wang *et al.* question the feasibility of antiviral drug prophylaxis therapy as recommended by us.

Regarding the first issue, the published article was limited by its scope as a retrospective study. As most dermatologists have traditionally neglected the risk of HBV infection and reactivation during corticosteroid therapy, only 21 of 98 patients (21%) were screened or recorded for serum hepatitis B markers status in this retrospective study. Thus, it was not possible to acquire a baseline HBV DNA viral titre. Even without a baseline HBV DNA viral titre for comparison, however, it is reasonable to conclude that there was a reactivation of HBV in these four patients based on the clinical history and course, as prednisolone is a known risk factor for HBV reactivation, as reported previously.[2]

Regarding the second issue, HBV reactivation is often encountered in lymphoma patients receiving chemo/immunosuppressive therapy. Currently, the consensus based on different studies noting reactivation of HBV in lymphoma recommends prophylactic use of antiviral therapy and monitoring of HBV DNA titre and liver function during lymphoma chemotherapy.[3–6] Certainly, more study is needed to demonstrate the optimal intervention time of antiviral therapy in patients with HBV treated with corticosteroids, but this would entail an extensive prospective cohort, preferably a randomized controlled trial, for definitive elucidation.

While we recognize the extensive research on the part of Wang *et al.*, it is our opinion that the points raised in their correspondence had been preliminarily addressed in our previous published paper. A prospective clinical study of HBV carriers undergoing systemic corticosteroid therapy along with a randomized controlled trial for analysis of optimal timing of antiviral drugs use would provide much insight into the phenomenon of HBV reactivation during immunosuppressive regimens.

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Unilateral segmental acneiform naevus: a model disorder towards understanding fibroblast growth factor receptor 2 function in acne?

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SIR, We present a 15-year-old boy with unilateral segmental acne on his right chest, trunk, shoulder and arm, including the extensor surface of the forearm (Fig. 1a). Multiple comedones as well as inflammatory papules and pustules were found in linear or whorled skin areas reflecting the lines of Blaschko.

