中文題目: 以 Rituximab 治療 MPO 陽性抗嗜中性白血球相關之血管炎併發帶狀泡疹病毒感染：個案報告

英文題目: Varicella zoster virus infection after rituximab treatment for myeloperoxidase (MPO)-positive ANCA associated vasculitis: A case report

作　　者: 張賀翔[1], 陳萱[2], 林威宏[1]

服務單位: [1]國立成功大學醫學院附設醫院內科部,
[2]國立成功大學醫學院附設醫院皮膚部

Introduction

Rituximab is an alternative induction agent for ANCA-associated vasculitis except cyclophosphamide. However, the infection rate within one year after the induction treatment remained high. The risk of herpes zoster reactivation increased with aging, and the risk may be higher after the use of rituximab.

Case presentation

A 78-year-old woman had history of MPO-Antineutrophil cytoplasmic antibody (ANCA)-associated crescentic glomerulonephritis (CGN), status post induction therapy with oral form cyclophosphamide. However, due to refractory condition, rituximab induction therapy was administered on 2020/11/12, 2020/11/19, and 2020/11/26. Besides, she also had stage 3b chronic kidney disease, dyslipidemia, and hypothyroidism.

She was admitted on 2020/12/03 for the forth cycle of rituximab administration originally. However, rituximab administration was hold, due to erythematous change with vesicles formation over the right breast, with extension to the right back, since 2020/12/01. She was diagnosed as herpes zoster infection, with right T1 and T2 dermatomes distribution. The patient was treated with Valaciclovir for 7 days, and crust formation was noted on 2021/12/08.

Discussion

Patients with ANCA-associated vasculitis (AAV) still had higher mortality than a matched general population despite advances in treatment in recent years[1]. The analysis of the early EUVAS trials showed the majority (28/59, 47.5%) of deaths within the first year of trial inclusion was contributed by infection[1]. All-cause mortality within one year of treatment for patients with AAV was associated with infections (% deaths: 0 infections 3%; 1–2 infections 10%, ≥3 infections 13%, P = 0.002)[2]. There was high risk of infections noted in the first year after immunosuppression, and respiratory infection was the most common[2]. And in RITUXVAS trial and RAVE trial, the rate of severe infections was similar in both rituximab and cyclophosphamide arm[3,4].

A single-center observational study including fifty-three patients with refractory granulomatosis with polyangiitis (GPA) treated with at least 2 courses of rituximab revealed 30 infections requiring antimicrobial therapy during the period of B cell depletion(the median time to return of B cells was 8.5 months (IQR 6–11 months)), and 4 herpes zoster infections were recorded[5]. Another single-center case-control study, including 9025 newly diagnosed and eligible patients with rheumatoid arthritis in Taiwan, revealed a higher proportion of ophthalmic herpes zoster in patients receiving therapy with non-TNF biologicals (rituximab/tocilizumab), compared with non-biologicals (20.0% vs 1.5%, $p<0.001$)[6]. Varicella-zoster virus (VZV)-specific memory T cells decline with age, and the peak incidence rate of herpes zoster in Taiwan was between 70 and 80 years old[78]. The major risk factors associated with herpes zoster are aging and immunosuppression through human immunodeficiency virus/acquired immune deficiency syndrome or malignancy[9]. CDC recommended Shingrix (recombinant Zoster vaccine) for all patient older than 50 years, and in patient having health condition, such as chronic renal failure, or taking low-dose immunosuppressive therapy (e.g., <20 mg/day of prednisone or equivalent, or using inhaled or topical steroids, azathioprine, mycophenolate mofetil), or in those anticipating immunosuppression (vaccinate ideally ≥4 weeks before treatment) [10].

Here, we reported an elderly woman, diagnosed with ANCA-associated crescentic glomerulonephritis, presented with herpes zoster after 3-cycle rituximab, which had not been reported in Taiwan. The association between herpes zoster infection and the use of rituximab in patient with AAV is unclear, and further study is needed.
For patients more than 50 years in whom immunosuppressive therapy including rituximab is planned, some experts suggest to immunize against HZ at least two to four weeks before planned treatment.

Conclusions: This case highlights the possibility of VZV reactivation in AAV patient with rituximab therapy, and recombinant zoster vaccine may be recommended before the beginning of the induction treatment with rituximab.

Figure 1. Multiple grouped clear-fluid containing vesicles erupted on erythematous

plaques along the right T4 dermatome (2020/12/03)

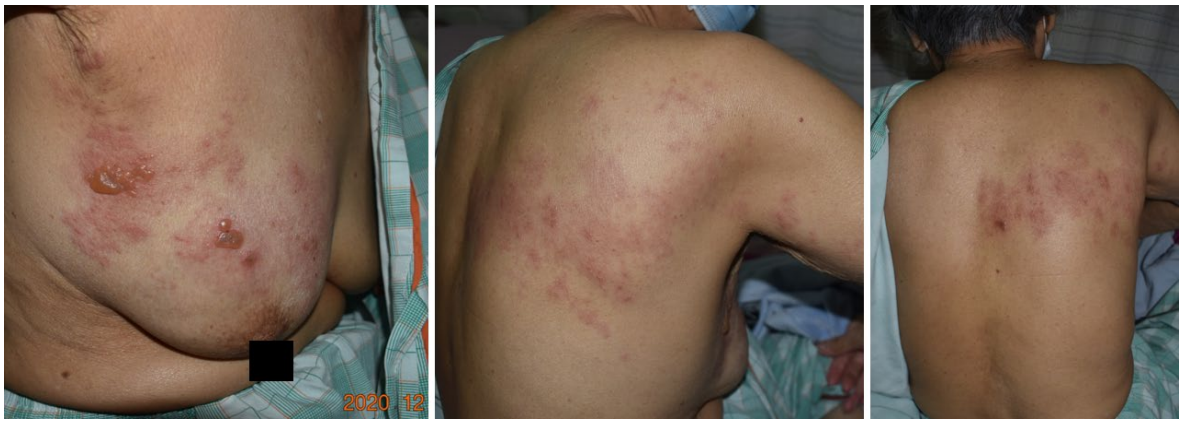
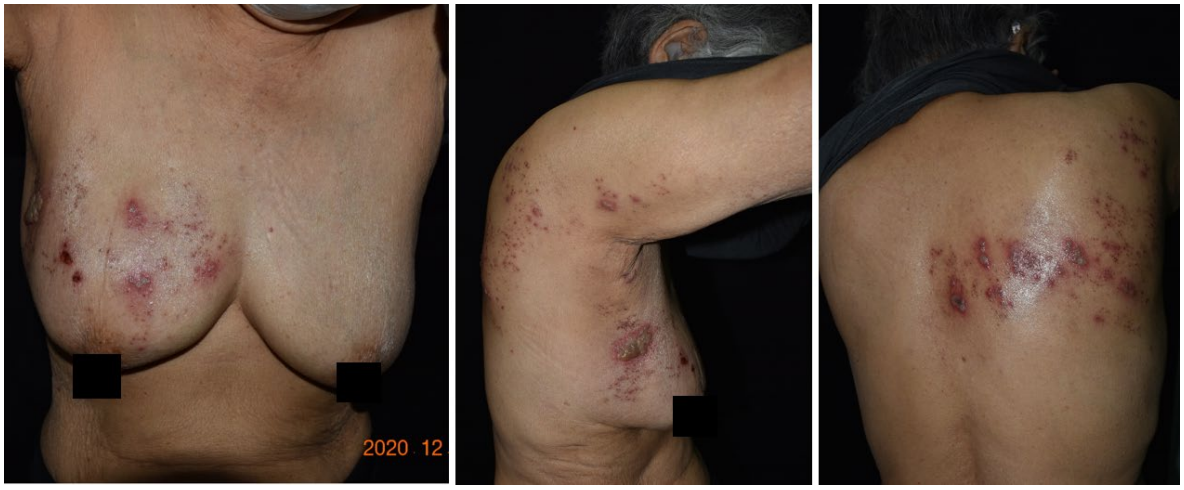


Figure 2. Significant remission of the background erythema with gradually dried out of the old vesicles after 5 days of antiviral therapy (2020/12/08)



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