Rituximab therapy in a case of pemphigus vulgaris triggering herpes simplex infection at varied sites

Sir,

Systemic glucocorticoids with or without adjuvant immunosuppressants has been the mainstay for the treatment of chronic blistering disorders such as pemphigus since decades; however, there are occasional cases that do not respond or have serious adverse events, requiring cessation of therapy. Novel agents such as rituximab, a chimeric monoclonal antibody against CD20 on B cells, have been used for the management of such refractory cases.

Rituximab was first used in paraneoplastic pemphigus by Borradori *et al*. for concurrent follicular B-cell lymphoma in 2001, with four infusions over one month.[1] Limited data is available on the efficacy and safety of rituximab in patients with pemphigus vulgaris (PV). Increasing incidence of various infections has been reported among patients treated with lymphoma and rheumatoid arthritis and the same may happen when rituximab is used in PV. Herein we report a case of a 32-year-old married woman diagnosed with PV who developed herpes simplex at an atypical site after treatment with rituximab.

A 32-year-old married woman presented with a history of recurrent erosions with crusting on the trunk, both upper limbs, and oral cavity, clinically suggestive of PV. The diagnosis was confirmed by biopsy. Serum antidesmoglein 1 and antidesmoglein 3 antibody levels (by ELISA) were also found to be raised above the normal range. Routine investigations including hemogram with erythrocyte sedimentation rate, urine examination, renal and liver function tests, chest X-ray, abdominal ultrasonography, and electrocardiogram were normal. The patient responded partially to treatment with systemic glucocorticoids and mycophenolate mofetil, but complete remission could not be achieved even a year after of treatment. Rituximab therapy planned in an intensive care set up. Injection dexamethasone (8 mg) intramuscularly, tablet paracetamol (500 mg) and oral domperidone (10 mg) orally were given as premedication. Rituximab was administered as intravenous infusion in the dose of 500 mg in 500 mL of normal saline at the rate of 50 mL/h over a period of 10 h. Vitals were stable and no adverse events were noted during the period of infusion. Four successive infusions were administered one week apart.

Three days after the first infusion the patient developed vesiculopustular lesions over her left palm [Figure 1]. Systemic

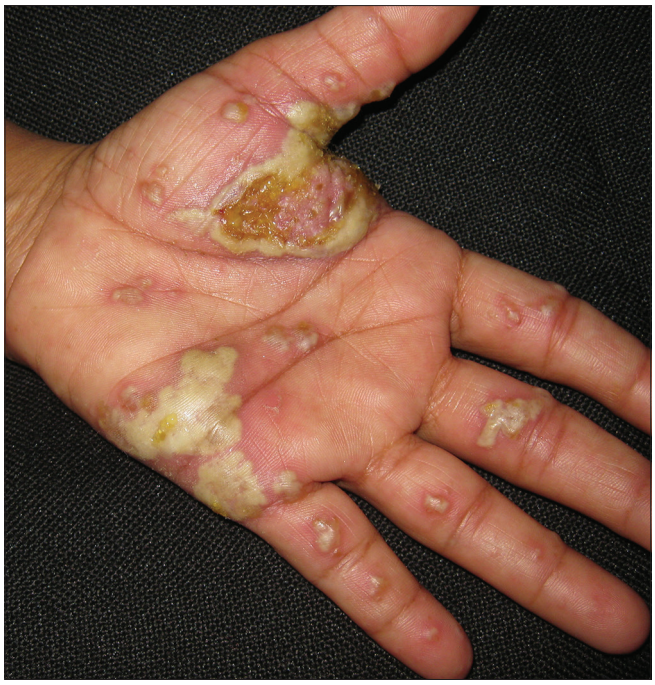

Figure 1: Vesiculopustular lesions on left hand after intravenous rituximab infusion—pretreatment

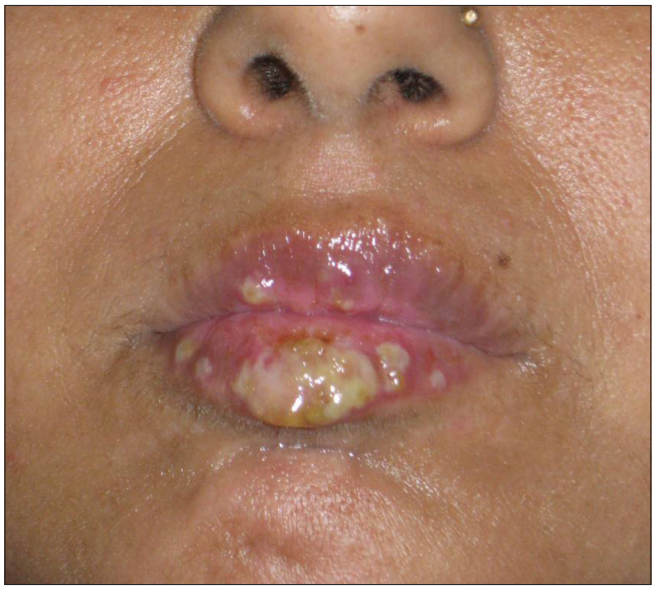

Figure 3: Herpes labialis

and local antibiotics were given, but there was no response. Subsequently, herpes simplex infection was suspected and Tzanck smear was found to be positive. Serum IgG and IgM Anti-HSV-I antibodies were found to be positive, although there was no past history of herpes labialis. The patient responded to oral acyclovir in the dose of 400 mg thrice a day for seven days with clearance of skin lesions over the palm within seven days [Figure 2].

Six days after the second infusion of rituximab, the patient developed vesiculopustular lesions on the lower lip with

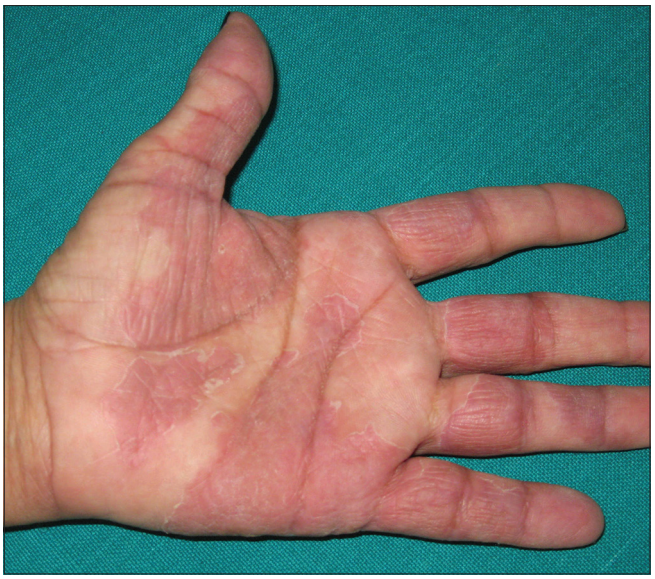

Figure 2: Clearance of lesions on left hand after oral acyclovir therapy for 7 days

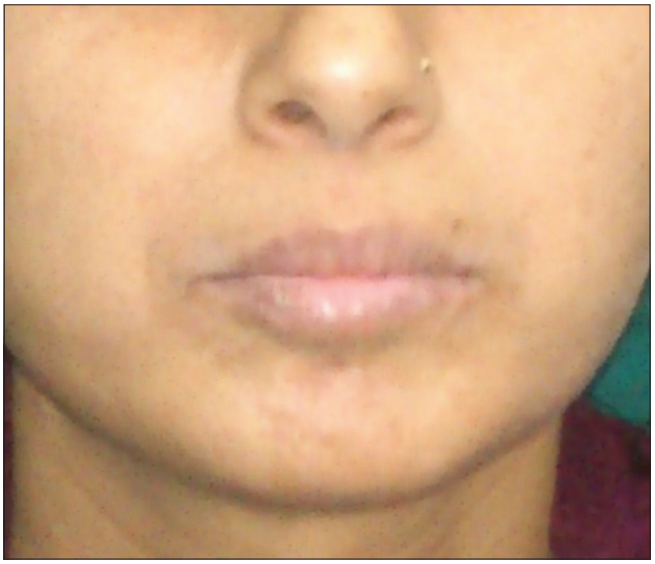

Figure 4: Herpes labialis—post treatment

oozing and crusting [Figure 3]. Recurrence of herpes labialis was suspected and the patient was treated with oral acyclovir 400 mg thrice a day for seven days to which she responded well [Figure 4]. This being a recurrent episode of herpes simplex infection, acyclovir was continued as prophylaxis till the last infusion, and one week thereafter. There was no episode of herpetic eruption during the subsequent infusions of rituximab. After 18 months of follow up without any medication, the patient remains symptom free for both herpes simplex infection and PV .

The US Food and Drug Administration have approved the use of rituximab in lymphoma, rheumatoid arthritis, chronic lymphocytic leukemia, and for Wegener's granulomatosis. Its use in PV is off label.[2] Chiu *et al*. reported concurrent

cytomegalovirus and herpes simplex virus infection in PV treated with rituximab and prednisolone.[3] Barnadas *et al*. also reported a case of paraneoplastic pemphigus associated with a CD20+ non-Hodgkin's lymphoma treated with rituximab, corticosteroids, and short courses of cyclosporine who developed sepsis due to *Listeria monocytogenes* and viral infections by human herpes virus 1 and 3 during the course of therapy.[4]

Our patient was in a constant state of immunosuppression due to systemic glucocorticoids and mycophenolate mofetil, compounded by her rituximab infusions. On first infusion, the diagnosis of herpetic lesions the over the palm could have been missed if it was not suspected and confirmed by serology and response to acyclovir therapy. Autoinoculation and reactivation of HSV may explain the change in site of infection after the second infusion of rituximab therapy. Thus, immunosuppression resulting from rituximab therapy may trigger recurrent viral and other infections that may occur at a different site each time; this should be looked for in every suspected case. All pemphigus patients must be probed for a past history of herpes simplex infection; if positive they should be offered prophylactic acyclovir therapy during therapy, especially rituximab infusions, to prevent recurrence and possible disseminated infection.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Borradori L, Lombardi T, Samson J, Girardet C, Saurat JH, Hügli A. Anti-CD20 monoclonal antibody (rituximab) for refractory erosive stomatitis secondary to CD20(+) follicular lymphoma associated paraneoplastic pemphigus. Arch Dermatol 2001;137:269-72.
2. Cianchini G, Lupi F, Masini C, Corona R, Puddu P, De Pità O. Therapy with rituximab for autoimmune pemphigus: Results from a single-center observational study on 42 cases with long-term follow-up. J Am Acad Dermatol 2012;67:617-22.
3. Chiu HY, Chang CY, Hsiao CH, Wang LF. Concurrent cytomegalovirus and herpes simplex virus infection in pemphigus vulgaris treated with rituximab and prednisolone. Acta Derm Venereol 2013;93:200-1.
4. Barnadas M, Roe E, Brunet S, Garcia P, Bergua P, Pimentel L, *et al*. Therapy of paraneoplastic pemphigus with Rituximab: A case report and review of literature. J Eur Acad Dermatol Venereol 2006;20:69-74.

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