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Bullous herpes zoster in a patient with bullous systemic lupus erythematosus

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Abstract

Bullous systemic lupus erythematosus (SLE) is a rare cutaneous manifestation of SLE characterized by sudden vesiculobullous eruptions. Herpes zoster infection may lead to rapid bullae development in patients with known bullous SLE. Herein, we describe a case of rapid development of bullous herpes zoster in a patient with bullous SLE. Patients with SLE and lupus nephritis exhibit an increased risk for herpes zoster infection. Bullous herpes zoster has been described in a previous patient with SLE and lupus nephritis. The current case illustrates that the presence of bullous SLE may have precipitated the development of bullous variant herpes zoster, as blisters leading to breakages in the skin increase risk for superinfection by viral pathogens. The current case highlights the importance of monitoring for skin changes in patients with SLE and maintaining a low threshold for infectious workup. Furthermore, it is important to recognize that the presence of bullae in SLE may confuse the diagnosis of bullous herpes zoster, leading to delays in diagnosis and management. Given high rates of morbidity and mortality in disseminated herpes zoster infection, the emergence of bullae in patients with SLE should raise a high index of suspicion for herpes zoster infection and prompt systemic workup.

Keywords: bullous, herpes zoster, lupus, lupus nephritis

Introduction

Bullous systemic lupus erythematosus is a rare autoimmune blistering condition characterized by an acute vesiculobullous eruption in patients with systemic lupus erythematosus (SLE). Individuals with SLE and lupus nephritis have a greater incidence of herpes zoster compared to the general population [1,2]. A rare clinical variant of herpes zoster known as bullous herpes zoster has been described in a case of a patient with SLE and lupus nephritis [2,3]. However, bullous herpes zoster in the setting of bullous SLE has not been described to date. Herein, we report a case of rapid development of bullous herpes zoster in a patient with well-established bullous SLE.

Case Synopsis

A 55-year-old woman with a history of SLE and biopsy-proven lupus nephritis on chronic immunosuppression presented to the dermatology clinic for evaluation of lesions on the abdomen. The patient was on 40mg prednisone daily, 1500mg mycophenolate mofetil daily, 200mg hydroxychloroquine daily, and belimumab 200mg subcutaneously weekly for SLE and lupus nephritis. Dermatologic examination revealed tense bullae on the left upper and lower abdomen (**Figure 1**). Two biopsies were performed for routine histology and direct immunofluorescence. Histologic findings

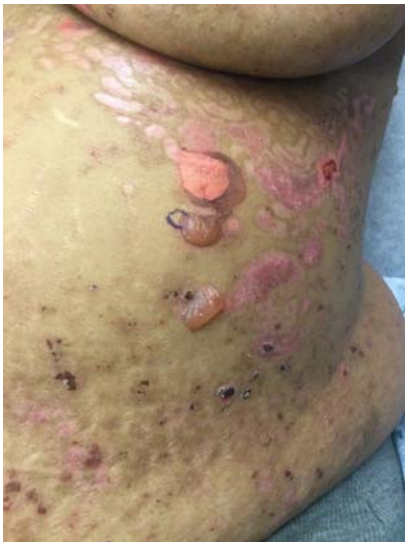

Figure 1. *Bullae on the left upper and lower abdomen.*

demonstrated subepidermal splitting with a neutrophil-rich infiltrate in the superficial dermis (**Figure 2**). Direct immunofluorescence demonstrated linear C3 deposits and equivocal IgG deposits at the basement membrane zone. These findings were consistent with the diagnosis of bullous systemic lupus. Type VII collagen antibodies were highly elevated at 98U/ml (normal <7U/ml). A baseline glucose-6-phosphate dehydrogenase level was 10.8U/gHb. The patient was started on treatment with dapsone 50mg, later increased to 100mg daily. One month later, the patient reported new lesions on the right side of the face, the roof of the mouth, and pain in the right eye region. On examination, there were coalescing bullae at the right temporal region extending toward the eye and scattered bullae with overlying yellow-brown crust

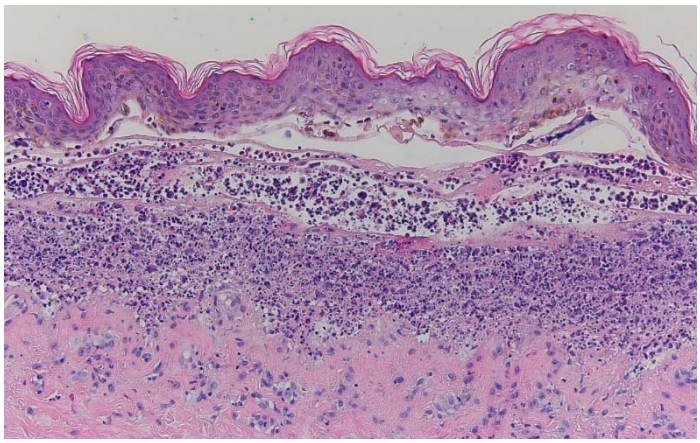

Figure 2. *Histologic findings demonstrating subepidermal splitting with a neutrophil-rich infiltrate in the superficial dermis.*

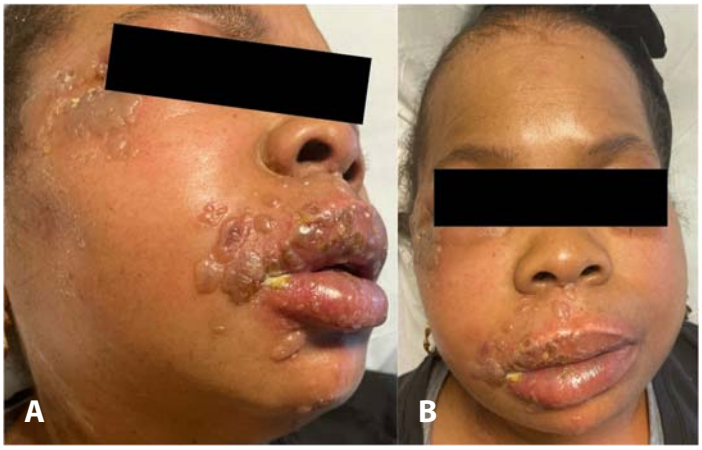

Figure 3. ***A)*** *Coalescing bullae at the right temporal region extending toward the eye and scattered bullae with overlying yellow-brown crust at the right side of the mouth extending into the lips.* ***B)*** *Swelling prominent on the right side of the face.*

at the right side of the mouth extending into the lips (**Figure 3A**). Swelling was prominent on the right side of the face (**Figure 3B**).

Due to concern for herpes zoster in an immunocompromised patient with secondary cellulitis, the patient was directly admitted to the hospital for renally-dosed IV acyclovir, vancomycin, and ampicillin-sulbactam. Viral polymerase chain reaction (PCR) of the facial bullae returned positive for varicella zoster virus (VZV) and bacterial culture returned positive for methicillin-susceptible *Staphylococcus aureus*. The patient was discharged on a 12-day course of valacyclovir (1000mg daily) with improvement of the lesions at follow-up.

Two months later, while she had not fully cleared bullous herpes zoster, she developed new large ulcerations in the right V3 distribution and pustular lesions on the scalp accompanied by postherpetic neuralgia, prompting dermatologic consultation. On examination, crusted, erythematous ulcers were present in the right mandibular region and right upper neck (**Figure 4A**). Pustules with underlying erythema were on the frontal and vertex scalp (**Figure 4B**). A viral PCR swab from the right neck ulcerations returned positive for VZV, and bacterial cultures from the ulcers and scalp pustules were positive for methicillin-resistant *Staphylococcus aureus*. The patient was admitted for non-healing herpes zoster with methicillin-resistant *Staphylococcus aureus* superinfection and began a

Figure 4. ***A)*** *Crusted, erythematous ulcers in the right mandibular region and right upper neck.* ***B)*** *Pustules with underlying erythema on the frontal and vertex scalp.*

14-day course of IV acyclovir (520mg every 12 hours) in addition to a 14-day course of IV linezolid (600mg every 12 hours). She also began treatment with oral doxycycline (100mg twice daily), mupirocin ointment, and gabapentin (300mg daily), with clinical improvement during hospitalization. She was discharged on valacyclovir (1000mg daily).

During follow-up one month later, there was healing of the right-sided facial and neck wounds, with post-inflammatory hyperpigmentation over regions of previous bullae formation and ulcerations (**Figure 5**).

Case Discussion

Bullous SLE is a rare cutaneous manifestation of systemic lupus erythematosus characterized by an acute vesiculobullous eruption that occurs owing to autoantibodies against type VII collagen at the dermoepidermal junction, resulting in subepidermal blistering [3]. Patients with SLE and lupus nephritis exhibit an increased risk for herpes zoster infection due to abnormal T cell cytotoxicity in the context of concomitant glucocorticoid and immunosuppressant use [1]. The bullous variant of herpes zoster has been described in few cases to date, with 63.6% (7 of 11) documented cases occurring in the setting of immunosuppression [2, 5-8], **Table 1**.

Immunosuppression may be a risk factor for bullous herpes zoster. Bullae formation in bullous herpes zoster may arise from superinfection with exfoliative-toxin-producing *Staphylococcus* [4]. Exfoliative toxin release by staphylococci superinfection, leading to

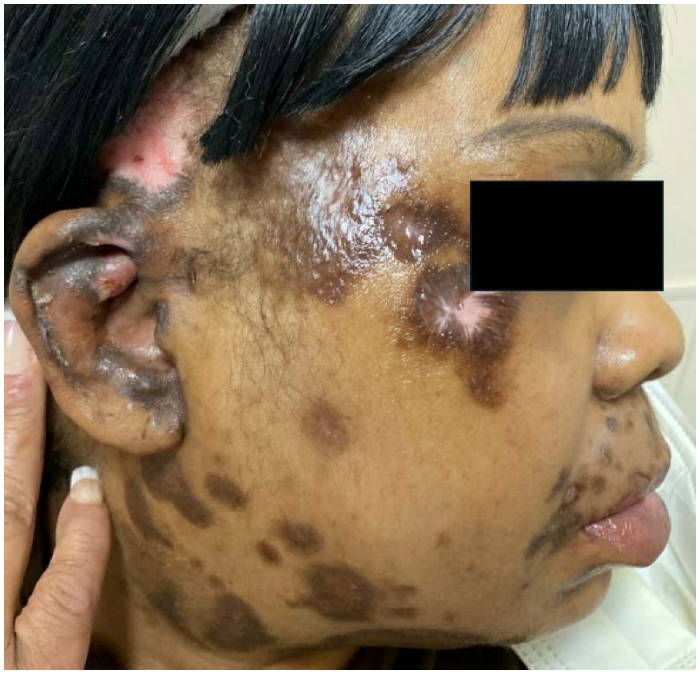

Figure 5. *Post-inflammatory hyperpigmentation over regions of previous bullae formation and ulcerations.*

cleavage of desmoglein 1, results in loss of keratinocyte adhesion in the stratum granulosum and subsequent bullae formation [8]. Patients with SLE may be predisposed to bullous herpes zoster owing to enhanced colonization by staphylococci species [9]. Bullous herpes zoster may also represent a distinct manifestation of herpes zoster, as cytological examination of bullous varicella demonstrated multinucleated giant cells lacking an abundance of polymorphonuclear leukocytes and bacteria [5].

Bullous herpes zoster has been described in a patient with a history of SLE and lupus nephritis on immunosuppressants in a reported case, with the case resulting in disseminated herpes zoster [2]. To the best of our knowledge, we report the first case of bullous herpes zoster in the setting of bullous SLE. In the current case, the presence of bullous SLE may have precipitated the rapid progression of disseminated herpes zoster. Disseminated herpes zoster may be more prevalent in severely immunosuppressed patients, including those with uncontrolled HIV infection [7]. Given high rates of morbidity and mortality in disseminated herpes zoster infection [6], especially among immunosuppressed patients [2], the presence of bullae development in patients with SLE should raise

a high index of suspicion for herpes zoster infection and prompt systemic workup.

Conclusion

The current case highlights the importance of monitoring for skin changes in patients with long-standing SLE and maintaining a low threshold for infectious workup. Furthermore, it is important to recognize that the presence of bullae in SLE may confuse the diagnosis of bullous herpes zoster, leading to delays in diagnosis and timely management. As morbidity and mortality in disseminated herpes zoster infection is high, prompt systemic workup is essential. The current case also illustrates that the presence of bullae in SLE may be a predisposing risk factor for bullous herpes zoster, as our patient developed herpes zoster with superimposed bacterial infection shortly after bullous SLE diagnosis. Blisters leading to breakages in the skin increase risk for superinfection by viral and bacterial pathogens, including VZV and *Staphylococcus*.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Chen D, Li H, Xie J, et al. Herpes zoster in patients with systemic lupus erythematosus: Clinical features, complications and risk factors. *Exp Ther Med.* 2017;14:6222-6228. [PMID: 29285180].
2. Widasmara D, Firdausiya F. Disseminated herpes zoster on a child with systemic lupus erythematosus and lupus nephritis. *Infect Drug Resist*. 2021;14:2777-2785. [PMID: 34321894].
3. Gammon WR, Briggaman RA. Bullous SLE: a phenotypically distinctive but immunologically heterogeneous bullous disorder. *J Invest Dermatol.* 1993;100:28S-34S. [PMID: 8423389].
4. Wong KJ, Osowicki J, Seaby E, Curtis N, Gwee A. Bullous herpes zoster. *J Pediatr Hematol Oncol.* 2004;26:587-590. [PMID: 24252791].
5. Haimi M, Ben-Arush MW, Kassis I, et al. Bullous herpes zoster in a child with leukemia: Case report and review of the literature. *J Pediatr Hematol Oncol.* 2004;26:587-590. [PMID: 15342986].
6. Jethwa T, Bertasi RAO, Kieneker L, Pattanaik S, Pujalte G. Bullous disseminated herpes zoster: An atypical presentation. *Cureus.* 2020;12:e9293. [PMID: 32832290].
7. Cohen PR, Beltrani VP, Grossman ME. Disseminated herpes zoster in patients with human immunodeficiency virus infection. *Am J Med*. 1988;84:1076-1080. [PMID: 3376978].
8. Brazel M, Desai A, Are A, Motaparthi K. Staphylococcal scalded skin syndrome and bullous impetigo. *Medicina (Kaunas).* 2021;57:1157. [PMID: 34833375].
9. Battaglia M, Garrett-Sinha LA. Bacterial infections in lupus: Roles in promoting immune activation and in pathogenesis of the disease. *J Transl Autoimmun.* 2020;4:100078. [PMID: 33490939].

Table 1. *Summary of demographic features, type of systemic lupus erythematosus, immunosuppressant treatment, distribution of herpes zoster, treatment of herpes zoster, and response to treatment among patients with a history of systemic lupus erythematosus and lupus nephritis presenting with bullous herpes zoster.*

Case	Age (Years)	Gender	Race	Type of SLE	Immunosuppressant treatment	Distribution of herpes zoster	Treatment of herpes zoster	Response to treatment
In-house	55	Female	Black	Systemic lupus erythematosus, lupus nephritis, and bullous systemic lupus erythematosus	Prednisone, mycophenolate mofetil, hydroxychloroquine, and belimumab for SLE and lupus nephritis; dapsone for bullous systemic lupus erythematosus	Right temporal region extending toward the right eye, right perioral region extending into the lips. Non-resolving herpes zoster on the scalp, right mandibular region, and right upper neck.	Treatment of bullous herpes zoster: IV acyclovir, vancomycin, and ampicillin-sulbactam; discharged on valacyclovir Treatment of non-resolving herpes zoster: IV acyclovir, IV linezolid, oral doxycycline, mupirocin ointment, and gabapentin; discharged on valacyclovir	Persistence of bullous herpes zoster following initial treatment; resolution of bullae and ulcerations following second round of treatment
Widasmara (2021)	14	Female	Asian	Systemic lupus erythematosus and lupus nephritis	Methylprednisolone	Face, anterior and posterior trunk, gluteus, bilateral upper extremities, dorsum of the hands, right lower extremity	Oral acyclovir	Resolution of bullae