

Herpes zoster in patients with systemic lupus erythematosus: Clinical features, complications and risk factors

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Received January 5, 2016; Accepted September 7, 2017

DOI: 10.3892/etm.2017.5297

Abstract. Herpes Zoster (HZ) is reported as the most prevalent viral infection in patients with systemic lupus erythematosus (SLE). The aim of the present study was to investigate the clinical features, complications, and potential risk factors of HZ in patients with SLE from Southern China. A retrospective study was performed among patients with SLE admitted to the First Affiliated Hospital of Sun Yet-Sen University (Guangzhou, China) between 2009 and 2013. Demographic information, clinical and laboratory data, and medications used were collected and analyzed. A total of 48 instances of HZ from 46 individuals in a cohort of 1,265 SLE patients during the follow-up period were identified, with an overall prevalence of 3.6%. Complications occurred in 23.9% of patients with HZ (11/46). The risk of HZ was highest within 3-6 months following SLE diagnosis and reduced thereafter. The multivariate logistic regression analysis demonstrated that lymphopenia (OR=4.6; 95% CI=1.5-13.8; P=0.006) and treatment with high-dose glucocorticoids (GC; OR=4.3; 95% CI=1.6-11.7; P=0.004) were both significantly associated with occurrence of HZ. Lymphopenia was the only independent risk factor for the occurrence of complicated HZ (OR=15.2; 95% CI=2.7-85.1; P=0.002). There are some notable characteristics of HZ in patients with SLE in Southern China, such as the tendency to manifest in an early stage of SLE, and frequent complications with benign outcomes. The present data supported the role of lymphopenia and high-dose of GC therapy as risk factors for the occurrence of HZ. Lymphopenia was also shown to contribute to complicated HZ.

Introduction

Herpes Zoster (HZ), which is a form of recurrent infection of varicella zoster virus (VZV), typically occurs decades after an instance of childhood VZV attack (1). It occurs most commonly in otherwise healthy, elderly individuals and immunocompromised hosts, including those with acquired immune deficiency syndrome, malignancies and systemic lupus erythematosus (SLE), amongst other conditions (2). The annual incidence of HZ is 1.5-3.0 per 1,000 persons in the general population in the United States and markedly increased to 6.4-32.5 per 1,000 person-years in patients with SLE (3-6). Furthermore, compared with healthy individuals, patients with SLE and HZ have a greater tendency to develop cutaneous and visceral dissemination of lesions (7), which are significantly associated with a poor prognosis (7,8). Furthermore, those with HZ are also more likely to develop bacterial superinfection during their disease course (9). At present, the most effective way to reduce the incidence and severity of HZ is zoster vaccination (10,11). Despite the overall efficacy of the zoster vaccine, this is uncertain in SLE patients and has a high financial cost (12,13). The zoster vaccine is currently not available in China, therefore patients who require treatment have to go abroad. Consequently, it is essential for clinicians to identify the risk factors that may predispose patients with SLE to the development of HZ. Risk factors predisposing SLE patients to HZ infection are not well established. A number of previous studies have attempted to identify risk factors for HZ in SLE; however, the findings of these studies were inconsistent (9,14,15). Furthermore, whereas the role of leucopenia has been extensively analyzed (15), lymphopenia as a risk factor for HZ is seldom discussed. However, incidence rates, patient history and risk factors differ markedly by geographical location and among different ethnic groups (3-6), possibly due to genetic and environmental factors. Little is known about the clinical features of SLE when complicated with HZ in Southern China.

It was hypothesized that a study of HZ in patients with SLE in Southern China may help increase the awareness of the extent and natural history of this disease in the region, assess therapeutic strategies on higher risk patients with HZ, and identify any subgroup(s) of patients who may benefit the most from the new zoster vaccine. In these regards, a retrospective study was performed to systematically examine the

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Key words: herpes zoster, systemic lupus erythematosus, complication, lymphopenia

prevalence, nature and complications of HZ in patients with SLE in a single rheumatology center. Clinical and laboratory features, as well as administered therapies were reviewed to determine their association with the occurrence of HZ as well as the complications of HZ.

Patients and methods

Study design and patients. A retrospective study was conducted using clinical records from the First Affiliated Hospital of Sun Yat-Sen University (Guangzhou, China) from January 2009-January 2013. A total of 1,265 patients recruited from the rheumatology outpatient clinics and inpatients department were diagnosed with SLE and fulfilled ≥ 4 of the American College of Rheumatology revised classification criteria for SLE (1997) (16). A diagnosis of HZ was clinically established by the presence of a typical vesicular eruption developing in a dermatomal distribution (14). Viral isolation by culture or serology was not done for confirmation of HZ. For the present study, only those patients with a history of HZ following the diagnosis of SLE were included. Patients with a history of HZ onset prior to SLE were excluded. Among these SLE patients, 46 were diagnosed with HZ, and another 48 age- and gender-matched SLE patients without history of HZ were randomly selected as control.

Review of the clinical files of these 94 SLE patients was performed and data was extracted. From the initial diagnosis of SLE, patients were subsequently followed-up until the occurrence of HZ. Follow-up also ended in instances of death or if there was no episode of HZ prior to the last documented visit.

Disease definitions. Complications of HZ were defined as the occurrence of one or more of the following conditions: i) Ocular, visceral or neurological involvements caused by VZV (17); ii) chronic (lasting for >30 days) atypical skin lesions; iii) postherpetic neuralgia (defined as pain persisting for >6 weeks following initial appearance of the rash) (8); iv) cutaneous dissemination (defined as vesicular lesions outside the primary and adjacent dermatomes) (7); and v) infections associated with HZ that required treatment with antibiotics.

Leucopenia was defined as a total white blood cell count $<4.0 \times 10^9/l$. Neutropenia was defined as a total neutrophil count $<1.5 \times 10^9/l$. Lymphopenia was defined as a total lymphocyte count $<1.0 \times 10^9/l$. Monocytosis was defined as a total monocyte count $>1.0 \times 10^9/l$.

Demographic, clinical, laboratory data and therapeutic variables. The following data were collected from medical records: Demographic information including gender and age at SLE diagnosis; duration between the onset of SLE and HZ; lupus disease activity; complications of HZ; clinical symptoms and signs; and laboratory findings such as blood routine test, various autoantibodies, erythrocyte sedimentation rate and C-reactive protein. The use of therapeutic agents including glucocorticoids (GC) and other immunosuppressive agents (ISA) within 1 month of HZ onset was also recorded. The dosage of GC was defined as none, low-dose (<30 mg prednisone or equivalent per day) or high-dose (≥ 30 mg

prednisone or equivalent per day). The SLE Disease Activity Index (SLEDAI) was used to evaluate SLE activity during HZ, and patients were defined as active SLE if the SLEDAI score was ≥ 6 (18).

Statistical analysis. Data was analyzed using SPSS 16.0 (SPSS, Inc., Chicago, IL, USA). Continuous data are presented as the mean \pm standard deviation. Categorical variables were presented as the absolute value and percentage. The Mann-Whitney U test was used to compare differences in continuous variables, and the chi-squared test was used for categorical variables. Variables that demonstrated significant associations with dependent variables in univariate analysis were included in a stepwise multivariate logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Demographic data. In the present retrospective analysis, from a total of 1,265 patients with SLE, 48 instances of HZ were recorded in 46 patients. In total, HZ patients accounted for a prevalence of 3.6%. Of these 48 patients, 2 experienced multiple episodes (2 each) of HZ, whereas the remaining 44 patients experienced only one episode during the follow-up period.

All subjects were of Chinese Han ethnicity. As presented in Table I, the majority of patients with HZ were female (95.7%) and mean age at the diagnosis of SLE was 35.0 ± 14.0 years (range, 18-75 years). The mean duration between the diagnosis of SLE and HZ was 9.1 ± 1.3 months, with a range from 0.5-36.0 months. Following SLE diagnosis, the risk of HZ was highest within 3-6 months and reduced thereafter (Fig. 1). The majority (31/46; 67.4%) of patients experienced HZ in this period, whereas the remaining 15 patients developed HZ in the chronic stage of SLE (>6 months).

Clinical characteristics of SLE patients with HZ. HZ skin lesions were most commonly located in the thoracic region (37/48; 77.1%), followed by the lumbar segment (6/48; 12.5%) and sacral area (3/48; 6.3%). The dermatome occurred in trigeminal regions in 2 instances (2/48, 4.2%), 1 in the inner corner of the eyelids and 1 on the tip of the ear.

A total of 35 patients exhibited typical skin lesions without complications. Of the remaining 11 patients who had complications in their disease course, 4 (8.7%) had superimposed infections that required antibiotic therapy (2 with pneumonia, 2 with sepsis and 1 with cellulitis), and 7 (15.2%) had postherpetic neuralgia. Only 2 of these 7 patients with postherpetic neuralgia had a course longer than 12 months. No patients in the present cohort experienced other serious complications, such as ocular, visceral or neurological involvement, chronic atypical skin lesions, and cutaneous dissemination.

Outcome and treatment. All patients received antiviral treatment with oral acyclovir or ganciclovir. A total of 10 patients (21.7%) were ultimately treated with intravenous ganciclovir due to clinical resistance to acyclovir. All cases had complete resolution of rash with no cutaneous scarring. There were no deaths attributed to HZ in the present cohort.

Table I. Comparison between SLE patients with and without HZ.

Characteristic	With HZ (n=46)	Without HZ (n=48)	P-value
Demographic characteristics			
Sex, male:female	2:44	7:41	0.2
Age at SLE diagnosis, years	35.0±14.0	33.8±14.4	0.7
Laboratory data			
ANA positive, n (%)	45 (97.8)	43 (89.6)	0.2
Anti-dsDNA positive, n (%)	27 (58.7)	24 (50.0)	0.4
Anti-Smith antibody positive, n (%)	3 (6.5)	8 (16.7)	0.2
ACL positive, n (%)	3 (6.5)	9 (18.8)	0.1
Leucopenia, n (%)	7 (15.2)	12 (25.0)	0.3
Neutropenia, n (%)	6 (13.0)	8 (16.7)	0.8
Lymphopenia, n (%)	17 (37.0)	6 (12.5)	0.008
Monocytosis, n (%)	18 (39.1)	14 (29.2)	0.4
Anemia, n (%)	29 (63.0)	24 (50.0)	0.2
Hypoproteinemia, n (%)	26 (56.5)	23 (47.9)	0.4
ESR, mm/h	36.8±30.7	44.1±23.9	0.2
CRP, mg/l	24.3±61.7	6.7±12.0	0.08
Clinical features			
Renal involvement, n (%)	36 (78.3)	27 (56.2)	0.03
Neuro-psychiatric manifestations, n (%)	3 (6.5)	3 (6.2)	1
Articular, n (%)	20 (43.5)	23 (47.9)	0.7
Mucocutaneous involvement, n (%)	21 (45.7)	26 (51.0)	0.6
Serositis, n (%)	5 (10.9)	7 (14.6)	0.7
SLEDAI	9.1±7.4	5.4±4.2	0.004
Active lupus, n (%)	25 (54.3)	14 (29.2)	0.02
Number of organs involved	2.4±1.3	2.3±1.2	0.6
Treatments prior to HZ onset			
Cyclophosphamide, n (%)	20 (43.5)	17 (35.4)	0.4
Mycophenolate mofetil, n (%)	8 (17.4)	9 (18.8)	0.9
Methotrexate, n (%)	6 (13.0)	7 (16.7)	0.4
Hydroxychloroquine, n (%)	38 (82.6)	32 (66.7)	0.08
Glucocorticoid, n (%)	42 (91.3)	42 (87.5)	0.7
Dosage, mg/day	34.8±38.4	13.9±11.7	<0.001
Low-dose ^a , n (%)	22 (47.8)	34 (70.8)	0.01
High-dose ^b , n (%)	20 (43.5)	8 (16.7)	0.004

Data are presented as the mean ± standard deviation unless otherwise stated. ^a<30 mg prednisone or equivalent per day; ^b≥30 mg prednisone or equivalent per day. SLE, systemic lupus erythematosus; HZ, herpes zoster; dsDNA, double stranded DNA; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SLEDAI, SLE Disease Activity Index; ANA, antinuclear antibodies; ACL, anticardiolipin antibody; Sm, Smith.

In total, 42 of the 46 patients (91.3%) were undergoing GC treatment at the time of HZ onset, at a mean equivalent dose of 34.8±38.4 mg (range, 5-200 mg) prednisone. A total of 20 patients (43.5%) received high-dose GC therapy, and the remaining 22 patients received low-dose GC therapy. Additional ISA were also administered in 40 patients prior to the onset of HZ, including 20 with cyclophosphamide (CYC), 8 with mycophenolate mofetil (MMF), 6 with methotrexate (MTX) and 38 with hydroxychloroquine (HCQ).

A total of 5 patients (10.9%) continued treatment with a previous dose of GC and the remaining 37 patients were treated with a decreased dose of GC (5.0-15.0 mg/day). Following the

onset of HZ, HCQ was continuously prescribed in 33 patients and discontinued in the remaining 5 patients. CYC and MMF were discontinued in all patients throughout their HZ episodes. MTX treatment was discontinued in 4 patients and continued in the remaining 2 patients.

Comparison of study variables between SLE patients with and without HZ. Demographic data, clinical characteristics and administered treatments were compared between SLE patients with and without HZ (Table I). SLE patients with HZ presented with a significantly higher SLEDAI score (9.1±7.4 vs. 5.4±4.2; P=0.004), a significantly higher proportion of active

lupus (54.3 vs. 29.2%; $P=0.02$), a significantly higher frequency of lymphopenia (37.0 vs. 12.5%; $P=0.008$), and a significantly higher percentage of renal involvement (78.3 vs. 56.2%; $P=0.03$) compared with SLE patients without HZ. Focusing on immunosuppressive treatment administered prior to the onset of HZ infection, the mean oral GC dose was significantly higher in SLE patients with HZ compared with non-HZ controls (34.8 ± 38.4 vs. 13.9 ± 11.7 mg/day; $P<0.001$). Instances of high-dose GC therapy prescription was significantly increased in HZ patients compared with non-HZ patients (43.5 vs. 16.7%; $P=0.004$). The frequency of patients who received ISA therapy was not significantly different between the two groups.

Factors associated with the occurrence of HZ in SLE patients. The risk of developing HZ was calculated for patients with SLE with various predisposing factors. All variables with a significant association with HZ in univariate analysis (Table II) were further included in a stepwise multivariate logistic regression analysis. The following variables were found to be risk factors for the development of HZ in patients with SLE in multiple analysis: Lymphopenia (OR=4.6; 95% CI=1.5-13.8; $P=0.006$) and high-dose GC therapy (OR=4.3; 95% CI=1.6-11.7; $P=0.004$). Therefore, these factors may act as predictors for the occurrence of HZ in patients with SLE.

Comparison of study variables between HZ patients with and without complications. Of the 46 SLE patients with HZ, 11 developed complications and 35 did not. The comparison of the study variables between these two groups is presented in Table III. Patients with complications of HZ exhibited significantly higher SLEDAI scores than patients without complications (13.0 ± 8.5 vs. 7.9 ± 6.8 ; $P=0.04$), which indicated that the disease was more active in patients with complications. Compared with patients without complications, patients with complications of HZ demonstrated a significantly higher percentage of lymphopenia (63.6 vs. 28.6%; $P=0.04$) and more abnormal hematologic findings (100 vs. 28.6%; $P<0.001$). The mean oral prednisone dose and the percentage of patients who received ISA therapy were similar between these two groups.

Factors associated with complications of HZ in SLE patients. Variables associated with the onset of HZ complications, i.e., lymphopenia and SLEDAI scores, were included in the multivariate logistic regression model. Lymphopenia was the only predictor of complicated HZ in the final model with an OR of 15.2 (95% CI=2.7-85.1; $P=0.002$). This finding indicated that SLE patients with lymphopenia were 15.2 times more likely to develop complications of HZ when compared with patients with normal lymphocyte count.

Discussion

VZV typically remains latent in cranial or spinal ganglia following resolution of a systemic infection (1). Reactivation, which tends to occur in elderly persons and immune compromised patients, induces a vesicular skin eruption accompanied by pruritus and dysesthesias (19). Minimal information is available in the literature describing the characteristics of HZ infection. To the best of our knowledge, the present study is the

Table II. Significant variables associated with occurrence of herpes zoster on univariate logistic regression.

Variable	Crude OR (95%CI)	P-value
Lymphopenia	4.1 (1.4-11.7)	0.008
Renal involvement	2.8 (1.1-6.9)	0.03
Active lupus ^a	2.9 (1.2-6.8)	0.01
High-dose GC ^b	3.8 (1.5-10.0)	0.006

^aSystemic lupus erythematosus disease activity index >6 ; ^b ≥ 30 mg prednisone or equivalent per day. OR, odds ratio; CI, confidence interval; GC, glucocorticoid.

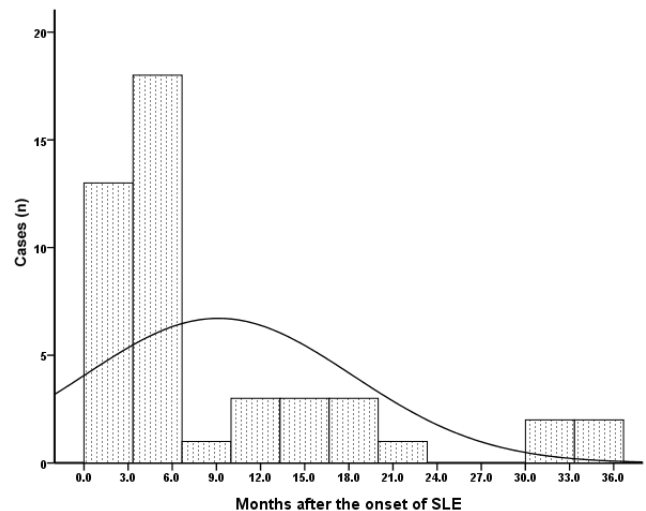


Figure 1. Time distribution of occurrence of HZ in relation to the onset of SLE. In the majority of patients (67.4%; 31/46), HZ was diagnosed within 3-6 months following SLE diagnosis, and rates reduced thereafter. HZ, herpes zoster; SLE, systemic lupus erythematosus.

first from Southern China to focus on SLE patients with HZ infection. Of note was the lower prevalence than that reported from other Asian regions. In a previous study from Saudi Arabia by Sayeeda *et al* (7), a total of 32 cases of HZ infection were identified among 624 SLE patients with a prevalence of 5.1%. Ishikawa *et al* (6) previously reported that Japanese patients with SLE were vulnerable to HZ with an incidence of 46.6%. There are two possible explanations for the lower prevalence in the present cohort. Firstly, the retrospective nature of the present study may have led to an underestimation of the incidence caused by mild HZ cases. Secondly, it may be due to the large number of patients who received HCQ, which had a wide range of antimicrobial effects. There are two previous studies that suggested that antimalarials may be protective against infections in patients with SLE (20,21).

The present study also indicated that most instances of HZ occurred early in the course of the disease, with the peak occurrence of HZ at 3-6 months following SLE diagnosis. This time period was earlier than other reports. Nagasawa *et al* (22) previously summarized that almost half of the Japanese adult patients developed HZ in the first year following SLE diagnosis. Borba *et al* (4) observed that HZ was typically a

Table III. Comparison of SLE patients with complicated and uncomplicated HZ.

Characteristic	Complicated HZ (n=11)	Uncomplicated HZ (n=35)	P-value
Demographic characteristics			
Sex, male:female	0:11	2:32	1.0
Age, years	32.1±13.4	35.8±14.5	0.5
Duration of SLE, years	3.4±5.1	2.9±4.4	0.8
Laboratory data			
ANA positive, n (%)	11 (100)	34 (97.14)	1.0
Anti-dsDNA positive, n (%)	7 (63.6)	20 (57.1)	0.7
Anti-Smith antibody positive, n (%)	1 (9.1)	2 (5.7)	0.7
ACL, n (%)	1 (9.1)	2 (5.7)	0.7
Leucopenia, n (%)	2 (18.2)	5 (14.3)	0.8
Neutropenia, n (%)	3 (27.3)	3 (8.6)	0.1
Lymphopenia, n (%)	7 (63.6)	10 (28.6)	0.04
Monocytosis, n (%)	7 (63.6)	11 (31.4)	0.06
Anemia, n (%)	8 (72.7)	21 (60.0)	0.5
Hypoproteinemia, n (%)	8 (72.7)	18 (51.4)	0.2
ESR, mm/h	32.5±25.8	38.4±32.5	0.6
CRP, mg/l	13.9±23.0	28.3±71.0	0.4
Clinical features			
Renal involvement, n (%)	8 (72.7)	28 (80.0)	0.7
Neuro-psychiatric manifestations, n (%)	2 (18.2)	1 (2.9)	0.1
Hematological involvement, n (%)	11 (100)	10 (28.6)	<0.001
Articular, n (%)	7 (63.6)	13 (37.1)	0.2
Mucocutaneous involvement, n (%)	7 (63.6)	14 (40.0)	0.2
Serositis, n (%)	1 (9.1)	4 (11.4)	1.0
SLEDAI	13.0±8.5	7.9±6.8	0.04
Lupus active, n (%)	8 (72.7)	17 (48.6)	0.2
Treatments prior to HZ onset			
Methotrexate, n (%)	2 (18.2)	4 (11.4)	0.6
Cyclophosphamide, n (%)	6 (54.5)	14 (40.0)	0.5
Mycophenolate mofetil, n (%)	3 (27.3)	5 (13.5)	0.4
Hydroxychloroquine, n (%)	8 (72.7)	30 (85.7)	0.4
Glucocorticoid, n (%)	10 (90.9)	32 (91.4)	1.0
Dosage, mg/day	43.9±28.9	46.7±44.3	0.7
High-dose ^a , n (%)	5 (45.5)	15 (42.9)	1.0

^a≥30 mg prednisone or equivalent per day. SLE, systemic lupus erythematosus; HZ, herpes zoster; dsDNA, double stranded DNA; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SLEDAI, SLE Disease Activity Index; ANA, antinuclear antibodies; ACL, anticardiolipin antibody; Sm, Smith.

late-SLE complication, as >50% of HZ events occurred over 5 years following SLE diagnosis and only 7.9% within the first 2 years. In the present study, 2/3 of HZ was developed within 6 months after SLE diagnosis, which may be associated with activity of lupus or drugs. Therefore, the present findings suggested that clinicians must pay close attention to the latent vesicular skin eruption, particularly within the initial 3-6 months following SLE diagnosis.

Another notable finding was the higher prevalence of complications of HZ among the present cohort than that based on general population. The most common complication was postherpetic neuralgia, followed by superimposed bacterial

infection. In the general population infected with HZ, postherpetic neuralgia occurs in 5-9% of people and is significantly more common in persons over age 60 (23,24). In the present study, the rate of postherpetic neuralgia was in accordance with previous studies in SLE patients (4,25), which was more frequent than that in the general population. Conversely, superimposed bacterial skin infection was observed in 8.7% of the present cohort, which was higher than the 1.4% reported in a previous general population-based study (3). All HZ patients in the present study exhibited full recovery and none of them experienced severe complications or succumbed to mortality. Therefore, despite a higher frequency of complications,

complications with HZ infections in SLE patients were relatively benign.

Only a small number of studies have explored predictors for developing HZ in patients with SLE (9,14,15), which have yielded inconsistent results. Furthermore, previous studies have rarely investigated the association between lymphopenia and HZ. The present study demonstrated that lymphopenia led to a risk of HZ infection and serious complications concomitant with HZ in patients with SLE. This finding was in accordance with two previous reports. Ng *et al* (26) demonstrated that HZ was more likely to develop in SLE patients with lymphopenia, and Hu *et al* (15) also suggested that in patients with SLE who developed HZ, the frequency of lymphopenia was increased compared with those without HZ. Although the exact mechanisms underlying the association between lymphopenia and VZV reactivation remain to be elucidated, it was hypothesized that decreased cell-mediated immunity serves a key role, as lymphopenia was a more specific reflection of defective cell-mediated immunity (CMI). The main defense against VZV reactivation in general populations was CMI rather than humoral immunity, as recurrent VZV infections occurred in patients with antibodies against VZV. A number of previous studies have demonstrated that CMI in patients with SLE may increase the risk of HZ. Nagasawa *et al* (22) suggested that the high incidence of HZ in patients with SLE was likely due to defects in CMI. Park *et al* (27) revealed that patients with lupus exhibited significantly lower VZV-specific cluster of differentiation T cell frequencies than rheumatoid arthritis patients and healthy controls. VZV-specific T cells have an important role in maintaining the equilibrium between the host and the virus during latency. A decline in the frequency of VZV-specific T cells has been demonstrated to be associated with an increased risk of VZV reactivation, leading to HZ (28). Furthermore, VZV itself has been reported to induce lymphopenia once reactivated, which may also have contributed to poor patient outcomes such as cutaneous dissemination, prolonged atypical skin lesions, ocular complications, and CNS involvement (29).

The present study demonstrated that high-dose GC (≥ 30 mg prednisone or equivalent per day) was an independent risk factor for infection with HZ in patients with SLE. Similar results were previously reported by Wu *et al* (14) and Manzi *et al* (25), who noted that steroid usage increased the risk of HZ in a dose-dependent manner. Consistent with findings from Wu *et al* (14) and Sayeeda *et al* (7), the present study also demonstrated that treatment with additional ISA, including CYC, MMF and MTX, did not appear to confer higher risk. The present results highlighted the relevance of GC as the most important immunosuppressive drug in terms of risk of HZ infections in SLE. This suggests that careful monitoring of HZ occurrence is warranted in patients with SLE taking high-dose GC, and that discontinuing ISA therapy may be unnecessary during instances of HZ in patients with SLE. A prospective study with a larger sample size may be required to confirm the validity of this therapeutic strategy by following up HZ-infected patients.

In conclusion, this is, to the best of our knowledge the first cohort in Southern Chinese patients with SLE to determine that HZ has features including a relatively low prevalence and more common complications with a relatively benign course. In addition, HZ was demonstrated to be an early complication of SLE,

with the highest risk of HZ within 3-6 months following SLE diagnosis. The present data supported the role of lymphopenia and high-dose GC therapy as risk factors for the occurrence HZ. Furthermore, lymphopenia was considered as an independent risk factor for severe HZ in patients with SLE. Therefore, these findings suggest that careful monitoring of HZ occurrence was warranted in SLE patients with risk factors. In addition, those with lymphopenia may benefit most from vaccination for HZ.

Acknowledgements

The present study was supported by grants from the Guangdong Technology Project (grant nos. 2014A020221009, and 2016A020215043) and a grant of National Natural Science Foundation of China (grant no. 81603435).

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