Post-Immunosuppression Imprinting in Systemic Lupus Erythematosus Complicated by Varicella-Zoster Virus Infection

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Abstract

Objective To investigate the clinical immunological characteristics and safety of physical therapy in systemic lupus erythematosus (SLE) patients complicated with herpes zoster (HZ) virus infection.

Methods A retrospective analysis was conducted on 10 SLE patients with HZ infection compared with 30 SLE patients without infection hospitalized during the same period. General data, laboratory indicators before onset, at onset, and after recovery, as well as T lymphocyte subset counts were observed in both groups.

Results There was no difference in general data between the two groups. Comparison of routine laboratory examination indicators: the SLE with HZ group showed statistically significant differences ($P<0.05$) in elevated absolute neutrophil count and white blood cell count before onset, and decreased lymphocyte percentage and elevated C-reactive protein at onset. Comparison of T lymphocyte subset examination indicators: before onset, the SLE with HZ group showed statistically significant differences ($P<0.01$) in elevated CD3+ percentage, decreased CD16+CD56+ percentage, and abnormal CD4+/CD8+ ratio, and statistically significant differences ($P<0.05$) in elevated CD8+ percentage, elevated CD8+ count, and decreased CD16+CD56+ count. At onset, there were statistically significant differences ($P<0.05$) in elevated CD3+ percentage, elevated CD8+ percentage, decreased CD4+ percentage, and abnormal CD4+/CD8+ ratio, and statistically significant differences ($P<0.01$) in decreased CD16+CD56+ percentage and elevated CD8+ count. After recovery, there was a statistically significant difference ($P<0.01$) in decreased CD16+CD56+ percentage. The treatment duration for HZ infection was 5 ± 1.3 days, with a cure rate of 100% and no occurrence of postherpetic neuralgia.

Conclusion SLE patients with HZ infection have an immunosuppressive state,

suggesting that monitoring of T lymphocyte subsets should be strengthened during SLE treatment. Antiviral drugs and physical therapy are safe and effective for the treatment of SLE patients with HZ infection.

Full Text

Analysis of Immune Suppression in Patients with Systemic Lupus Erythematosus Complicated by Herpes Zoster Virus Infection

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Abstract

Objective: To investigate the clinical and immunological characteristics and the safety of physical therapy in patients with systemic lupus erythematosus (SLE) complicated by herpes zoster (HZ) virus infection. **Methods:** We retrospectively analyzed 10 SLE patients with HZ infection and compared them with 30 SLE patients without infection who were hospitalized during the same period. General patient data, laboratory indicators, and T lymphocyte subset counts were examined before, during, and after infection. **Results:** No significant differences were found in general patient data between the two groups. In routine laboratory tests, the SLE+HZ group showed statistically significant differences in the proportion of patients with elevated absolute neutrophil count and white blood cell count before HZ onset, and decreased lymphocyte percentage and elevated C-reactive protein during infection ($P<0.05$). For T lymphocyte subsets, significant differences were observed before HZ onset in elevated CD3+ percentage, decreased CD16+CD56+ percentage, and abnormal 4/8 ratio ($P<0.01$), as well as in elevated CD8+ percentage, elevated CD8+ count, and decreased CD16+CD56+ count ($P<0.05$). During HZ infection, significant differences were found in elevated CD3+ percentage, elevated CD8+ percentage, decreased CD4+ percentage, and abnormal 4/8 ratio ($P<0.05$), along with decreased CD16+CD56+ percentage and elevated CD8+ count ($P<0.01$). After cure, the proportion of patients with decreased CD16+CD56+ percentage remained significantly different ($P<0.01$). The average treatment duration for HZ infection was 5 ± 1.3 days, with a 100% cure rate and no postherpetic neuralgia. **Conclusion:** SLE patients with HZ infection exhibit an immunosuppressive state, suggesting that monitoring of T lymphocyte subsets should be strengthened during SLE treatment. Antiviral drugs combined with physical therapy are safe and effective for treating SLE complicated by HZ infection.

Key words: systemic lupus erythematosus; herpes zoster; immunity; physical therapy

Introduction

In clinical practice, rehabilitation departments frequently encounter SLE patients with concurrent HZ infection. SLE complicated by HZ infection is characterized by clustered vesicles that tend to merge into large patches, often affecting half of the body, accompanied by severe pain that disrupts sleep and prolonged disease course. These features impact routine SLE treatment and prognosis, potentially leading to disease exacerbation. Ramos-Casals et al. reported that among 88 SLE patients with viral infections, one died from varicella-zoster infection [1]. Studies have shown that the incidence of HZ infection in SLE patients is relatively high, reaching 10% in children and 4% in 1,830 adult SLE patients [2-5]. The onset may be associated with high-dose corticosteroids and immunosuppressant use, active lupus disease, fever, positive anti-double-stranded DNA antibodies, decreased complement levels, and lupus nephritis. While some studies have analyzed the compromised immune status during HZ infection [6], and others have suggested that varicella-zoster virus can alter immune system indicators in pediatric SLE patients [7], previous research has lacked investigation into the immune status of SLE patients *before* and *after* HZ infection—whether it represents insufficient or excessive immunosuppression. Therefore, this study employed a retrospective analysis to examine the clinical and immunological characteristics, as well as the efficacy and safety of physical therapy, in SLE patients with HZ infection hospitalized in our rheumatology and immunology department. We aimed to explore strategies to reduce the incidence of HZ infection in SLE patients and identify optimal treatment approaches to rapidly control infection, promote lesion healing, and minimize impact on SLE management, thereby providing references for future treatment and prevention.

Methods

1.1 Study Population We collected data from 201 SLE patients hospitalized in our rheumatology and immunology department from January 2012 to December 2015. Among them, 10 SLE patients with HZ infection who received physical therapy in the rehabilitation department were designated as the observation group. From the remaining 191 SLE patients without HZ infection, we used SPSS 13.0 statistical software to randomly select 30 patients as the control group at a 1:3 ratio. All patients met the 1997 American College of Rheumatology SLE diagnostic criteria [8], and HZ diagnosis conformed to the criteria established by Zhao Bian in *Clinical Dermatology* [9].

1.2 Data Collection and Treatment Protocols 1.2.1 Clinical Data Collection

We collected demographic information including gender, age, disease duration, number of affected organ systems, average daily corticosteroid dosage during infection, average daily hydroxychloroquine dosage, and cumulative immunosuppressant dose. Laboratory results were recorded for the observation group at three time points: the last examination before HZ onset, during infection, and

one month after cure, and for the control group at corresponding intervals. Parameters included white blood cell count, neutrophils, lymphocytes, hemoglobin, platelets, serum albumin, erythrocyte sedimentation rate, C-reactive protein, complement C3 and C4, immunoglobulins IgA, IgG, IgM, antinuclear antibodies (ANA), anti-double-stranded DNA antibodies, and T lymphocyte subset counts.

1.2.2 HZ Treatment Methods

The observation group received standard lupus medications plus oral acyclovir 0.12 g five times daily, combined with physical therapy. The physical therapy protocol consisted of: (1) For the first two days, short-wave ultraviolet (UV) therapy (wavelength 253-260 nm) applied to the herpes area. Before irradiation, vesicle fluid was aspirated with a syringe. The irradiation field extended 1 cm beyond the lesion margin at a lamp distance of 1 cm, using a minimal erythema dose (MED). The initial exposure was 10-20 seconds (1-2.5 MED), with 25-50% dose escalation on day two. Concurrently, water-filtered infrared A (wIRA) therapy was administered at the spinal nerve root segment above the lesion using a German wIRA device. (2) From day three onward, all lesions received wIRA irradiation at 30 cm distance, 20 cm^2 spot size, for 20 minutes once daily for five days. Patients were followed up one month after discharge to assess skin lesions and postherpetic neuralgia.

1.2.3 Efficacy Evaluation

Patients were followed up daily to monitor vesicle number, erythema extent, erosion presence, pain relief time, and crusting time. Pain was assessed using the Visual Analogue Scale (VAS). Cure criteria were: *Cure*—pain disappearance with complete lesion resolution; *Markedly effective*—pain substantially relieved with >75% lesion resolution; *Effective*—pain reduction with 50-75% lesion resolution; *Ineffective*—no pain relief with <50% lesion resolution. Effective rate was calculated as [(cure cases + markedly effective cases)/total patients] × 100%.

1.2.4 Statistical Analysis

SPSS 13.0 software was used for statistical analysis. Count data were expressed as rates (%) and analyzed using the chi-square test. Measurement data were expressed as mean ± standard deviation and analyzed using t-tests. $P<0.05$ was considered statistically significant.

Results

2.1 Comparison of General Data and Medication Use The observation group comprised 2 males and 8 females, with mean age 32.7±8.8 years and SLE disease duration 36.3±44.5 months. The number of affected organ systems ranged from 1-4 (2.6±1.4). The control group included 2 males and 28 females, mean age 33.4±10.2 years, disease duration 38.7±31.3 months, and 1-4 affected systems (2.3±0.7). No significant differences were found between groups in gender, age, disease duration, number of affected systems, average daily corticosteroid dose, or cumulative cyclophosphamide dose ($P>0.05$). How-

ever, average daily hydroxychloroquine dosage differed significantly (P=0.041). All patients in both groups had inactive disease (Table 1).

2.2 Routine Laboratory Examination Results Compared with the control group, the observation group showed significantly higher proportions of patients with elevated absolute neutrophil count and white blood cell count before HZ onset (P<0.05). During HZ infection, significantly higher proportions exhibited decreased lymphocyte percentage and elevated high-sensitivity C-reactive protein (P<0.05). No significant differences were observed in other indicators (Table 2).

2.3 T Lymphocyte Subset Examination Results Before HZ onset, the observation group showed significantly higher proportions of patients with elevated CD3+ percentage, decreased CD16+CD56+ percentage, and abnormal 4/8 ratio (P<0.01), as well as elevated CD8+ percentage, elevated CD8+ count, and decreased CD16+CD56+ count (P<0.05) compared with controls. During HZ infection, significant differences persisted in elevated CD3+ percentage, elevated CD8+ percentage, decreased CD4+ percentage, and abnormal 4/8 ratio (P<0.05), with more pronounced differences in decreased CD16+CD56+ percentage and elevated CD8+ count (P<0.01). After cure, only the proportion of patients with decreased CD16+CD56+ percentage remained significantly different (P<0.01) (Table 3).

2.4 Clinical Distribution and Prognosis of HZ Infection Among 201 SLE hospitalizations, 10 cases (4.98%) were complicated by HZ infection. Five patients presented with fever at consultation. Lesion distribution was: head, face, and neck (2 cases); neck, shoulder, chest, back, and upper extremities (3 cases); lumbar and abdominal region (3 cases); and sacral, gluteal, and lower extremity region (2 cases). Lesion area ranged from 20×30 cm to 30×50 cm, with vesicles appearing in clusters that merged into confluent patches. The mean treatment duration was 5±1.3 days, with pain relief occurring at 2.6±0.8 days and crusting at 4.8±1.2 days. All HZ patients achieved cure, yielding a 100% effective rate, with no postherpetic neuralgia observed.

Discussion

Herpes zoster is a viral skin disease caused by reactivation of latent varicella-zoster virus (VZV) along dermatomal distributions, presenting with erythema, vesicles, and pain. Its pathogenesis is associated with immunosuppression [10]. Studies have confirmed that long-term corticosteroid and immunosuppressant use in SLE patients suppresses the immune system, leading to compromised immunity and increased infection risk [11-14]. Epidemiological data show SLE patients have an HZ incidence of 15-91 per 1,000 person-years, indicating HZ is a common complication of SLE treatment. The 4.98% incidence in our study aligns with these reports.

Our study found no differences between HZ-infected and non-infected groups in age, gender, disease duration, number of affected systems, or cumulative cyclophosphamide and corticosteroid doses. Although daily hydroxychloroquine dosage differed, this cannot explain HZ occurrence. The cumulative cyclophosphamide dose and daily corticosteroid dose during HZ infection were consistent with doses used during SLE induction and maintenance therapy, and all patients had inactive disease. This contrasts with previous studies [15-17] showing HZ primarily occurred in SLE patients with multi-system involvement, where SLE Disease Activity Index (SLEDAI) score, thrombocytopenia, hypoalbuminemia, average corticosteroid dose within one month, and cyclophosphamide pulse therapy were risk factors for HZ infection. This discrepancy may be attributed to well-controlled disease in our cohort, whereas previously reported SLE+HZ patients often had active disease. Routine laboratory tests revealed that before rash onset, the HZ group had higher proportions of neutrophilia and leukocytosis, possibly reflecting inflammatory responses to viral reactivation. During infection, lymphopenia and elevated C-reactive protein were significantly different. While C-reactive protein is an acute-phase reactant in many inflammatory and autoimmune diseases, most studies show it rarely elevates in SLE and correlates poorly with disease activity [18-19], but increases significantly during infections.

During HZ pathogenesis, T lymphocyte subsets undergo characteristic changes. CD3+ represents total T cells, including CD4+ and CD8+ subsets, which play dual regulatory roles. Research indicates that decreased absolute lymphocyte count, CD3+ and CD4+ values, reduced CD4+/CD8+ ratio, and elevated CD8+ are risk factors for SLE complicated by HZ [6,20]. However, previous studies only examined differences during active HZ infection compared with SLE controls, without investigating whether changes before onset and after cure were specific. Our study focused on T lymphocyte subset changes before, during, and after HZ infection. Results showed that CD8+ and CD3+ percentages were already elevated before HZ onset, while normalizing after cure and in controls ($P<0.05$). CD16+CD56+ percentage decreased and 4/8 ratio became abnormal before and during infection, whereas these normalized in controls and post-cure patients ($P<0.05$). These findings suggest patients were in a state of low or excessive immunosuppression before HZ onset, which may predispose to viral and other infections. Since patients were in induction or maintenance phases, this pattern may reflect hypersensitivity to immunosuppressants, where standard or low doses induced excessive immunosuppression. Therefore, clinical practice should monitor T lymphocyte subset changes and consider individual patient differences to adjust medication dosages for optimal immune status.

Previous studies have confirmed that short-wave or medium-wave UV therapy for HZ can localize inflammation, promote inflammatory exudate absorption, accelerate lesion healing, and upregulate immune function [21-22]. Low-dose, short-duration UV irradiation does not induce phototoxic reactions or trigger SLE flares, proving safe and effective for SLE+HZ. Water-filtered infrared-A (wIRA) has a wavelength of 580-1400 nm, power of 750 W, and penetration

depth up to 7 cm, encompassing anti-inflammatory infrared light, super-laser that reduces inflammatory mediators like serotonin and decreases sympathetic nerve excitation for analgesia, and red light that modulates immune function, enhances mitochondrial oxygen utilization, and promotes wound healing [23-24]. Given that our HZ lesions were extensive, clustered, confluent, severely painful, and highly inflammatory, UV therapy alone might not rapidly control inflammation, and high UV doses could trigger lupus activity. Therefore, we employed a progressive approach combining UV and wIRA to leverage both modalities for rapid inflammation control without affecting SLE disease activity. Our results showed superior lesion healing time, pain relief, and cure rate compared to the average 15.7±2.5 days reported in literature [17]. The normalization of routine laboratory and T lymphocyte subset indicators before and after treatment suggests the regimen does not adversely affect T lymphocyte subsets and may help regulate immune dysfunction.

In summary, SLE patients with HZ infection in our cohort showed no differences from controls in age, gender, disease duration, affected systems, or corticosteroid/immunosuppressant dosages. Before HZ onset, patients exhibited low or excessive immunosuppression, possibly due to hypersensitivity to immunosuppressants where standard doses caused excessive suppression. This immunocompromised state likely predisposed patients to viral and other infections, while HZ infection further perturbed immune function. Antiviral therapy combined with physical therapy rapidly, effectively, and safely controlled inflammation, relieved pain, and promoted lesion healing. These findings underscore the importance of enhanced T lymphocyte subset monitoring during SLE treatment to optimize therapy and reduce medication side effects and infectious complications.

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