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CASE SERIES

Comparative Case Series of Herpes Zoster in Older Immunocompromised Chinese Adults: Clinical, Immunological, and Treatment Profiles in Four Cases Over 60

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Purpose: Herpes zoster poses severe complications in elderly immunocompromised patients, particularly those with altered drug metabolism and renal impairment, impacting quality of life.

Patients and Methods: To evaluate brivudine's efficacy and safety in such cases, we conducted a retrospective case series at Shanghai Skin Disease Hospital, analyzing four Chinese patients (aged 64–84 years) with complex herpes zoster, including systemic lupus erythematosus, diabetes nephropathy, multiple comorbidities, and trigeminal nerve involvement. Selected for their immunocompromised status and prior antiviral failure or renal concerns, patients received oral brivudine (125 mg once daily) with or without intravenous acyclovir, with outcomes assessed via clinical examination, pain scores, and laboratory monitoring over 7–14 days.

Results: All patients experienced rapid symptom relief, lesion resolution, and pain reduction with minimal side effects. Compared to previous use of other antivirals, brivudine was better tolerated and did not require renal dose adjustment.

Conclusion: In summary, brivudine appears to be a promising option for elderly immunocompromised patients with herpes zoster, offering effective viral control, favorable safety, and improved clinical outcomes.

Plain Language Summary:

- Brivudine is effective in immunocompromised and elderly patients and yields better results than acyclovir or valaciclovir, particularly in patients with severe or disseminated herpes zoster.
- Brivudine has a favorable safety profile in patients with renal impairment, unlike acyclovir and valacyclovir, which can accumulate and cause toxicity.
- Early antiviral therapy can lead to rapid symptom relief, lesion resolution, and pain management, particularly in patients with high risk.
- Combining brivudine with pain management (eg, pregabalin and mecobalamin) enhances treatment outcomes in complex cases.

Keywords: antivirals, brivudine, case report, herpes zoster, immunocompromised, older Chinese adults

Introduction

Herpes zoster (HZ), also known as shingles, is a form of reactivation of the varicella-zoster virus (VZV) that typically occurs decades after primary infection. VZV is a ubiquitous, double-stranded DNA virus from the human alpha herpesvirus subfamily.[1] Like other herpesviruses, it causes both primary and recurrent infections and remains latent in sensory ganglia. VZV is responsible for two major human diseases: varicella and HZ. Primary infection causes mild, self-limited varicella, after which the virus becomes latent. HZ results from reactivation, often preceded by prodromal symptoms, including fatigue, headache, low-grade fever, and abnormal skin sensations.[2] It presents as a painful, dermatomal rash and can significantly impair quality of life. Approximately 20% of patients develop postherpetic

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neuralgia, persistent pain that continues after rash resolution. Unlike primary infection, HZ is associated with prolonged discomfort and chronic pain. Older adults, particularly those aged >60 years, are at a considerably high risk because of age-related immunosenescence, which impairs the body's ability to suppress latent VZV.[3,4] In this population, HZ exhibits a high incidence and is often severe, with prolonged recovery and a high risk of complications.[5,6]

Particularly, facial HZ involving the ophthalmic branch of the trigeminal nerve (HZ ophthalmicus) is a serious manifestation in older adults and can cause various complications, including keratitis, uveitis, scleritis, and, in rare cases, chorioretinopathy, all of which may cause substantial visual impairment if not promptly managed.[7] Furthermore, older individuals are at a greater risk of postherpetic neuralgia (PHN), which is a debilitating condition affecting up to 40% of those aged > 60 years. Common risk factors for HZ are age > 50 years, immunosuppression, physical trauma, irradiation, infections, and metal stress.[8]

These symptoms can persist for months or years, severely affecting the quality of life.[9,10] The burden of HZ is particularly pronounced in Asian populations, including Chinese adults, in which traditional barriers to healthcare access and potential underreporting of atypical presentations can delay timely diagnosis and treatment. Immunocompromised conditions, such as systemic lupus erythematosus (SLE) and type 2 diabetes mellitus (T2DM), and the use of immunomodulatory therapies, such as Janus kinase (JAK) inhibitors, notably heighten the risk of HZ reactivation and its complications. T2DM is associated with impaired cellular immunity, predisposing patients to severe presentations of HZ and complications, such as PHN, bacterial superinfections, and VZV-related vasculopathy, including stroke.[11,12] Similarly, patients with SLE are particularly vulnerable to HZ considering the immune dysregulation nature of the disease and the therapies often required for its management.[13] The increasing prescription of JAK inhibitors for autoimmune conditions, such as rheumatoid arthritis and SLE, further intensifies these risks.[14,15] JAK inhibitors disrupt key cytokine signaling pathways that are crucial for antiviral immunity, which substantially increases the incidence of HZ among treated patients. A meta-analysis demonstrated that patients receiving JAK inhibitors had a higher risk of HZ than those receiving other immunosuppressive therapies.[14,15] These findings underscore the importance of prophylaxis and close monitoring for the early signs of HZ in this special population.

Although vaccination has considerably reduced HZ incidence and severity in some populations, many older Chinese adults are vulnerable to severe disease owing to limited vaccine coverage in this group.[16] Atypical and rare presentations, such as facial HZ, are less frequently documented and may complicate timely diagnosis and management, particularly in older patients with multiple comorbidities.[17] Given the elevated risk of severe HZ in these patients, effective and well-tolerated antiviral treatment options are essential. Brivudine, a nucleoside analogue antiviral, selectively inhibits herpesvirus DNA synthesis by competitively blinding to viral DNA polymerase, with potent activity against VZV.[18] Administered orally once daily, it's convenient dosing regimen enhances patient compliance. Unlike acyclovir or valacyclovir, brivudine does not require dose adjustment in patients with renal impairment, making it particularly suitable for elderly patients or those with comorbidities.[19] Its high bioavailability and enhanced tissue penetration compared to traditional antivirals promote rapid viral suppression, accelerate lesion resolution, and may reduce the risk of PHN in high-risk individuals. Brivudine's favorable safety profile further supports its use in managing VZV infections.[19] This report describes four cases of HZ in Chinese adults aged >60 years, emphasizing the clinical presentation, complications, and management strategies for enhanced understanding and improved outcomes in this vulnerable group.

Case Presentation

This descriptive case series included four patients diagnosed and treated at our institution. Relevant clinical data were collected retrospectively from medical records and presented in chronological order for each case. All patients were managed according to standard institutional protocols. This study was approved by ethic committee of Shanghai Skin Disease Hospital (Approval No. 2025–04), institutional approval was not needed to publish the case details. Written informed consents were obtained from all four participates, including consent for publication of detailed clinical information and treatment course, as well as patient images with eyes appropriately covered to ensure anonymity. The summary characteristics of the four cases were presented in the Table 1.

Table 1 Characteristics of the Four HZ Cases

Case	Age / Sex	Immunological Status / Comorbidities	Presentation	Treatment	Outcome	Notable Points
Case 1	65 / Male	CD4/CD8: 0.63 (suggestive of immunosuppression); prior influenza	Unilateral herpes zoster (HZ) on left face with vesicles and crusting; no dissemination	Brivudine 125 mg daily for 7 days; pregabalin; vitamin B12	Rash scabbed in 7 days; pain subsided in 3 weeks	Rapid improvement with no recurrence; no lab abnormalities
Case 2	64 / Male	Poorly controlled type 2 diabetes (HbA1c 10.2%)	Right-sided HZ with extensive facial involvement, otalgia, and ocular symptoms; low-grade fever	Brivudine; cefixime; ganciclovir eye drops; symptomatic support	Rash scabbed in 6–7 days; no sequelae	Brivudine well-tolerated in diabetic patient with rapid resolution
Case 3	76 / Male	Hypertension, AF, emphysema, hyperuricemia; multi-lab abnormalities	Severe facial and disseminated HZ; pain and tenderness; vesicles on face, ear, trunk, limbs	Acyclovir (initial); switched to brivudine; pregabalin; mecobalamin; topical eye ointment	Rash resolved with scabbing; reduced pain; minor residual pain at 1 month	Brivudine effective despite extensive disease and comorbidities
Case 4	82 / Female	Parkinson's, diabetes, chronic bronchitis	Left-sided facial HZ with periorbital swelling and pain; fever, fatigue	Brivudine; celecoxib; mecobalamin; eye drops and cream	Rapid symptom relief; rash scabbed by day 5	Safe and effective use in elderly with neurodegenerative and metabolic disease

Case 1: Lupus and Immunosuppressants

A 65-year-old man with a known history of SLE was receiving long-term immunosuppressant therapy, including the JAK inhibitor tofacitinib. The patient presented with a 6-day history of progressive pain a rash localized to the left-sided head and neck. He had initially been started on oral famciclovir for HZ, but his symptoms continued to worsen over 3 days. Physical examination revealed banded erythema with scattered, partly fused blisters. Some blisters were cloudy with relaxed walls, whereas others had dried and formed scabs, which were surrounded by redness. The skin lesions were limited to one side (Figure 1). The patient experienced disease progression after 3 days of oral famciclovir treatment.

Laboratory tests revealed decreased levels of erythrocytes, hemoglobin, thrombocytes, apolipoprotein B, prealbumin, albumin, total protein, and potassium, along with increased cystatin C and monocyte percentages. Additionally, amyloid proteins were detected in the serum. Systemic treatment was initiated with intravenous acyclovir, brivudine (despite contraindication in immunocompromised patients), mecobalamin, pregabalin, potassium chloride (1.5 g/30 mL in 500mL normal saline), and pantoprazole sodium for gastric protection. Although brivudine is contraindicated in immunocompromised patients due to limited safety data from Phase III clinical trials, its use in this 65-yrs-old man with SLE and sever craniofacial HZ was justified by a careful risk-benefit evaluation. The patients, on long-term immunosuppression with tofacitinib, exhibited disease progression after 3 days of oral famciclovir, alongside significant proteinuria and elevated cystatin C, indicating renal impairment. These factors restricted the use of renal-cleared antivirals like acyclovir or valacyvlovir due to nephrotoxicity risks and the need for dose adjustments. Brivudine, a potent nucleoside analogue, offered high bioavailability, once-daily dosing, and no requirement for renal dose adjustment, making it suitable for rapid viral suppression in this setting. Administered with intravenous acyclovir under close clinical and laboratory monitoring, brivudine effectively controlled HZ progression without adverse events, potentially reducing the risk of PHN in this high-risk patient.

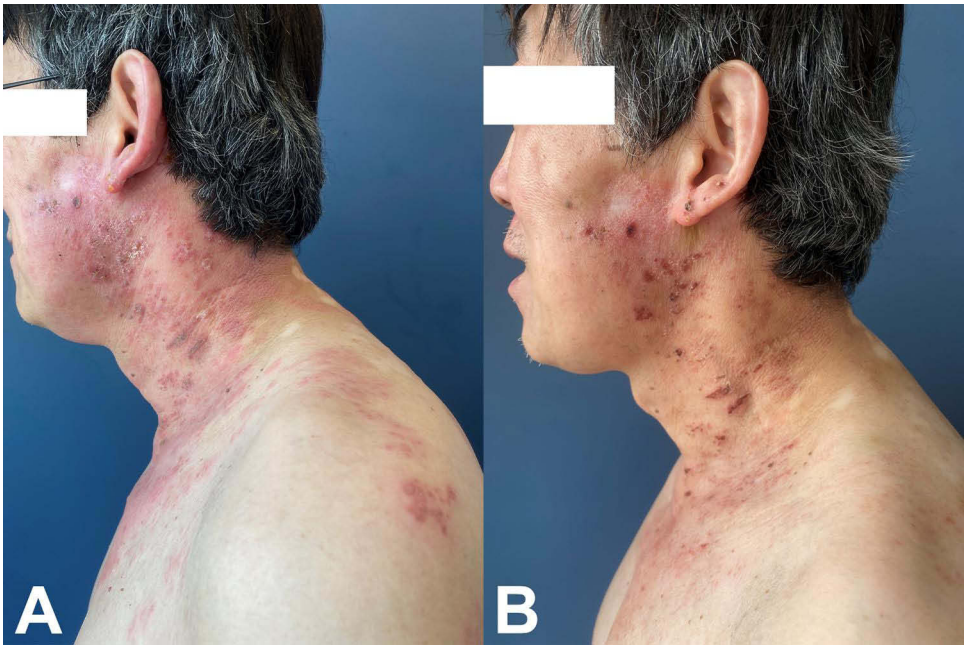

Figure 1 A 65-year-old man with systemic lupus erythematosus (SLE) and facial herpes zoster: (**A**) before treatment; (**B**) after treatment at discharge.

On day 2 of treatment, immune function tests revealed a lower-than-normal ratio of CD19 (B cells) percentage (%) and CD4/CD8 ratios, whereas CD3 (T cells) percentage (%), absolute counts of CD3 (T cells), and absolute CB8 (inhibiting T cells) counts were elevated. Interferon, interleukin, and tumor necrosis factor levels were within normal ranges. Blood potassium levels normalized, and the patient reported notable symptom relief. After 7 days of treatment, blood potassium levels stabilized at the low–normal limit. The patient's rash and pain improved, with banded erythema and scabbing on the left side of the head and neck.

Despite its contraindication in immunocompromised patients, brivudine was effective and well tolerated, leading to remarkable symptom improvement. Laboratory findings revealed abnormal complement levels, suggesting immune dysregulation rather than overt immunodeficiency. This case highlights the efficacy of brivudine in patients with SLE receiving immunosuppressants and underscores the need to critically evaluate routine immune function tests while assessing immune status.

Case 2: Type 2 Diabetes and Renal Impairment

A 64-year-old man with a history of T2DM and chronic renal impairment was presented with severe HZ affecting the left chest and back, with pain persisting for 5 days. Physical examination revealed erythema in a banded distribution on the left thoracic spine, with scattered turbid blisters, some relaxed and others dried and scabbed, which were surrounded by a red halo (Figure 2). The patient reported persistent, severe, and unbearable pain (visual analogy score not determined).

Laboratory tests revealed elevated serum amyloid protein, C-reactive protein, D-dimer, fibrinogen, and glycosylated hemoglobin levels. The absolute monocyte value and percentage increased, whereas the thrombocyte count was decreased. Renal function tests revealed increased creatinine and urea levels and decreased albumin and total protein levels. Fecal occult blood was positive, and interleukin and CD4/CD8 ratios were abnormally elevated.

The patient was initially treated with valaciclovir (300 mg twice daily), pregabalin, and topical calamine. However, the patient's condition progressed, and he was admitted to the hospital. Intravenous acyclovir (250 mg three times daily) was initiated but could not control the symptoms. On the same day, oral brivudine (125 mg once daily for 7 days) was administered, along with oral pregabalin (3.75 mL twice daily, increased to 7.5 mL twice daily on day 3), Lugac (500 mg once every night), and mecobalamin tablets (0.5 mg three times daily).

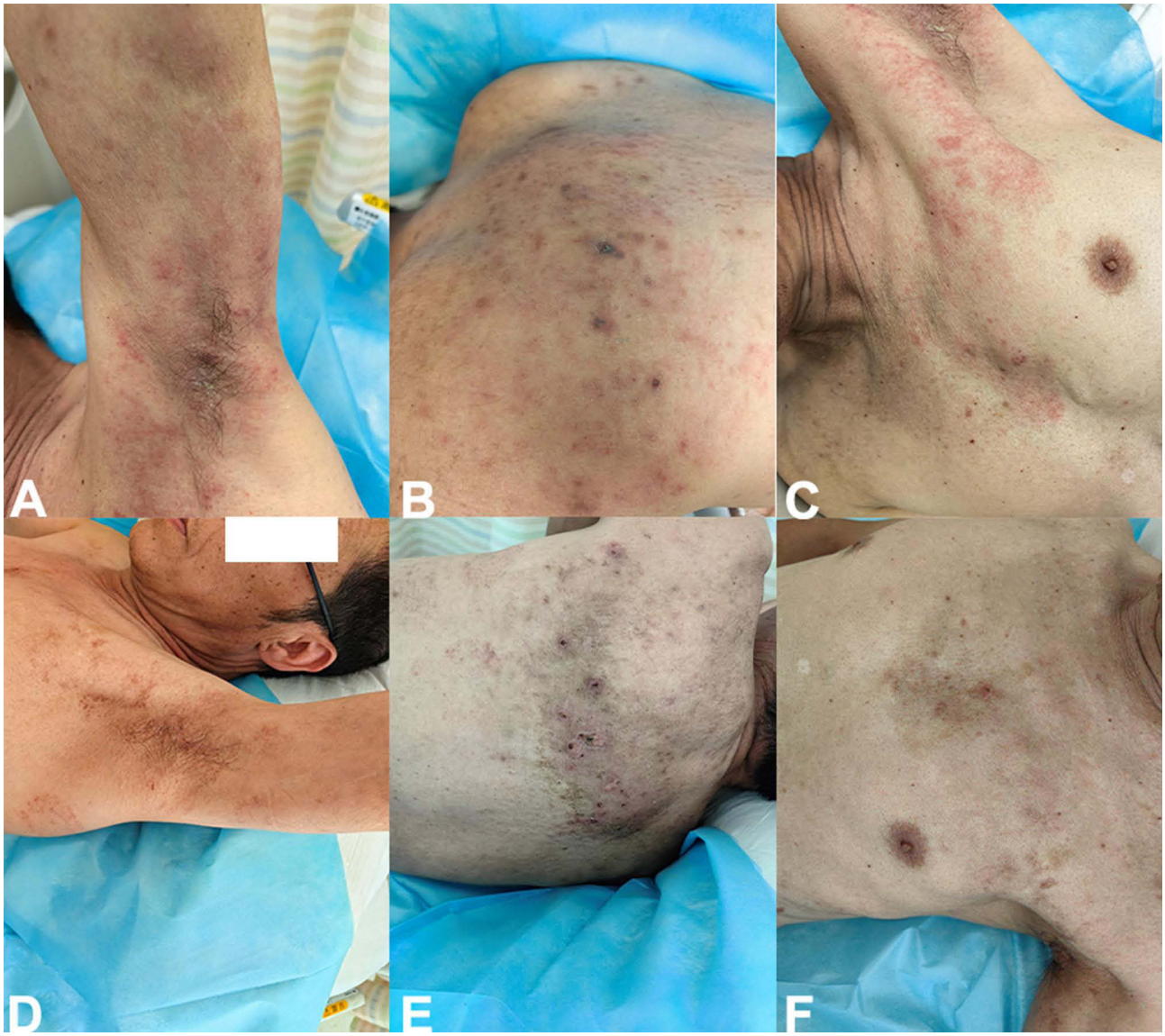

Figure 2 A 64-year-old man with type 2 diabetes and renal impairment presented with severe herpes zoster in the back and neck areas: (**A**–**C**) before treatment; (**D**–**F**) after treatment.

The patient's symptoms substantially improved after transitioning to brivudine. Pain subsided, vesicle formation was arrested, and lesion healing was observed. Renal function remained stable, with estimated glomerular filtration rate values of 54.69 and 60.74 mL/min/1.73m^2 and creatinine levels of 120.20 µmol/L and 110.20 µmol/L on days 1 and 2, respectively. Oral valacyclovir and intravenous acyclovir were ineffective, whereas brivudine successfully controlled symptoms without requiring dose adjustments or adverse renal effects.

This case highlights the efficacy and safety of brivudine for patients with T2DM and renal impairment, highlighting its suitability as a therapeutic option when antiviral treatments fail.

Case 3: Disseminated Zoster with Chronic Comorbidities

A 76-year-old man with multiple chronic conditions, including hypertension, atrial fibrillation, pulmonary emphysema, and hyperuricemia, presented with severe facial HZ and dissemination. The patient exhibited scattered blisters with banded erythema on the left side of the face, ear, abdomen, and lower limbs. The lesions were turbid, with some blisters

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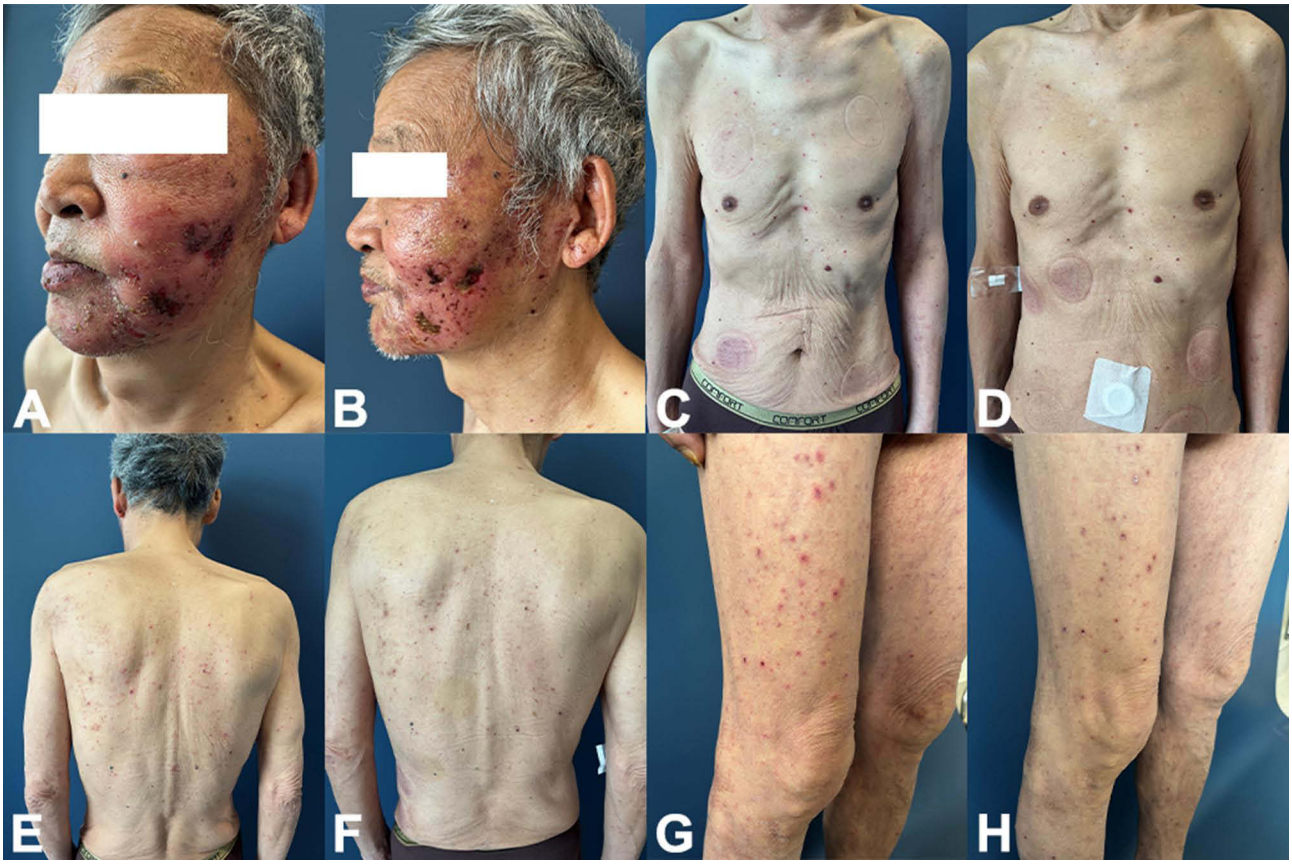

Figure 3 A 76-year-old man with multiple chronic conditions, including hypertension, atrial fibrillation, pulmonary emphysema, and hyperuricemia, presented with severe facial herpes zoster and dissemination: (**A, C, E, G**) before treatment; (**B, D, F, H**) after treatment.

relaxed, dried, and crusted, whereas the skin lesions remained confined to one side of the body without crossing the midline (Figure 3). The local skin temperature was slightly elevated, and tenderness was marked by intense pain.

Laboratory tests revealed abnormalities in several parameters: decreased eosinophils, lymphocytes, and thrombocytes; increased neutrophils and platelet pressure; and the presence of serum amyloid protein. Urinalysis revealed occult blood and elevated urine sugar levels. Furthermore, abnormalities were noted in thyroid function tests (TSH, T3, and FT3); creatinine uric acid; complement C3, C4, IgG, IgM, and total prostate-specific antigen; coagulation markers; pro-benign prostatic hyperplasia; and troponin-T (TN-T).

Initial anti-VZV treatment with oral acyclovir was administered; however, because of extensive involvement of the left face and body, brivudine was subsequently administered. The patient was also prescribed oral mecobalamin and pregabalin for pain management, along with topical aureomycin eye ointment for the affected area. After 3 days of treatment, the patient's rash and pain considerably improved. The skin and maculopapular lesions on the left side of the face and across the body started to crush and scab, respectively. The pain intensity significantly reduced, and at the end of treatment, the rash was mostly resolved with scabbing.

The patient continued to receive brivudine and pregabalin after discharge, and an outpatient follow-up 1 month later revealed mild residual pain and localized scarring. The pregabalin dosage was reduced to once daily because the pain had significantly subsided compared with that at discharge.

Notably, brivudine treatment did not have any considerable effect on the patient's blood glucose levels, renal function, or other comorbidities. Brivudine therapy resulted in rapid symptom improvement, lesion resolution, and minimal adverse effects, highlighting its superior efficacy over valacyclovir for treating facial HZ in elderly patients with multiple comorbidities.

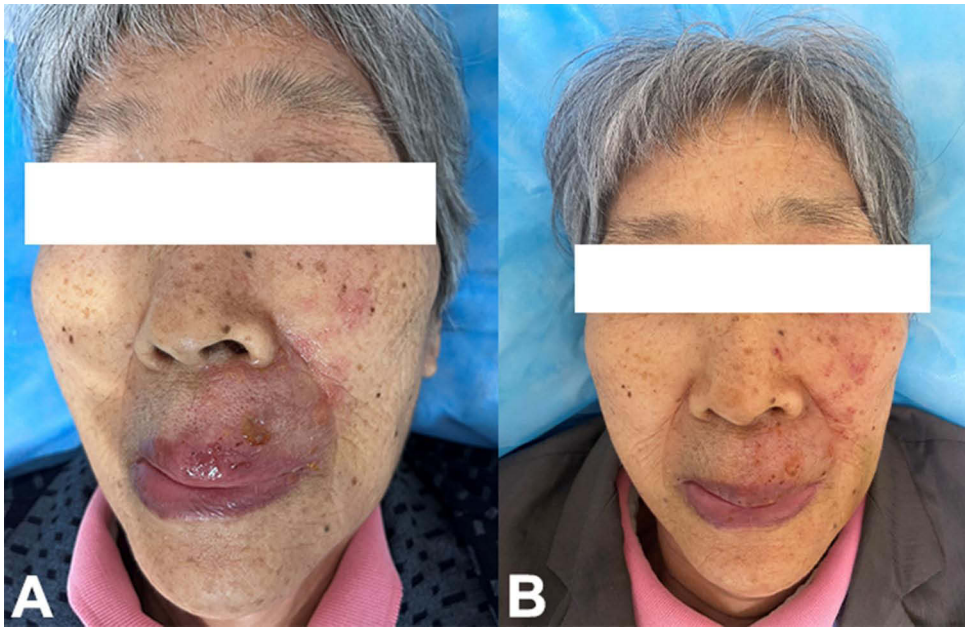

Figure 4 An 82-year-old woman presented with erythematous blisters on the left side of the head and face: (**A**) before treatment; (**B**) after treatment.

This case highlights the potential advantages of brivudine in treating severe facial HZ, particularly in older patients with complex medical histories, owing to its efficacy, safety profile, and minimal impact on existing comorbid conditions.

Case 4: Elderly Patient with Trigeminal Zoster

An 82-year-old woman was presented with erythematous blisters on the left side of her head and face, which were accompanied by pain for 5 days. The patient had no obvious predisposing factors. Clinical examination revealed banded erythema with scattered blisters on the forehead, some of which were fused. The blisters appeared cloudy and relaxed, with a few dried and crusted, which were surrounded by a red halo (Figure 4). The lesions were confined to the left side of the head and face and did not cross the midline. The local skin temperature was slightly elevated, and tenderness was pronounced.

Laboratory tests revealed a notable decrease in hemoglobin levels, positive urine occult blood, decreased free and total triiodothyronine (T3) levels, and decreased albumin levels. After admission, brivudine (125 mg once daily for 7 days), gabapentin (0.3 g three times daily), mecobalamin (0.5 mg three times daily), and symptomatic management were initiated.

After treatment, the patient's rash and pain considerably improved. Band-like erythema remained on the left side of the head and face, with a few blisters drying up and forming scabs. Brivudine therapy resulted in rapid symptom relief, cessation of vesicle formation, and lesion healing without adverse events.

This case demonstrates the potent antiviral efficacy, selective action, and safety of brivudine in elderly patients. It is a viable alternative to other antivirals for managing trigeminal HZ, particularly in this age group with limited treatment options.

Comparison with Current Published Cases

Based PubMed and China National Knowledge Infrastructure (CNCI) review, we identified a total of 6 observational studies (sample size range: 20–64, aged 3–70 years)[20–25] and 9 case reports (aged 30–81 years)[26–34] on the use of brivudine in HZ (Table 2). Most patients were immunocompromised due to malignant disease. Several cases involved individuals who were immunosuppressed due to human immunodeficiency virus (HIV) infection, kidney transplantation with associated immunological abnormalities, or immunosenescence. The majority of patients were diagnosed clinically, with only a small number confirmed by virological testing, such as VZV isolation from lesions, polymerase chain

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Table 2 Characteristics of the Current Published HZ Cases with Brivudine Therapy

Study ID (First Author, Publish Year, Country)	Sample Size, Age, Sex, Patients Status	Diagnosis of Zoster Infection	Severity of the Zoster, Place of Zoster	BVDU Types (Brand and Manufacture), Dose	Outcomes	Safety
Y. Benoit, 1985, Belgium.[20]	21 malignant children (10 males, aged 3–14 yrs) acute lymphoblastic leukaemia, malignant lymphoma, solid tumour, histiocytosis X.	Typical papulovesicular lesions and isolated VZV in vesicle fluid and raised VZV antibodies	Dissemination and single cranial, thoracic, cervical or cervicobrachial	NR, orally in capsules at 15 mg/kg daily for 5 d in 2 or 3 doses daily	Recovered completely without complications. At 3 weeks, all patients complete recovery	Liver dysfunction, blood count alterations, thrombocytopenia, granulocytopenia, lymphocytopenia, elevated transaminases
Wildiers, 1985, Belgium (Clinical trial)[21]	20 Immunocompromised patients with malignancies aged 48.5 yrs (range 16–70) 8M/12F	Clinical diagnosis of severe localized or disseminated HZ	Severe localized or disseminatedThoracic, cervical, sacral, cranial, abdominal/leg	NR, Synthesized at Rega Institute, 7.5 mg/kg/d orally (125 mg capsules t.i.d. or q.i.d). ×5 d	New lesions stopped: 1.83 d, Complete healing at 3 wks: 11/20; clinical response: good/ above: 12, moderate: 5, failure: 1	Vomiting (due to dosing error)
Wutzler, 1988, Germany (Clinical study)[22]	20 patients with malignancies	NR	Severe zoster, cutaneous lesions	NR	Most, 13/20, cessation of new vesicle, fever resolution, crusting, and complete healing. Delayed treatment (> 48h after onset) failed to prevent lesion spread	Well tolerated, laboratory abnormalities in few cases
Heidl, 1990, Germany (Prospective RCT)[23]	43 immunocompromised children: 21:22, age: 8.4 vs.7.6 yrs; 11 males vs 10. Malignancies: 83.7% and post-BMT: 7/43	Clinical VZV infection + serum creatinine <120 μmol/L	NR, cervical, thoracic, lumbar/sacral	NR 15 mg/kg/d orally in 3 divided doses ×5 d Aciclovir: 1500 mg/m²/ d IV in 3 divided doses ×5 d	Lesions crusted: 1–5 days bothDefervescence: 1–9 days both Complete remission: 5–6 days bothTreatment failure: 2 both	Adverse events: nausea/ vomiting
Wutzler, 1995, Germany/ Belgium (RCT)[24]	48 immunocompromised adults (1:1) aged 36.7± 18.0 yrs vs 43.6±20.1 yrs, 50% female vs 41.7%, malignant diseases	Herpes zoster rash <72h, with malignant disease, immunocompromised status	Severity score: 2.37 vs 2.41, thoracic, lumbar, generalized rash	Helpin®, Berlin Chemie AG, Germany, 125 mg every 6 h (500mg/ d) ×5 d, Zovirax®: 10mg/kg IV every 8 h ×5 d	Pain score lower for Brivudin on days 1,2,5 (P< 0.05). New lesions by day 3: 12.5% vs 13%, full crusting by day 12: 83% vs 78% non-sig	AE: 25% vs 8.7% Nausea, loss of appetite

Vogel, 2023, Germany (Retrospective cohort)[25]	64 immunocompromised children, Median 14 yrs, 36M/28F, hematologic or solid tumors, genetic diseases	Vesicular rash and PCR-confirmed VZV in vesicle fluid and blood	Unilateral dermatomal lesions, painful/burning sensation, thoracic/ abdominal, extremities, cranial	NR, 2 mg/kg once daily ×7-21 d (median 14 d)	Full crusting: Median 6 d (78.1% 1 wk), complete healing: wk 1: 17.2%, wk 2: 60.9%, wk 3: 21.9%, no postherpetic neuralgia	NR, 1 vaccine-strain HZ resolved
Vinckier, 1987, Belgium (Case report)[26]	55-yr male with chronic lymphocytic leukemia and B-cell malignancy	Presentation chronic oral lesions, repeated HSV-1 isolation from lesions, virological confirmation	Life-threatening progression, bronchopneumonia. Mandibular gingiva, maxillary labial mucosa, soft palate	NR, 125 mg/d orally (divided q.i.d). ×20 d	No improvement, HSV-1 persistently isolated, isolate showed >5000-fold resistance	NR
Husak, 1998, Germany (Case report)[27]	30-yr male HIV-1 infection, Immunosuppressed status, recurrent perianal HSV-2, oral candidosis, oral hairy leukoplakia	PCR-confirmed HSV-2 in smears and tissue biopsy	NR, left lateral tongue	NR 300 mg/d orally ×5 d	Rapid regression within 5 days, complete resolution of tumor	Successful despite CD4+ count >200 cells/μL
Ran, 2017, China (Case report)[28]	62-yr female, tinea capitis by Trichophyton violaceum, Immunological abnormalities (ANA+, SSA +++), valacyclovir failed	Clustery tension blisters	Painful tension blisters, Involved trigeminal nerve, scalp, preauricular, cheek, lips, submandibular	Zostex, 125 mg once daily ×9 d, pregabalin (75mg bid)	D 9: Complete blister resolution, complete resolution at 16 wks, no recurrence at 1-yr	NR
Tian, 2020, China (Case report)[29]	80-yr male, hypertension, diabetes mellitus (poorly controlled), Immunological status: CD4/CD8: 0.63	Clinical diagnosis	Hemorrhagic bullae and confluent vesicles, systemic dissemination, severe pain, Left lumbar/back dermatome, face/ trunk/ upper limbs	NR 125 mg once daily ×7 d+ mecobalamin / VitB1+polymyxin B ointment	D 1: Vesicle cessation, crust formation, pain reduction, D 5: Complete lesion resolution, D 7: Pain disappearance, Zero PHN at follow-up	NR
Yu Hong, 2021, China (Case report)[30]	45-yrs male, Kidney transplant (8 m), Immunosuppressants, hepatitis B history	Ear pain + ear canal vesicles + facial paralysis, met Ramsay-Hunt syndrome criteria	Constant electroshock-like pain with vertigo, nausea, facial nerve paralysis, right auricle and ear canal	NR, 125 mg once daily × 10 d+prednisone 25 mg/d × 3 d → 10 mg/d, mecobalamin 0.5 mg/d IV × 14 d+ red light	D 1: Significant pain reduction D 6: Ear swelling resolved, glossal numbness disappeared D 8: Lesions crusted, taste recovered D 10: Pain resolved, facial palsy slightly improved Month 4: Complete facial recovery	No treatment-related events reported

(*Continued*)

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Table 2 (Continued).

Study ID (First Author, Publish Year, Country)	Sample Size, Age, Sex, Patients Status	Diagnosis of Zoster Infection	Severity of the Zoster, Place of Zoster	BVDU Types (Brand and Manufacture), Dose	Outcomes	Safety
Sterz, 2021, Germany (Case report)[31]	37-yr male metastatic osteosarcoma, Immunocompromised status	Clinical diagnosis	Mild right facial palsy without systemic complications, NR	NR, Standard 7-day course	Successful resolution without recurrence, immunotherapy-maintained efficacy	No AEs, no interaction with checkpoint inhibitors
Wang, 2021, China (Case report)[32]	65-yr male, chronic renal failure, hypertension, proteinuria history, no immunomodulator use	Disseminated rash and typical dermatomal progression	Hemorrhagic bullae, >50 disseminated pustules, urinary difficulty; Left gluteal dermatome, face/ trunk/limbs /perineum	NR, 125 mg once daily ×7 d, mecobalamin/ VitB1, renal protection agents	D 7: Lesions crusted, hemorrhagic plaques resolved D 14: Complete scab detachment Renal function: Cr decreased	NR
Zhang, 2022, China (Case report)[33]	70-yr male immunosenescence, disseminated herpes zoster, herpetic conjunctivitis, viral pneumonia	Virologic confirmation (implied)	Severe facial edema, purulent discharge dissemination. Right trigeminal dermatome, disseminated to trunk/ limbs	NR, 1 tablet (125 mg) once daily, combined Foscarnet 3g IV q8h, and mecobalamin	D 3: Fever resolved, no new vesicles, D 7: Complete crusting of lesions, pain reduction	NR
Osman Köstek, 2022, Turkey[34]	81-yr male with undifferentiated pleomorphic sarcoma	Zona lesions	NR; right neck and chest wall with a mass lesion	NR	Completed response tested by thorax and abdomen CT at 4 wks. 27 m, pneumonia and died with recurrences on bilateral pleural	NR

reaction (PCR), or serological antibody elevation. Most patients presented in the acute phase of HZ, typically within 72 hours of the rash onset. Lesion distribution varied widely, including cervical, thoracic, sacral, lumbar, and facial dermatomes, as well as the mandibular gingiva, maxillary labial mucosa, soft palate, tongue, scalp, preauricular region, lips, submandibular area, trunk, auricle, ear canal, perineum, and chest wall. Few cases assessed severity using standardized score systems.

Brivudine dosing in children was typically 15 mg/kg administered two or three times daily for 5–7 days, while adults received 125 mg every 6 hours for 5 to 20 days. Most patients achieved full recovery within 3 weeks. Reported clinical milestones included cessation of new lesions within 1–5 days, resolution of fever within 1–9 days, and complete remission of skin lesions in 5–6 days. Severe cases, such as one case involving the ear canal, showed delayed recovery: pain relief and ear swelling subsided by day 6, facial palsy improved by day 10, and complete facial recovery was observed after 4 months. Long-term outcomes were favorable in most reports, with no recurrences noted at 1-year follow-up in several studies. However, treatment failures were also documented. For example, a 55-year-old male with chronic lymphocytic leukemia and B-cell malignancy developed chronic, progressive oral lesions despite 20 days of brivudine therapy; HSV-1 was persistently isolated with no clinical improvement.[26] Reported adverse effects included gastrointestinal symptoms (vomiting, nausea, anorexia), hepatic dysfunction, and hematological abnormalities such as granulocytopenia, granulocytopenia, lymphocytopenia, and elevated transaminases. No interaction with immune inhibitors were reported.

Discussion

The presented cases highlight the efficacy and safety of brivudine for treating HZ in patients with varying underlying conditions, including SLE, T2DM, chronic comorbidities, and aging. These cases demonstrate the potential advantages of brivudine over standard antiviral treatments, such as acyclovir and valaciclovir, particularly in populations with compromised immune systems or renal impairment.

In case 1, a 65-year-old man with SLE receiving immunosuppressive therapy responded well to brivudine after failed initial therapies such as acyclovir. This case highlights the importance of brivudine in patients with autoimmune conditions who are receiving immunosuppressants. SLE, an autoimmune disorder, predisposes individuals to viral infections because of immune system dysregulation, making HZ a predominant concern. The combination of immunosuppressive therapy and underlying autoimmune condition may have hindered the effectiveness of acyclovir in this patient, which is a known limitation in patients who are immunocompromised. In contrast, brivudine demonstrated rapid symptom relief, lesion healing, and minimal adverse effects, reinforcing that brivudine may be a superior alternative to acyclovir in such populations, similar to other studies.[35]

Similarly, case 2 involved a 64-year-old patient with T2DM and renal impairment who exhibited an inadequate response to anti-VZV treatments (ie, valacyclovir and acyclovir). After transitioning to brivudine, improvements in symptoms and lesion resolution were observed without renal complications. T2DM and renal dysfunction pose considerable challenges in HZ management, considering that these conditions often result in immunosuppression and altered drug metabolism. Reportedly, brivudine is effective in controlling viral replication and has a favorable safety profile in patients with renal impairment.[16] In contrast, acyclovir can accumulate in patients with poor renal function, potentially leading to toxicity.

In case 3, an elderly patient with multiple chronic comorbidities, including hypertension, atrial fibrillation, and pulmonary emphysema, exhibited widespread HZ. Despite the severity of the condition, the patient experienced notable relief after brivudine therapy. This finding supports results from previous studies, suggesting that brivudine is particularly beneficial in elderly patients with complex medical histories in whom the immune system is already compromised. A previous study emphasized the antiviral potency of brivudine in the elderly, highlighting its superior efficacy over acyclovir, particularly in patients with systemic comorbidities that may impair the effectiveness of standard antivirals.[36]

Finally, case 4 involved an 82-year-old woman with trigeminal HZ for whom brivudine therapy led to rapid symptom relief and lesion healing without complications. Trigeminal zoster, owing to its involvement in the facial nerve and the potential for severe complications such as PHN, can be particularly debilitating in elderly patients. The ability of brivudine to rapidly halt vesicle formation and promote healing aligns with findings from studies that demonstrate its efficacy in treating HZ, particularly in preventing PHN, a common and painful sequelae of HZ, particularly in older adults.[13]

Compared with previous research, these cases corroborate the findings that brivudine is a potent antiviral agent with superior efficacy in managing HZ in elderly patients who are immunocompromised. The contraindication for brivudine in immunocompromised populations was established during its phase III clinical trials in which patients with congenital, acquired, or drug-induced immunodeficiencies, including malignancies, were excluded from the study enrollment.[35,37] This contraindication remains unchanged because of the absence of subsequent phase III studies in these populations. However, subsequent case reports and observational studies have suggested that brivudine is effective and safe in patients who are immunocompromised, although more robust evidence is required to revise its current labeling. Notably, brivudine is absolutely contraindicated in patients who have recently received or are currently receiving cancer chemotherapy involving 5-fluorouracil (5-FU) or related fluoropyrimidine within the last 4 weeks because of the risk of fatal toxicity.[38] Despite these limitations, the ability of brivudine to provide rapid symptom relief and lesion resolution and its safety profile, particularly in populations with renal dysfunction or multimorbidity, highlight its potential as a valuable treatment option. The absence of significant renal toxicity and reduced incidence of side effects observed in these cases support its use as a preferred option in selected high-risk populations.

Existing research supports these observations have demonstrated the efficacy of brivudine in elderly patients who are immunocompromised, highlighting its ability to reduce pain, prevent vesicle formation, and promote rapid healing compared with autoimmune diseases and other chronic conditions, further supporting the role of brivudine in these high-risk populations.[25,31,34]

Conclusion

In conclusion, when considered along with the published literature, these cases provide compelling evidence for the use of brivudine in treating HZ in vulnerable patient groups. The rapid onset of action, particularly in pain relief, by brivudine enhanced efficacy in immunocompromised populations, and favorable safety profile make it an important therapeutic option in managing HZ, particularly in patients with comorbid conditions, such as T2DM, autoimmune diseases, and renal impairment. Further randomized controlled trials are needed to establish its safety and efficacy in immunosuppressed populations.

Disclosure

The authors report no conflicts of interest in this work.

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