Dermatol Ther (Heidelb) (2023) 13:2461–2471
https://doi.org/10.1007/s13555-023-01019-6

CASE SERIES

Varicella Zoster Virus-Specific Hyperimmunoglobulin in the Adjuvant Treatment of Immunocompromised Herpes Zoster Patients: A Case Series

Patrick Terheyden · Cord Sunderkötter · Franz-Dietmar Söhngen · Linda Golle · Sonja Schimo · Ralf Baron · Christian Maihöfner · Andreas Binder · Wolfram Pönisch

Received: July 5, 2023 / Accepted: August 21, 2023 / Published online: September 13, 2023

ABSTRACT

Introduction: Immunocompromised patients are at increased risk for herpes zoster (HZ)-associated complications. Despite standard therapy with systemic antiviral drugs and analgesics, complications are frequently encountered, including generalization of lesions or persistent neuropathic pain, so-called post-herpetic neuralgia (PHN). Given the scarcity of literature and awareness of therapeutic options to improve patient outcomes, especially for vulnerable patient groups, here we describe a strategy based on early intensification of treatment with a varicella zoster virus-specific hyperimmunoglobulin (VZV-IgG), which is approved in the adjuvant treatment of HZ.

Methods: For this case series, we selected four cases of HZ in patients with impaired immunity due to hemato-oncologic disease or immunosuppressive treatment who presented with either existing generalized lesions and/or severe pain or with other risk factors for a complicated HZ course such as PHN. They were considered to be representative examples of different patient profiles eligible for intensification of treatment by the addition of VZV-IgG to virostatic therapy.

Case Report: All patients showed a rapid response to combined treatment with VZV-IgG and a virostatic agent. In two patients who had generalized lesions, the formation of new

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13555-023-01019-6.

P. Terheyden
Department of Dermatology, University of Lübeck, Lübeck, Germany

C. Sunderkötter · L. Golle
Department of Dermatology and Venereology, University Hospital Halle (Saale), Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

F.-D. Söhngen
Department of Hematology and Oncology, Hospital Altenburger Land GmbH, Altenburg, Germany

S. Schimo (✉)
Biotest AG, Landsteinerstraße 5, 63303 Dreieich, Hessen, Germany
e-mail: Sonja.Schimo@biotest.com

R. Baron
Division of Neurological Pain Research and Therapy, Department of Neurology, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

C. Maihöfner
Department of Neurology, General Fürth Hospital, University of Erlangen, Fürth, Germany

A. Binder
Department of Neurology, Hospital Saarbrücken gGmbH, Saarbrücken, Germany

W. Pönisch
Hematology and Cell Therapy, Medical Clinic and Policlinic 1, University Hospital Leipzig, University of Leipzig, Leipzig, Germany

lesions ceased 1 day after VZV-IgG infusion. One patient, with mantle cell lymphoma, achieved complete healing of the lesions 9 days after diagnosis of HZ, a rare occurrence compared to similar cases or cohorts. A patient with HZ in the cervical region showed a good response after a single dose of VZV-IgG. None of the patients developed post-zoster-related complications. Combination therapy of a virostatic agent and VZV-IgG was well tolerated in these four cases.

Conclusion: This case series demonstrates highly satisfactory treatment effectiveness and tolerability for VZV-IgG in the adjuvant treatment of immunocompromised HZ patients and supports early intensification of HZ therapy in patients at high risk of severe disease progression.

Keywords: Generalized lesions; Herpes zoster; Hyperimmunoglobulin; Immunocompromised; VZV; Varitect CP; VZV-IgG

Key Summary Points

Complications of herpes zoster (HZ) are frequently seen in immunocompromised patients; however, besides standard treatment with antiviral drugs and analgesics, data on alternative approaches to allow optimized HZ therapy are scarce

Here we describe a strategy based on early intensification of treatment with a varicella zoster virus-specific hyperimmunoglobulin (VZV-IgG, Varitect® CP), the only approved adjuvant therapy for patients with HZ, which should be considered, particularly in immunocompromised patients at risk of dissemination

We present four HZ patients each with individual risk factors for a complicated course of disease, in which all patients were immunocompromised because of either hemato-oncologic disease or immunosuppressive treatment

Treatment of HZ with a combination of virostatic agent and VZV-IgG proved to be both well tolerated and effective; despite the high-risk constellations, none of the patients went on to develop complications such as post-herpetic neuralgia

Our case series supports the early use of VZV-IgG in combination with antiviral drugs for the intensification of treatment of HZ in immunocompromised patients, with the potential to improve patient outcomes, and offers guidance on the use of VZV-IgG in eligible patients

INTRODUCTION

Herpes zoster (HZ) is a painful disease caused by reactivation of the varicella zoster virus (VZV) from latently infected ganglionic neurons [1]. Despite mainstay therapy with early systemic antiviral agents and analgesics, zoster patients are at risk of developing complications [1–3]. These include neurologic, cutaneous and vascular manifestations up to permanent impairment and a diminished quality of life [1, 4]. Although acute neuropathic pain often precedes or accompanies cutaneous eruptions, the most common long-term complication of HZ is a chronic neuropathic pain syndrome, also referred to as post-herpetic neuralgia or PHN [1]. PHN occurs in 5 to > 30% of patients and persists for at least 3 months after the resolution of acute HZ lesions [1, 4].

The substantial burden of disease associated with HZ emphasizes the need for better risk stratification of patients and refinement of standard therapy. Time is considered a critical factor; if the virus is left untreated and contact with the trigeminal and or spinal ganglia persists, there may be a higher probability of nerve injury and other complications [5]. This is especially reflected in immunodeficient patients who are at increased risk for a severe course of disease with viral dissemination and long-term sequelae [1]. Early intensification of therapy should be considered in this vulnerable patient

group; this can be achieved with a varicella zoster virus-specific hyperimmunoglobulin (VZV-IgG, Varitect® CP, Biotest AG, Germany), which is approved in the adjuvant treatment of HZ [6].

In the last 20 years, to our knowledge, there have been no publications on the use of VZV-IgG in HZ; consequently, there is limited awareness of this therapeutic option in the medical community. However, its usefulness was demonstrated in a small number of earlier studies reporting effectivity and safety [7–10] with the potentially beneficial effect of reducing the incidence of PHN [7].

Given this paucity of publications covering approved treatment options to optimize HZ therapy, we initiated a meeting of physicians from different specialties in October 2021 to discuss VZV-IgG and its value in the therapeutic management of HZ. The main focus was on patients with impaired immunity due to immunosuppression or hemato-oncologic disease. The four selected cases presented here each received a combined treatment approach consisting of a virostatic agent and VZV-IgG; they were nominated by this group as being representative examples of different patient profiles at risk of HZ-related complications and offer insights on the use of VZV-IgG in eligible patients to improve therapeutic management.

Ethical approval was not required for this study in accordance with local/national guidelines. Written informed consent was obtained from all patients for publication of their case and any accompanying images. The publication of this case series was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

CASE SERIES

Case 1

A 72-year-old Caucasian man with a 5-year history of chronic lymphocytic leukemia (CLL), receiving treatment with venetoclax, presented to the hospital with slightly painful lesions on the upper left side of his face. According to the patient, the first lesions had appeared 5 days before.

Physical examination revealed erythematous grouped vesicles in a left-sided V1 dermatomal distribution as well as diffusely spread aberrant vesicles (> 50) on the trunk. The left side of the face showed mild swelling and several necrotic plaques in the supraorbital region associated with slight pain, grade 2, on an 11-point numerical analog scale (NAS). Ocular involvement was excluded. Laboratory examination revealed a slightly elevated C-reactive protein (CRP: 10.1 mg/l; normal range: < 5.0 mg/l) and serum creatinine (123 µmol/l; no. 59–104 µmol/l) with an estimated glomerular filtration rate of 51 ml/min (no. > 90 ml/min, later improved to 88 ml/min) as well as lymphocytopenia (lymphocytes: 590/µl; no. 1100–4000/µl).

Disseminated HZ was diagnosed, and the patient was admitted to the dermatology clinic. Treatment was started with 5 mg/kg acyclovir (renal dose adjustment) intravenously three times a day for 7 days along with adequate pain treatment (metamizole 4 × 500 mg/day). Skin lesions were treated with zinc sulfate gel, which was later replaced by fusidic acid cream. Due to the advanced manifestations on the skin (dissemination, necrosis) 2 days later the patient received an additional single dose of 1.6 ml/kg (3750 IU) intravenous VZV-IgG (Fig. 1a–c, Supplementary Table S1). The VZV-IgG infusion was well tolerated. Within 1 day, cessation of new lesion formation was noted, and within 5 days, complete crusting of lesions was observed; the patient was pain free (NAS = 0) and discharged (Fig. 1a–c*). The treatment of the hematologic disease was not interrupted. At the outpatient follow-up examination 84 days after hospital admission, the patient showed complete healing of HZ. The skin lesions had healed with only discrete erythema remaining on the left side of the forehead. The pain medication had been terminated, and only a low level of tightness and itching on the left facial area was reported to be remaining.

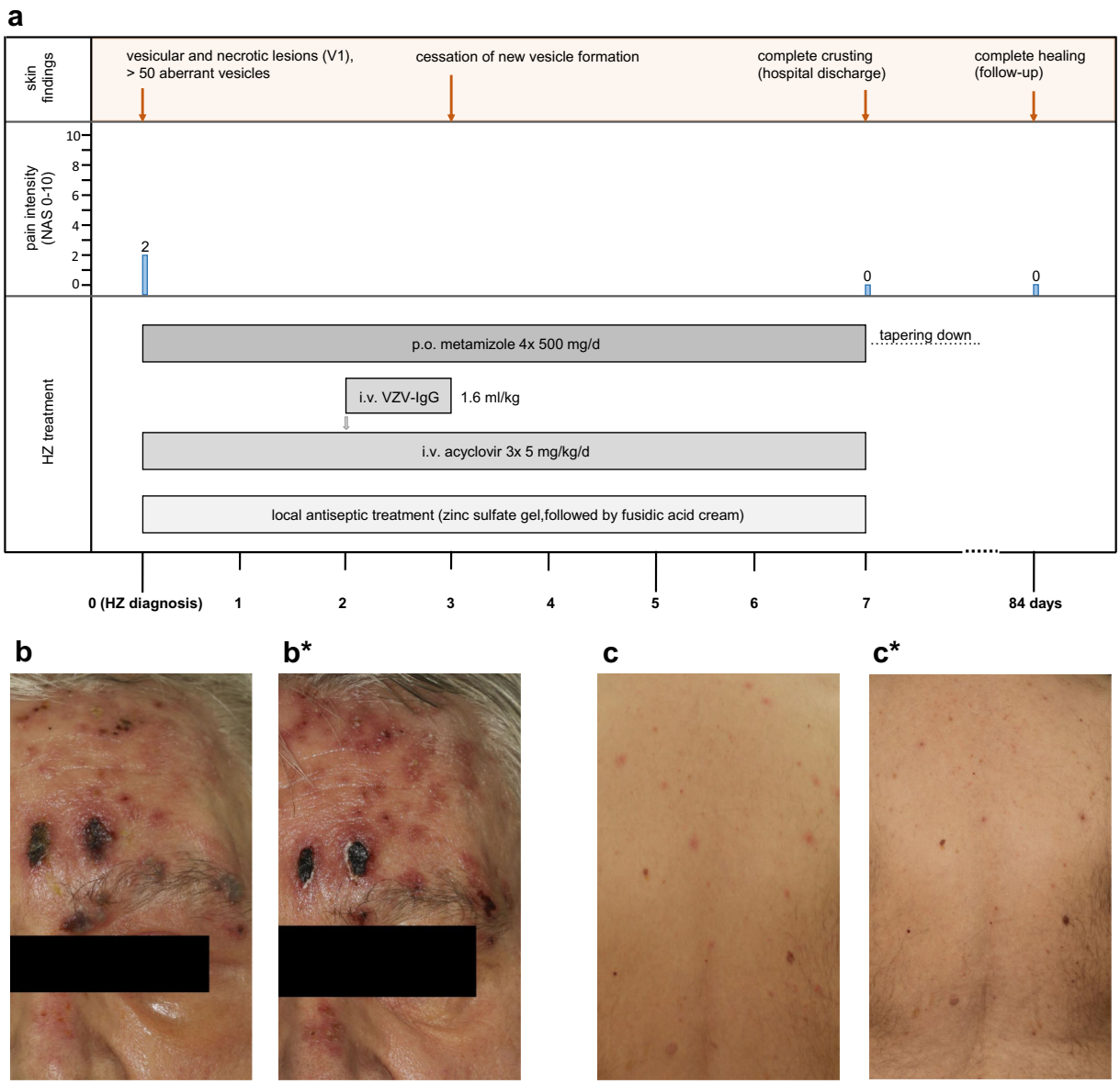

Fig. 1 Case 1: timeline of interventions and outcomes (**a**) and clinical presentation of HZ with lesions on the left side of the face and dissemination over the trunk (back view) 2 (**b**, **c**) and 7 days (**b***, **c***) after diagnosis, respectively. The swelling below the eyes had decreased significantly after 7 days, and the lesions on the back were completely crusted. *HZ* herpes zoster, *NAS* numerical analog scale, *VZV-IgG* varicella zoster virus-specific hyperimmunoglobulin

Case 2

A 61-year-old man was admitted to our hemato-oncology department with general weakness, increasing fatigue, fever and night sweats. Initial examination revealed lymphadenopathy, splenomegaly and pronounced lymphocytosis. Lymph node and bone marrow biopsy followed by immunohistochemical and cytogenetic analysis showed overexpression of cyclin D1 and translocation t(11;14)(q13;q32). The patient was diagnosed with mantle cell lymphoma stage IV B. A curative treatment approach with three double cycles of alternating R-CHOP (rituximab

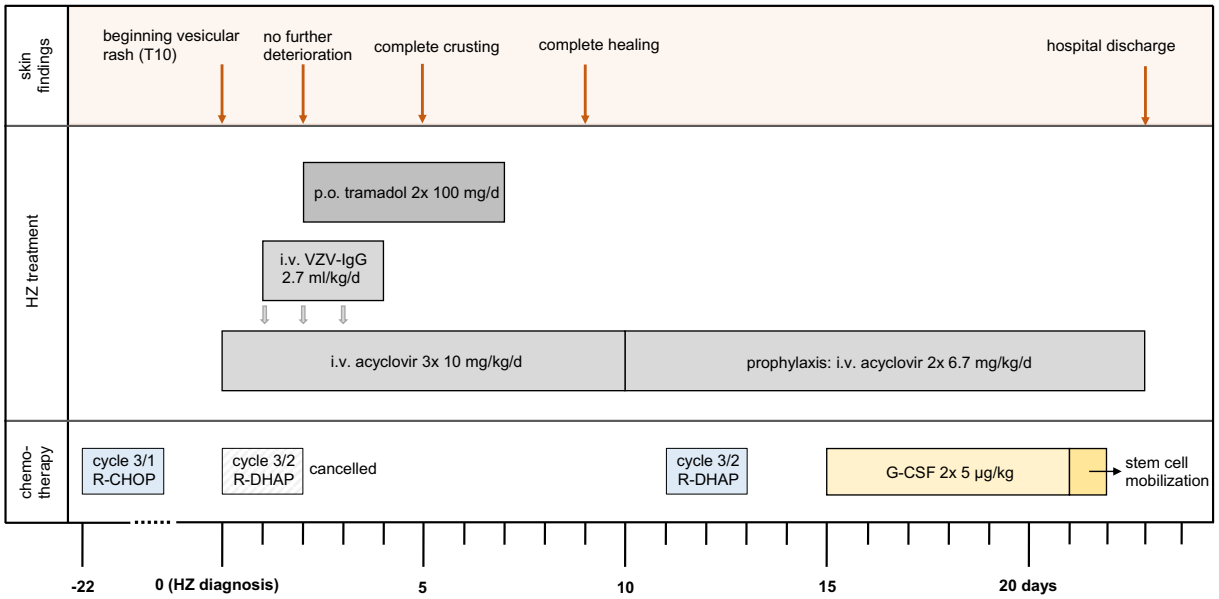

Fig. 2 Case 2: timeline of interventions and outcomes. *G-CSF* granulocyte-colony stimulating factor, *HZ* herpes zoster, *R-CHOP* rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisone, *R-DHAP* rituximab plus dexamethasone, high-dose cytarabine and cisplatin, *VZV-IgG* varicella zoster virus-specific hyperimmunoglobulin

plus cyclophosphamide, doxorubicin, vincristine and prednisone) and R-DHAP (rituximab plus dexamethasone, high-dose cytarabine and cisplatin) was initiated. The patient tolerated the immunochemotherapy well; however, at his planned admission for the third R-DHAP cycle, the patient was diagnosed with HZ presenting with a unilateral, commencing confluent vesicular rash in a right-sided T10 dermatomal distribution. According to the patient, the rash had started the previous day and was not accompanied by pain. Chemotherapy was discontinued, and antiviral therapy with intravenous acyclovir 3×10 mg/kg per day over 10 days was started (Fig. 2, Supplementary Table S1). An immune status analysis was conducted. The results were available the next day and confirmed that the patient had a severe combined humoral and cellular immunodeficiency [IgG: 4.31 g/l (no. 7.0–14.6 g/l), IgA: 0.21 g/l (no. 0.2–3.8 g/l), IgM: 0.18 g/l (no. 0.5–2.3 g/l), $CD4^+$ lymphocytes: 65/µl (no. 510–1614/µl), $CD8^+$ lymphocytes: 122/µl (no. 231–918/µl), $CD19^+$ lymphocytes: 3/µl (no. 109–411/µl), natural killer cells: 56/µl (no. 93–615/µl)]. Due to this high-risk constellation, the antiviral therapy was intensified, and the patient additionally received 2.7 ml/kg intravenous VZV-IgG (5000 IU) per day over 3 consecutive days. This therapy was well tolerated. One day after the start of VZV-IgG, cessation of new vesicle formation was observed. Additionally, due to the onset of moderate HZ-associated pain, therapy was complemented with 2×100 mg/day p.o. tramadol over 5 days. Thereafter, pain therapy was no longer necessary. Within 9 days of HZ diagnosis, complete healing of the skin lesions was observed; on day 10 intravenous acyclovir was switched to a prophylactic dosage with 500 mg two times per day. One day later, immunochemotherapy with R-DHAP was continued followed by successful stem cell mobilization and subsequent autologous stem cell transplantation. Twenty-three days after HZ diagnosis, the patient was discharged from the hospital without HZ-associated complications.

Case 3

A 48-year-old Caucasian woman with atopic dermatitis, who had undergone radioiodine

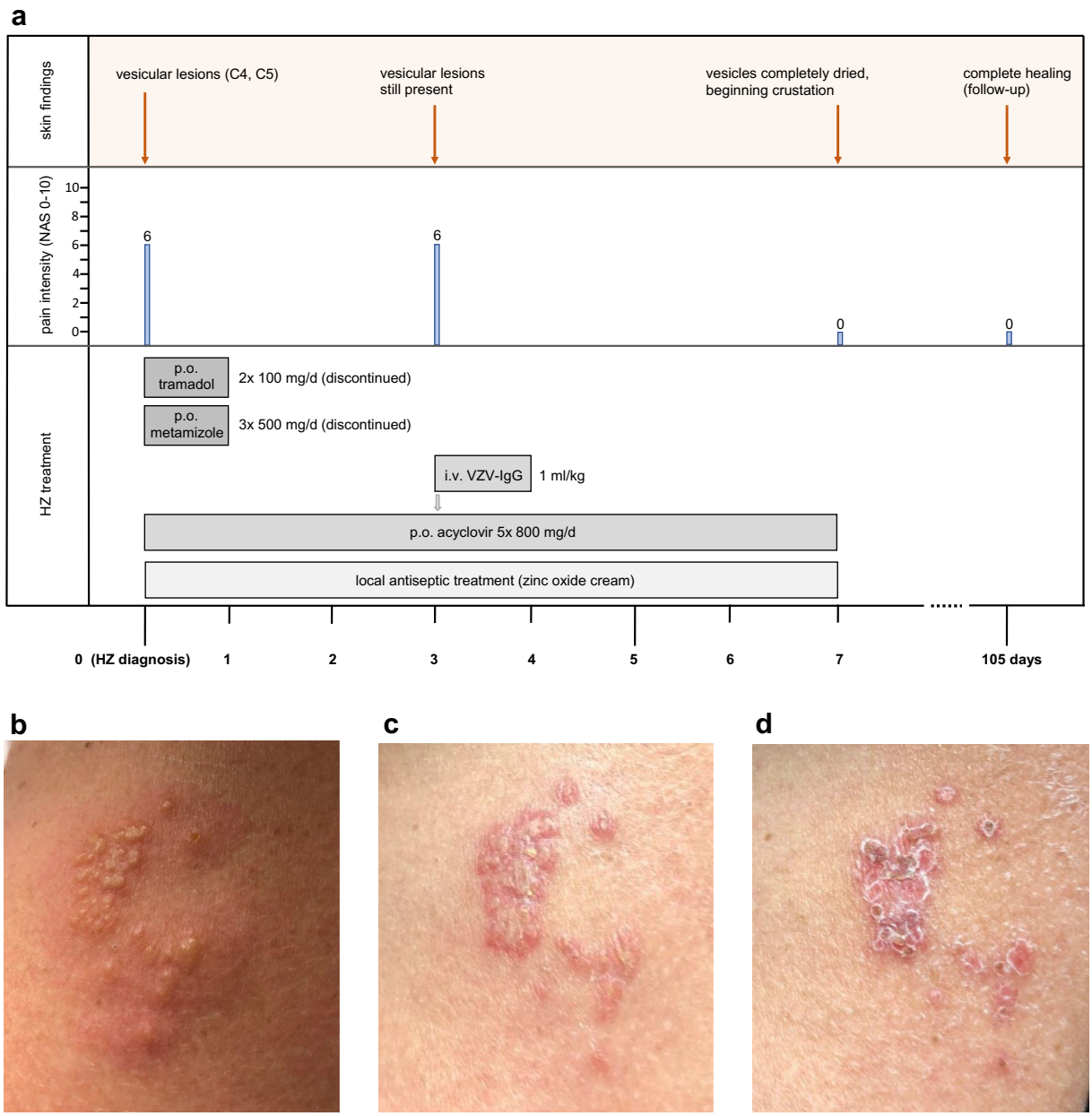

Fig. 3 Case 3: timeline of interventions and outcomes (**a**) and clinical presentation of HZ with erythematous grouped vesicles on the left side of the neck at treatment start (**b**), during treatment on day 3 (**c**) and on day 7 (**d**). *HZ* herpes zoster, *NAS* numerical analog scale, *VZV-IgG* varicella zoster virus-specific hyperimmunoglobulin

treatment for autonomous adenoma 1 month previously, was transferred to the hemato-oncologic clinic for further examination of a previously diagnosed thrombocytosis. Comprehensive examination additionally revealed a mild cellular immunodeficiency ($CD19^+$ lymphocytes: 83/µl; $CD8^+$ lymphocytes: 178/µl), likely related to the radioiodine treatment, but no other abnormal findings.

On follow-up 6 months after radioiodine treatment, the patient presented with a left-sided supraclavicular itching and burning blistering rash (C4-C5 dermatomes) with a pain

intensity of 6 on an 11-point NAS (Fig. 3a, b; Supplementary Table S1). According to the patient, the first lesions appeared a few days previously.

Laboratory examination revealed no increase of inflammatory markers [leukocytes: 7300/µl (no. 4000–10,400/µl); CRP: 0.5 mg/l]. There was no evidence of impaired humoral immunity, but $CD19^+$ lymphocytes (96/µl) and $CD8^+$ lymphocytes were reduced (188/µl). Serum VZV antibody titers were positive for IgG (1001 IU/l; negative cutoff: < 80 IU/l) and negative for IgM, indicative of a previous VZV infection. Based on these findings the patient was diagnosed with HZ.

Antiviral treatment was initiated with 800 mg oral acyclovir five times a day for 7 days and complemented with zinc oxide cream for treatment of the skin lesions. Pain treatment was started with 2 × 100 mg/day tramadol and 3 × 500 mg/day metamizole but discontinued on the patient's request. After telephone consultation 2 days later, the patient was requested to present at the department the following day. Active HZ lesions were still present, and pain symptoms were unchanged (Fig. 3a, c). Due to poor response to initial treatment, the cervical risk location (risk factor for neurologic involvement and long-term sequelae) and the diagnosed mild cellular immunodeficiency, the patient received an additional single dose of 1 ml/kg (1750 IU) intravenous VZV-IgG. No adverse reactions occurred. On follow-up 4 days later, blisters were completely dried and were beginning to form crusts (Fig. 3a, d). The patient was and remained pain free thereafter. After some weeks, the skin lesions healed completely without scarring.

Case 4

A 67-year-old Caucasian man with rheumatoid arthritis (RA), who had previously been hospitalized for myocardial infarction, was transferred to the dermatology department with HZ mandibularis. The patient had several comorbidities, including coronary artery disease, other cardiac and pulmonary morbidities, and type-2 diabetes mellitus. For the treatment of his RA he received immunosuppressive treatment with adalimumab and methotrexate.

The patient reported pain in the jaw region, followed by the appearance of vesicles in the left mandibular region and subsequently the spreading of vesicles over his whole body. He presented at the dermatology unit 1–2 weeks after the onset of pain.

Physical examination revealed multiple papular and vesicular eruptions with erythema as well as single necrotic lesions localized unilaterally along the left side of the mandibular nerve (V3) including the retroauricular area, accompanied by allodynia and severe burning pain, grade 8, on an 11-point NAS. The oral mucosa was not affected. In addition, the presence of over 50 aberrant vesicles on the trunk indicated generalization of lesions.

Laboratory analysis showed an elevation of CRP plasma levels (11.4 mg/l) with mild leukocytosis (12,130/µl). Serum creatinine was in the normal range (80 µmol/l).

Based on the typical clinical picture, HZ with generalization was diagnosed. Due to immunosuppression and signs of disease aggravation (generalization, necrotic lesions, severe pain), antiviral treatment was immediately started with 750 mg intravenous acyclovir three times a day for 10 days and a single dose of 1.2 ml/kg (2500 IU) intravenous VZV-IgG. The infusion was well tolerated; only a new headache was reported by the patient later on in the course of the day. Antiviral treatment was accompanied by the department's standard analgesic treatment regimen with 3 g/day metamizole and pregabalin (25 mg/day followed by slow titration to a therapeutic dose), which is initiated whenever pain intensity is > 4 or in presence of other risk factors for neuropathic pain. The skin lesions were treated with local antiseptic therapy (Fig. 4, Supplementary Table S1).

One day after start of treatment, the eruption of new vesicles ceased, and the patient reported an instant relief of pain. Renal function was stable, and no involvement of visceral organs was detected. On day 6, the patient reported a reduced pain intensity of 3; within 10 days of treatment, complete crusting of lesions was observed. The patient was discharged. On

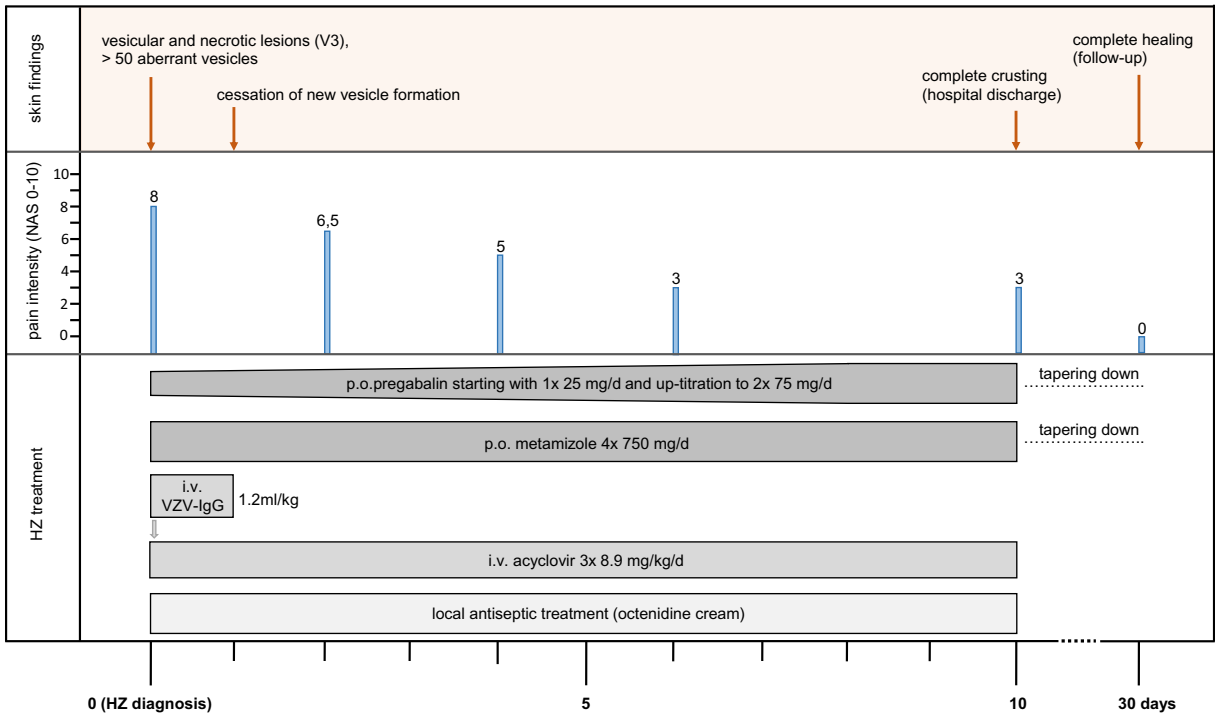

Fig. 4 Case 4: timeline of interventions and outcomes. *HZ* herpes zoster, *NAS* numerical analog scale, *VZV-IgG* varicella zoster virus-specific hyperimmunoglobulin

follow-up, 1 month post diagnosis, the patient was pain free and the skin lesions had completely healed; coincidentally, the patient was newly diagnosed with CLL (Binet stage B).

DISCUSSION

We describe a case series of immunocompromised patients who received combination therapy with VZV-IgG in addition to a virostatic agent because of their increased risk of severe disease progression. Risk factors associated with a severe course of HZ include age > 50 years, immunodeficiency, HZ of the head and/or neck region, HZ with hemorrhagic or necrotic vesicles and/or signs of cutaneous dissemination, CNS and/or visceral involvement, moderate to severe prodromal or acute zoster-associated pain as well as HZ in patients with severe predisposing skin diseases [1]. Guideline-based treatment includes virostatic therapy, topical antiseptics and rigorous pain management [1].

Despite treatment compliance with guidelines, e.g. starting antiviral chemotherapy within 72 h of rash onset and early pain management, PHN incidences reported in randomized controlled trials (RCT) varied between 1.0% and 20.2% [1–3, 11]. RCTs typically focus on a highly homogeneous subset of patients excluding complex or comorbid HZ patients such as patients with immunosuppression and/or renal impairment and/or disseminated and/or opthalmic HZ. Published PHN incidences may therefore only poorly reflect real-world settings [2, 3, 11].

Real-world data consistently demonstrate that complications such as severe neuropathic pain or PHN are significantly more common in immunosuppressed patients [12, 13]. An analysis of data from the German Pharmacoepidemiological Research Database showed a more frequent occurrence of PHN in immunocompromised patients than in immunocompetent individuals (33.8% vs. 22.5%) [12]. For different groups of immunosuppressed patients, including patients with stem cell transplantation,

hematologic malignancies, solid tumors and HIV, a PHN risk ranging from 6% to 45% was identified [13]. Therefore, intensifying HZ therapy in vulnerable patient groups such as immunocompromised patients is highly recommended.

In Germany, passive immunotherapy with VZV-IgG (Varitect® CP) is approved for the adjuvant treatment of HZ, particularly in immunocompromised patients at risk of dissemination [6]. VZV-IgG is a hyperimmunoglobulin containing purified immunoglobulins derived from pooled human plasma with standardized high levels of VZV antibodies. Depending on the severity and clinical course of disease, a dosage of 1–2 ml/kg is recommended [6]. The medical decision on dosage, frequency and duration of use depends on the severity of the disease and its course as well as on the underlying disease and its treatment. As shown in the second case, if curative chemotherapy is interrupted because of HZ and severe immunodeficiency, a higher dosage and repeated administration of VZV-IgG can be useful in parallel with virostatics with the aim to halt the progression of the disease and to limit neural damage, without jeopardizing the curative therapeutic approach of the patient.

In general, immunity to VZV is thought to be driven by T-cells particularly in the maintenance of latent VZV in a subclinical state. However, when there is a decline in the immune system of the host, which can occur with iatrogenic immune suppression or aging, reactivation of latent virus may occur [14]. Another component contributing to immunity against VZV appears to be antibody-dependent cellular cytotoxicity (ADCC), since patients with defects in natural killer cells, which are central to ADCC, suffer from severe and recurrent, often fatal VZV infections [14].

Virostatic drugs and VZV-IgG have a synergistic mode of action in the treatment of VZV; while the virostatic drug prevents viral replication inside the cell, VZV-specific IgGs mediate ADCC towards infected cells and also neutralize viral particles, thus preventing further dissemination [14–16].

The usefulness of VZV-IgG in the treatment of HZ was demonstrated in previous studies. A retrospective study in 113 adults, 67 of whom were immunocompromised, concluded that both VZV-IgG and acyclovir are effective therapeutics in the treatment of varicella and HZ [10]. In a small double-blind placebo-controlled randomized study, early combination of intravenous acyclovir and VZV-IgG in HZ patients was well tolerated and shown to be superior to placebo, with the incidence of PHN at day 42 reduced by 50% ($p = 0.027$) [7]. Two other smaller studies support the use of VZV-IgG in the treatment of HZ reporting satisfactory effectivity and safety [8, 9].

In all the cases presented here, there was a rapid response to the combination therapy with antiviral agent and VZV-IgG, particularly regarding disseminated or generalized HZ. In patients with generalized HZ (cases 1 and 4), cessation of new lesion formation was observed within 1 day of administration of VZV-IgG. In a similar cohort, a median time to cessation of new lesion formation of 2.2 days was reported after commencing i.v. acyclovir, while new lesion formation outside the primary dermatome by day 5 and 7 persisted in 19% and 3% of patients, respectively [17]. Early high-dose administration of VZV-IgG for 3 days (case 2) rapidly led to complete healing of lesions by day 9 after treatment start, notably shorter than a median of 17 days previously reported in a group of immunocompromised oncology patients [18]. In patient 3, a good response was observed after a single dose of VZV-IgG. Despite the high-risk constellations in this series, including impaired immunity, generalization of HZ, necrotic lesions and/or acute HZ-associated pain, no patient went on to develop further complications of HZ such as PHN. Overall, VZV-IgG co-administered with acyclovir showed good effectiveness and tolerability.

CONCLUSION

In clinical practice, immunocompromised patients with a high risk of a complicated course of HZ are common. For some of these patients, HZ may interrupt primary oncologic therapy and consequently worsen prognosis and health. The cases described here show that early addition of VZV-IgG to virostatic treatment has the

potential to shorten interruptions to curative therapy as well as to reduce or treat complications of HZ in this vulnerable patient group. As demonstrated, in this case series combination therapy resulted in rapid cessation of vesiculations and the absence of post-zoster-related complications. These results merit well-designed clinical studies to confirm the favourable effects of VZV-IgG and to further refine and personalize therapy in terms of dose, interval and duration according to individual risk constellations for patients who would particularly benefit from adjuvant treatment with VZV-IgG.

ACKNOWLEDGEMENTS

The authors extend thanks to the patients for agreeing to the presentation of their medical data.

Medical Writing/Editorial Assistance Editorial assistance in the preparation of this manuscript was provided by Sigrid Schwarz of MedWiss.Institut. Support for this assistance was funded by Biotest AG. We also thank Michelle Isele and Peter Griffiths, Biotest AG, for assistance with medical writing.

Author Contributions. All authors contributed to the conception of the work. Linda Golle, Wolfram Pönisch, Franz-Dietmar Söhngen, Cord Sunderkötter and Patrick Terheyden were involved in the acquisition, analysis and interpretation of data and directly involved in the care of patients. The first draft of the manuscript was written by Sonja Schimo and all authors critically revised the initial manuscript and commented on previous versions. All authors read and approved the final manuscript.

Funding. Funding for the journal's Rapid Service Fee, and the editorial assistance received was provided by Biotest AG.

Data Availability. The datasets generated during and/or analyzed in this case series are available from the corresponding author on reasonable request made within 6 months following publication. Additional patient data are not publicly available on legal and ethical grounds.

Declarations

Conflict of Interest. Linda Golle has no conflict of interest to declare. Ralf Baron, Andreas Binder, Christian Maihöfner, Wolfram Pönisch, Franz-Dietmar Söhngen, Cord Sunderkötter and Patrick Terheyden received advisory board honoraria from Biotest AG. Ralf Baron, Cord Sunderkötter and Patrick Terheyden received consultancy fees from Biotest AG. Andreas Binder received consultancy fees from Biotest AG, Pfizer and BMS. In the past 3 years Christian Maihöfner has worked as a consultant and/or speaker for the following companies: Allergan, Biotest AG, Daiichi Sankyo, Bionorica ethics, Grünenthal, GSK, Novartis, Lilly, Lundbeck, Pfizer, TEVA. Wolfram Pönisch received consultancy fees and speaker fees from Biotest AG. Franz-Dietmar Söhngen has since moved to the Paracelsus Hospital, Bad Suderode GmbH, Germany. Sonja Schimo is an employee of Biotest AG.

Ethical Approval. Ethical approval was not required for this study in accordance with local/national guidelines. Written informed consent was obtained from all patients for publication of their case and any accompanying images. The publication of this case series was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

REFERENCES

1. Gross GE, Eisert L, Doerr HW, et al. S2k guidelines for the diagnosis and treatment of herpes zoster and postherpetic neuralgia. J Dtsch Dermatol Ges. 2020;18(1):55–78. https://doi.org/10.1111/ddg.14013.

2. Bulilete O, Leiva A, Rullan M, Roca A, Llobera J, Group PHN. Efficacy of gabapentin for the prevention of postherpetic neuralgia in patients with acute herpes zoster: a double blind, randomized controlled trial. PLoS ONE. 2019;14(6): e0217335. https://doi.org/10.1371/journal.pone.0217335.

3. Tyring SK, Lee P, Hill GT Jr, Silverfield JC, Moore AY, Matkovits T, et al. FV-100 versus valacyclovir for the prevention of post-herpetic neuralgia and the treatment of acute herpes zoster-associated pain: a randomized-controlled trial. J Med Virol. 2017;89(7):1255–64. https://doi.org/10.1002/jmv.24750.

4. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014;4(6): e004833. https://doi.org/10.1136/bmjopen-2014-004833.

5. Andrei G, Snoeck R. Advances and perspectives in the management of varicella-zoster virus infections. Molecules (Basel, Switzerland). 2021;26(4):1132. https://doi.org/10.3390/molecules26041132.

6. Biotest Pharma GmbH. Summary of product characteristics (Fachinformation) Varitect® CP, German version 09/2022.

7. Hügler P, Siebrecht P, Hoffmann K, Stucker M, Windeler J, Altmeyer P, et al. Prevention of postherpetic neuralgia with varicella-zoster hyperimmune globulin. Eur J Pain. 2002;6(6):435–45. https://doi.org/10.1016/s1090-3801(02)00046-0.

8. Scarsella A, Scarsella S, Di Stanislao C. Immunoglobuline umane anti-varicella zoster virus nella terapia dell´herpes zoster e delle nevriti posterpetiche. Giornale Italiano Di Ricerche Cliniche E Terapeutiche. 1993;10:10–7.

9. Agostini G, Agostini S. Immunoglobulins in the treatment of herpes zoster. Clin Ter. 1992;141:11–6.

10. Senneville E, Chidiac C, Brouillard M, et al. Acyclovir and specific anti-varicella-herpes zoster immunoglobulins in the treatment of varicella-zoster virus infection in 113 adults. Pathol Biol (Paris). 1990;38(5(Pt 2)):568–71.

11. Kawashima M, Nemoto O, Honda M, Watanabe D, Nakayama J, Imafuku S, et al. Amenamevir, a novel helicase-primase inhibitor, for treatment of herpes zoster: a randomized, double-blind, valaciclovir-controlled phase 3 study. J Dermatol. 2017;44(11):1219–27. https://doi.org/10.1111/1346-8138.13948.

12. Schröder C, Enders D, Schink T, Riedel O. Incidence of herpes zoster amongst adults varies by severity of immunosuppression. J Infect. 2017;75(3):207–15. https://doi.org/10.1016/j.jinf.2017.06.010.

13. McKay SL, Guo A, Pergam SA, Dooling K. Herpes zoster risk in immunocompromised adults in the United States: a systematic review. Clin Infect Dis. 2020;71(7):e125–34. https://doi.org/10.1093/cid/ciz1090.

14. Park SY, Levin MJ, Canniff J, Johnson M, Schmid DS, Weinberg A. Development of antibody-dependent cellular cytotoxicity in response to recombinant and live-attenuated herpes zoster vaccines. NPJ Vaccines. 2022;7(1):123. https://doi.org/10.1038/s41541-022-00545-2.

15. Aiba N, Shiraki A, Yajima M, Oyama Y, Yoshida Y, Ohno A, et al. Interaction of immunoglobulin with cytomegalovirus-infected cells. Viral Immunol. 2017;30(7):500–7. https://doi.org/10.1089/vim.2016.0151.

16. Bozzo J, Jorquera JI. Use of human immunoglobulins as an anti-infective treatment: the experience so far and their possible re-emerging role. Expert Rev Anti Infect Ther. 2017;15(6):585–604. https://doi.org/10.1080/14787210.2017.1328278.

17. Whitley RJ, Gnann JW Jr., Hinthorn D, et al. Disseminated herpes zoster in the immunocompromised host: a comparative trial of acyclovir and vidarabine. The NIAID Collaborative Antiviral Study Group. J Infect Dis. 1992;165(3):450–5. https://doi.org/10.1093/infdis/165.3.450.

18. Shepp DH, Dandliker PS, Meyers JD. Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. N Engl J Med. 1986;314(4):208–12. https://doi.org/10.1056/NEJM198601233140404.