

A case study:

The treatment of an acute herpes zoster outbreak with an herbal, anti-viral remedy in an immunocompromised individual.

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Abstract

Objective: This case study demonstrates the safety and efficacy of the treatment of an acute herpes zoster outbreak with Peaceful Mountain Shingles Rescue (PMSR), an herbal antiviral remedy.

Design: A case report is considered and discussed. The symptoms of the subject were tracked using self-report surveys filled out daily. Weekly clinic visits entailed a detailed weekly survey, interview, and collection of photographic data.

Subjects: A 60-year old Caucasian woman, undergoing radiation therapy for a recently removed cancerous tumor, presented to her physician typical symptoms of herpes zoster rash. After four days on valaciclovir, a nurse in her doctor's office referred her to this study.

Interventions:

-Treatment phase I (5/20/04-7/18/04)

-Placebo phase (7/19/04-7/30/04)

-Treatment phase II (7/31/04-10/4/04)

Outcome measures: Severity of sleep disturbance, severity of pain, severity of tingling, severity of soreness, severity of redness, severity of shooting pain, severity of burning pain, discomfort, interference with daily activities, and overall severity of shingles symptoms were the primary, quantitative outcome measures. A secondary outcome measure was the qualitative analysis of photographs.

Results: Over the study period, the subject experienced reductions in all dimensions of symptoms. During the washout phase, where a placebo was administered, the condition worsened and symptoms began to return. This reoccurrence abated upon reinstatement of

the active treatment. Patient satisfaction with the treatment was excellent throughout the study.

Conclusion: PMSR is an effective treatment for reducing the severity and discomfort associated with herpes zoster rash in the immunocompromised population, even in the absence of concomitant systemic anti-viral therapy.

Key words: herpes zoster, immunocompromised, naturopathic, antiviral, treatment, case report.

Introduction:

The varicella-zoster virus (VZV) is responsible for herpes zoster, a viral infection of the peripheral nervous system commonly referred to as shingles. Common in the elderly and individuals of compromised immune status, symptoms of a herpes zoster rash typically include burning, itching skin accompanied by shooting nerve pain, increased skin sensitivity, and damage to the skin. The rash typically abates two to six weeks after the first symptoms depending on how quickly treatment of the rash began [1]. Individuals with compromised immune systems, due either to disease or chemotherapy, are at risk of prolonged symptoms, dissemination, and bacterial superinfection [1, 6, 9]. Balfour et al and Tying et al investigated the duration of VZV infection in immunocompromised individuals treated intravenously with antiviral medication, and found the median duration until complete healing of lesions to be 22.4 days and 21 days respectively [2, 14]. The persistent nature of viral infections in this population presents clinicians with the problem of how to efficiently treat these individuals, while minimizing discomfort. The treatment assessed in the current case study is a topical herbal gel with antiviral, cell proliferative, and nerve quelling properties [7]. It is the intent of this study to demonstrate the safety and efficacy of the gel while illustrating its ability to reduce discomfort, prevent dissemination of the virus, and minimize the need for repeated courses of antiviral therapy.

Case Report:

The subject discussed in the current case study presented symptoms of herpes zoster to her doctor shortly after undergoing chemotherapy. She was referred by a nurse in her doctor's office to the clinical research department at Klearsen Corporation. The subject

was a 60-year-old female who received a hysterectomy in March of 2004. A cancerous tumor had penetrated over 75% of her uterine wall. A course of radiation therapy was initiated to clear surgical margins of any remaining cancerous cells. Toward the end of her six-week radiation treatment course, the subject noticed a sharp neuralgia in her right shoulder. Within 48 hours of this initial neuralgia, the subject was at her doctor's office presenting with symptoms of herpes zoster rash. Due to the common occurrence of VZV infections in oncology patients treated with chemotherapy, and the typical presentation of symptoms, a diagnosis of zoster was made in the absence of a viral culture. The subject was placed on valaciclovir anti-viral therapy. As she left the office of her doctor, she was referred to the clinical research department of Klearsen Corporation for a trial therapy on shingles and postherpetic neuralgia. The following protocol was adapted from a study on post herpetic neuralgia (PHN) to accommodate the unique situation of the subject.

Materials and Methods:

The subject was treated with PMSR for 12 weeks after an acute outbreak of herpes zoster. Medical history was obtained from the subject during a recorded interview on her first visit to the clinic. Symptoms were tracked with daily, self-administered surveys that tracked the following dimensions of pain and quality of life as reported by the subject: Severity of sleep disturbance, severity of pain, severity of tingling, severity of soreness, severity of redness, severity of shooting pain, severity of burning pain, discomfort, interference with daily activities, and overall severity of shingles symptoms. The subject was also asked to record the times of application each day to ensure compliance with the recommended treatment protocol. Clinic visits were conducted approximately every 7 days. These visits consisted of a verbal interview, a detailed weekly survey, a picture of

the rash, and solicitation of adverse events. In addition to the standard daily questions, the detailed weekly survey asked the subject to rate her overall status as compared to the beginning of the study, and her satisfaction with the treatment. The inclusion of a washout phase (no active treatment applied) was included in the study to serve as a means of comparison. During the washout phase, the subject was given a placebo gel that had the same look and feel as the PMSR, but with no active ingredients.

Results:

On the fourth day of valaciclovir therapy, the subject came to the clinic for her first visit (see Fig. 1 for a timeline of treatment), baseline photos were taken (Fig. 1a), a verbal interview was given and recorded, and the subject filled out the first symptoms survey. Her average score of all dimensions of pain or life interference scales on the first day of the study was an eight (on a one to nine scale, nine being “as bad as it could be”, and one being “None at all”). The subject was seen again four days later (5/24/04), and a third time four days after that (5/28/04). The severity of her symptoms, as extrapolated from her symptoms surveys and visual assessment, changed very little in these first three visits. After nineteen days of valaciclovir anti-viral therapy and fifteen days in the study, the subject was taken off of valaciclovir due to failure to respond to treatment. At this point in the study, the average score on any one dimension of pain was an 8. Over the next three weeks of PMSR treatment, a slow yet consistent tapering of symptoms was observed (Fig. 2), until all lesions on the subject’s arm and hand had fully healed (Fig. 1b). This time frame suggested the possibility of a spontaneous remission of the infection [1]. To control for this possibility, the subject was started on a twelve-day

washout phase (WOP) wherein only a placebo gel would be applied to the affected region. The subject was asked to return the remaining portion of her PMSR, and told to apply a similar, “new and improved” preparation for the next several days while continuing to fill out the symptoms surveys. This hope of a “new and improved” preparation induced in the subject a clear placebo effect in the first three days of the WOP as symptom severity ratings dropped slightly for the first time in three weeks. Three days after the beginning of the WOP, nearly all symptom dimensions reversed their rate of decline and rose to levels higher than those preceding the WOP. Photograph data shows the distinct breakout of a new lesion on the subject’s anterior wrist (Fig. 1c). The effect of removing treatment was more detrimental to the rash than a simple placebo effect could counter for. When PMSR therapy was resumed after twelve days of placebo application, all dimensions of pain, and life interference began to decrease to the same level as prior to the placebo intervention. The lesion began to quickly heal, and previous reports of tingling and burning by the subject were replaced by descriptions of the soothing effects of the PMSR (Fig. 1d).

Figure 1: Timeline of Treatment and Symptoms

Fig. 1a (5/20/04) pre-treatment

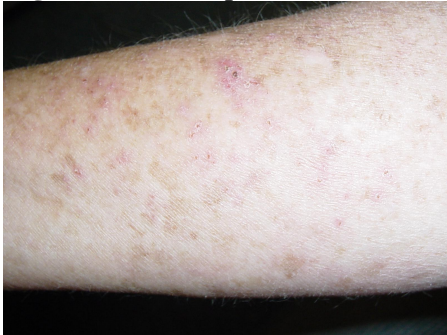


Fig. 1b (7/19/04) end of treatment phase 1
Placebo phase day 1



Fig. 1c (8/2/04) after 13 days of placebo



Fig. 1d (10/4/04) 2 months after
reintroduction of the active treatment.

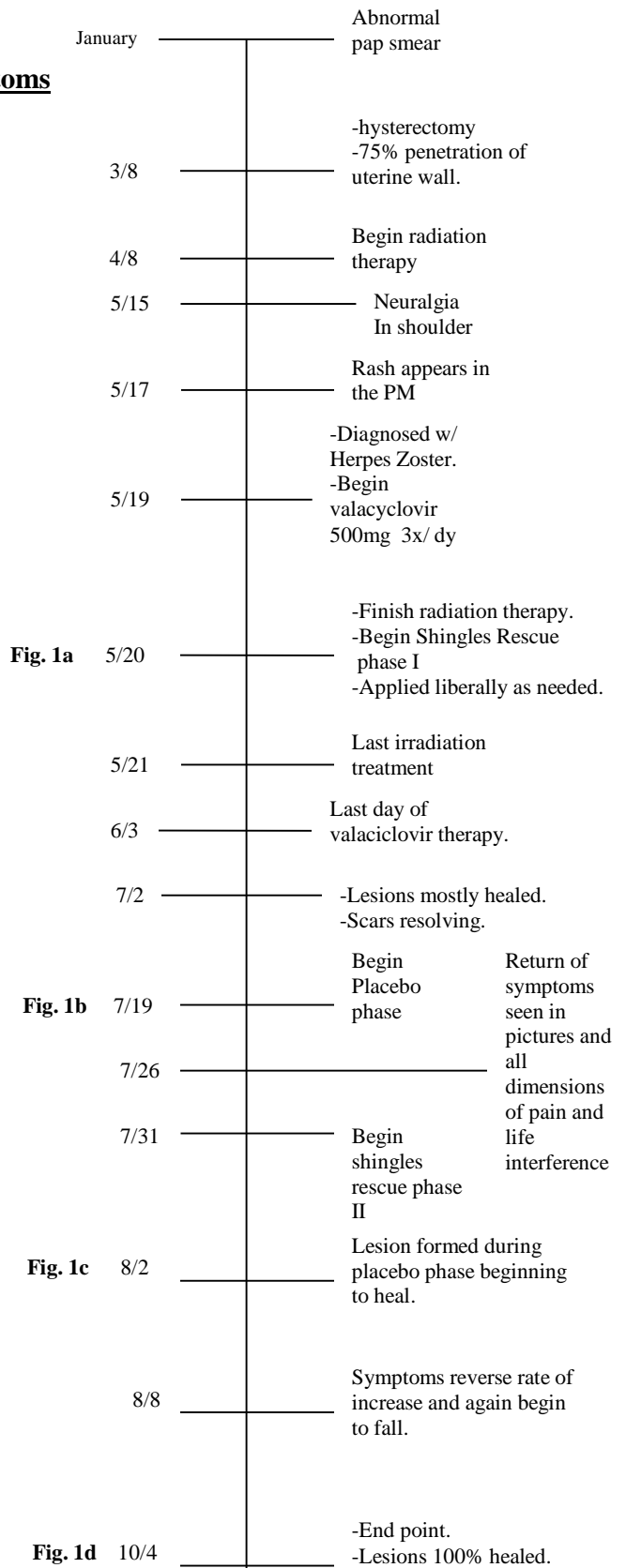
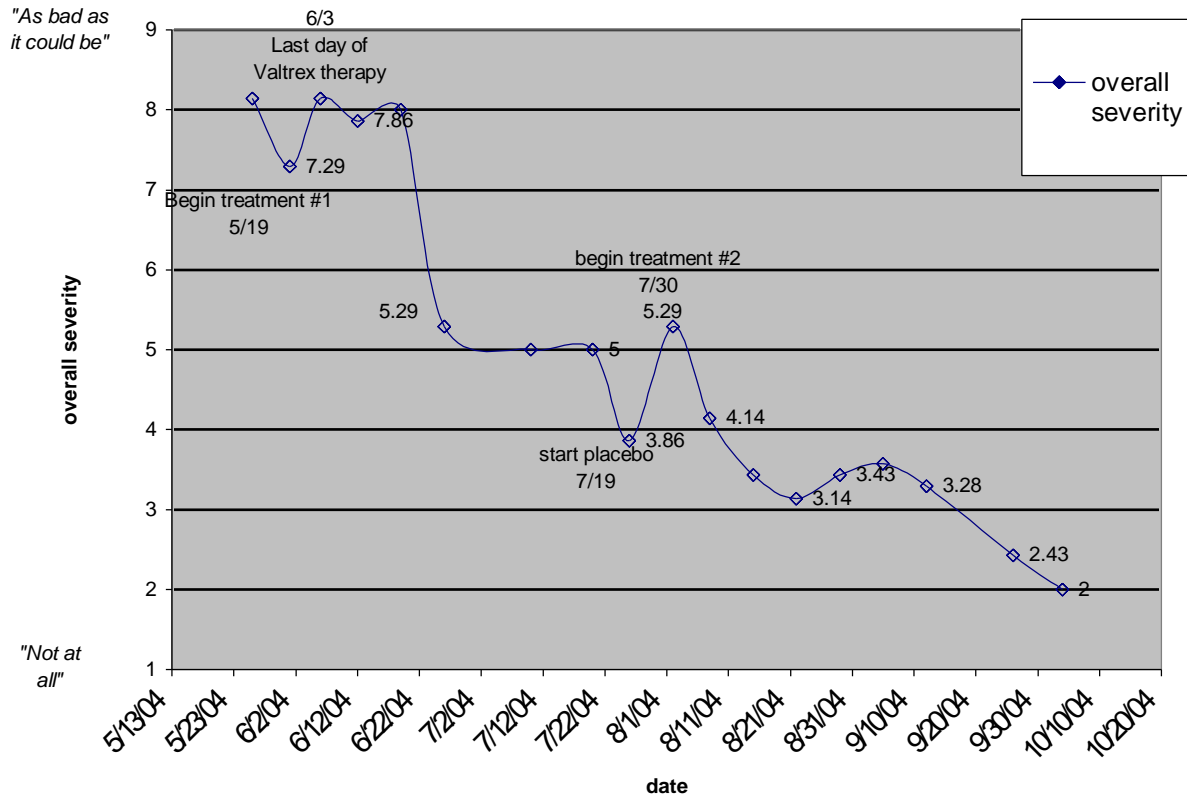


Fig. 2
Patient rated overall severity of Shingles outbreak
average of every 7 days



Discussion:

The high frequency occurrence of varicella zoster virus (VZV) outbreaks in immunocompromised individuals receiving either chemo or radiation therapy for solid tumors has raised many interesting issues for clinicians. Among them is the dilemma of how to treat VZV outbreaks recalcitrant to traditional antiviral therapy such as acyclovir, valaciclovir, and vidarabine. Clinical studies have shown these medicines to be highly effective in immunocompetent individuals when administered within 72 hours of symptom presentation [2, 12, 13]. Additionally, anti-viral cocktails have been questionably shown to reduce the occurrence of post-herpetic neuralgia (PHN) in

immunocompromised individuals as long as treatment is initiated within the same 72-hour grace period [12]. However, in the immunocompromised population, outbreaks often last longer than the typical seven-day treatment period, and new lesions continue to appear. Long-term antiviral administration is an unattractive option in this particular population, as resistant strains of herpes viruses are increasingly being isolated in immuno-deficient populations [8]. Clinicians must therefore develop a manner of treatment for this immuno-deficient population that will minimize viral activity, repair damaged cells, and help to alleviate discomfort, all while avoiding the pitfalls of frequent administration of antiviral therapy.

Minimizing viral activity

As with any treatment, efficacy starts with alleviating the discomfort of the patient. VZV infections can be excruciatingly painful, and often patients are inclined to use painkillers as an aid. Unfortunately, the preferred treatment regimen to alleviate the pain associated with VZV infections involves regular doses of analgesics often with the inclusion of a prescribed narcotic, which can become addictive. The pathophysiology of a VZV infection suggests that the prevention of pain begins by minimizing the amount of damage the virus is able to inflict on the sensory nerves [13]. This objective is, in immunocompetent individuals, often accomplished by initiating oral anti-viral therapy within 72 hours of the outbreak. A study of 1,141 immunocompetent patients treated with either acyclovir or valaciclovir within 72 hours of rash onset determined the median time to cessation of new lesion formation and median time to greater than 50% crusting or healing of lesions in all groups as 3 and 5 days respectively. In immunocompromised

individuals, however, infections can last for months, and anti-viral therapy has been shown to confer no additional therapeutic effect when maintained past 7 days in immunocompetent individuals [3]. The herbal preparation used by the subject in this case study contains an extract of *Phytolacca americana* (poke berry) which acts as a strong anti-viral to push the virus back into dormancy [7]. Topical pharmaceutical antiviral creams have been shown to be effective in both immunocompromised and immunocompetent populations at reducing pain and time to healing of lesions [6]. The anti-viral, and anti-herpetic actions of PMSR applied at a topical level may help to reduce damaging viral action in the nerves of the involved dermatome.

Even when anti-viral therapy is initiated within 72 hours of VZV rash onset, preventing recurrent viral outbreaks in the immunocompromised population is of great concern to clinicians. Results from the current case study demonstrate that topical application of the anti-herpetic, anti-viral, and anti-microbial preparation helps to stave off viral outbreaks and complicating infections. Two weeks after the initiation of treatment with PMSR (6/3/04), the subject was instructed by her physician to discontinue valaciclovir therapy (see Fig. 1). After a brief relapse of symptoms in the absence of the virostatic actions of the drug [5], the subject experienced a sharp remission of symptoms. This remission of symptoms is likely due to the use of PMSR for two reasons. One, the pharmacokinetics of valaciclovir are such that plasma concentrations of aciclovir after administration are down to approximately 1 ug/mL only 8 hours after the last dose [3]. Given this rapid half-life, it is unlikely that blood plasma concentrations of aciclovir would still be at virostatic levels more than two weeks after the last administered dose. It is unlikely that a sharp drop in symptoms, two weeks after cessation of valaciclovir therapy, can be

attributed to the mechanisms of valaciclovir. Secondly, one week after initiation of the placebo phase (Fig. 1c), the subject was seen in the clinic with a new lesion broken out on her right wrist. This relapse was seen after two months of steadily decreasing symptoms in all dimensions of pain and quality of life. Upon resuming treatment, the subject's symptoms as well as sleep and activity disturbance ratings once again began to fall. Since no concomitant anti-viral therapy was being administered, the conclusion that four to five times daily application of PMSR reduces new lesion formation, and the discomfort associated with VZV infection is plausible and paves the way for future investigation.

Alleviating pain

Viral damage inflicted on the nervous system due to a VZV infection can be accompanied by crippling pain, prompting sufferers to often utilize powerful painkillers and anti-depressants that can modulate the response of the sensory nervous system. The *Hypericum perforatum* (St. John's Wort) in PMSR provides two mechanisms of action to control pain without the dangers of frequent oral painkiller use, including addiction. First, the anti-inflammatory action of St. John's Wort works in a similar way to that of oral corticosteroids. By locally blocking the release of such chemical mediators as kinin and histamine, both the inflammation response and the activation of pain receptors are prevented resulting in a reduction of the burning, swollen feeling of a VZV rash [11]. This allows the subject relief from discomfort without having to keep a constant level of systemic anti-inflammatory medication in their system. While several studies have correlated corticosteroid administration with reduced pain and incidence of PHN, the

possible implications of suppressing the body's ability to fight off viral infection have made its clinical use rare [6, 10]. By keeping the anti-inflammatory actions of the PMSR local to the rash, rather than administering them systemically as with corticosteroids, sufferers of VZV rash can hope to avoid the suppression of cell-mediated immunity theoretically involved with corticosteroids.

In addition to the anti-inflammatory properties offered by St. John's Wort, the herb has also been shown to increase levels of norepinephrine, an important neuromodulator of the sympathetic nervous system [7]. This increase of available norepinephrine could theoretically increase the action potential threshold for pain receptors associated with the VZV infection [11]. Certainly, a higher threshold needed to trigger pain would result in fewer afferent signals of shooting, burning, and tingling pains commonly associated with VZV infection. Clinical trials investigating the effects of topically applied preparations of St. John's Wort on levels of neurotransmitters would lend credibility to this conclusion.

Repair of damage and prevention of complications

In addition to the prevention of tissue damage, repairing the inevitable nerve and epithelial damage incurred by viral activity can impede the development of many complications of VZV infection. *Symphytum officinale* (Comfrey), an herb with proven regenerative and cell proliferation properties, aids in treatment of a VZV infection in two ways [7]. First, by promoting regeneration of the skin epithelium damaged by the rash, the integrity of the of the body's primary defense against bacterial superinfection is

maintained. This supportive function may aid the body in preserving its own prophylaxis against dangerous common pathogens that frequently complicate VZV infections [6].

Allantoin, one of the active compounds in Comfrey, has been shown to have a significant enhancing effect on cellular proliferation in degenerating and regenerating nerve tissue of the peripheral nervous system [7].

Another complication associated with VZV infection that has become of great concern to clinicians is bacterial superinfection of a zoster rash. Infections by common pathogens, such as strains of Staphylococcus and Streptococcus, are common among patients suffering from VZV infection [6]. The ability of PMSR to stave off bacterial infection is due to the herb Larrea tridentate (Chaparral). The active chemical in Chaparral, nordihydroguaiaretic acid, acts as a strong antiseptic, and has been proven to reduce tooth decay and gum disease when used as a mouthwash [4]. Three to five times daily application of PMSR keeps the VZV rash associated area inhospitable to opportunistic pathogens.

Conclusion:

Based on the current case study, it can be tentatively concluded that the herbal preparation Peaceful Mountain Shingles Rescue can be used safely and effectively to treat a durative VZV infection in an immunocompromised individual. Worthy of mention in this conclusion is the lengthy nature of this infection as compared to most VZV infections reported in immunocompromised populations. The ability of the product to halt lesion formation and reduce pain in the absence of a healthy immune system

should highlight the clinical importance of herbal remedies in the treatment of VZV infections.

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