

A protracted, postherpetic neuralgic ulcer treated with risperidone and intranasal butorphanol



Giuseppe Ingrassi, BS, Michael Arbrook, MD, Karyn Haitz, MD, Robert Kirsner, MD, PhD, and Gil Yosipovitch, MD
Miami, Florida

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INTRODUCTION

Postherpetic neuralgia (PHN) represents a type of peripheral neuropathic pruritus that occurs after an episode of shingles and is characterized by localized pain, paresthesia, and itch, termed postherpetic itch (PHI); all may simultaneously exist within the same dermatomal distribution.¹ Although PHI has been reported to affect up to 58% of patients with shingles,² its exact pathophysiologic mechanism is poorly understood, and there are no proven specific treatments. Herein, we describe the case of a patient who presented with a painful and severely pruritic ulcer located on the left side of the neck that developed in the setting of PHN refractory to conventional treatments. Although many standard treatments moderately reduced the associated pain, successful treatment of the pruritus and scratching frequency was achieved only with risperidone and intranasal butorphanol, which ultimately led to the resolution of the ulcer.

CASE REPORT

A 67-year-old woman with end-stage renal disease currently on maintenance hemodialysis presented to the dermatology clinic in January 2020 endorsing a 2-year history of progressively worsening ulcer on the left side of her neck with associated moderate pain and intense pruritus. The patient quantified the pruritus on the peak pruritus numerical rating scale (PP-NRS) as an average of 10 (0-10) that worsened at night and disrupted her sleep. In 2017, the patient experienced an episode of

Abbreviations used:

PHI:	postherpetic itch
PHN:	postherpetic neuralgia
PP-NRS:	peak pruritus numerical rating scale

herpes zoster that affected the left side of her neck with resultant pruritus and pain that she described as a constant burning and shock-like sensation that led to regular picking, rubbing, and scratching of the affected area. A biopsy of the affected area was performed, and histopathologic analysis revealed marked hyperkeratosis with foci of parakeratosis, epidermal acanthosis with irregular elongation of the rete ridges, hypergranulosis, a prominent stratum lucidum, and a patchy lymphocytic infiltrate distributed in perivascular collections within the papillary dermis consistent with neurodermatitis. Treatments from that time to the time of presentation to our clinic included pregabalin 50 mg once daily for 1 year, mirtazapine 15 mg nightly for 8 months, oxycodone 30 mg daily for 1 month, cyclosporine 100 mg twice daily for 1 month, botulinum toxin injections, and a left stellate ganglion block. Of these, pregabalin, oxycodone, botulinum toxin injections, and the stellate ganglion block produced a moderate reduction in pain but no effect on pruritus. Oxycodone worsened the pruritus.

When the patient presented to our clinic in January 2020, dermatologic examination revealed a 7 × 3-cm eroded plaque on the left side of the neck with ulceration and sharply demarcated angular

From the Dr. Phillip Frost Department of Dermatology and Miami Itch Center, University of Miami.

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Correspondence to: Giuseppe Ingrassi, BS, Department of Dermatology and Cutaneous Surgery, University of Miami, 1600 NW 10th Ave RMSB Building 2067B, Miami, FL 33131.

E-mail: g.ingrasci1@med.miami.edu.

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Fig 1. Photograph from January 2020 displayed a 7 × 3-cm eroded plaque on the left side of the neck with ulceration and sharply demarcated angular borders. The medication regimen at that time included pregabalin 50 mg once daily for 1 year, mirtazapine 15 mg nightly for 8 months, oxycodone 30 mg daily for 1 month, and cyclosporine 100 mg twice daily for 1 month.

borders (Fig 1). Considering the patient's history of herpes zoster with concomitant pain, paresthesia, and pruritus in the same dermatomal distribution, a diagnosis of PHN with PHI was made. Treatment with risperidone 0.5 mg nightly and topical lidocaine twice daily was started. Over the course of 7 months, the dose of risperidone was increased to 4 mg nightly with reported improvements in pruritus severity, nighttime awakenings, and scratching frequency. By October 2020, the ulcer had reduced in size and measured 6 × 1 cm (Fig 2), and the patient reported an average PP-NRS of 6. At that time, intranasal butorphanol 1 mg daily was added, and the patient reported further improvements in pruritus severity and scratching frequency. As of March 2021, the patient's medication regimen included risperidone 4 mg nightly, intranasal butorphanol 1 mg daily, and topical lidocaine twice daily. At this time, the ulcer had resolved and epithelialized (Fig 3) with significant reductions in pain and scratching frequency and an average PP-NRS of 0. Table I summarizes the



Fig 2. Photograph from October 2020 displayed a 6 × 1-cm ulcer. The medication regimen at that time included risperidone 4 mg nightly for 2 months at the current dose and topical lidocaine twice daily for 7 months. Risperidone was started 7 months prior at a dose of 0.5 mg and was slowly increased to the current dose over a 5-month period.

changes in treatments, ulcer size, and PP-NRS over time.

DISCUSSION

Treatments for PHN include anticonvulsants such as pregabalin and gabapentin, tricyclic antidepressants, topical agents such as 8% capsaicin and anesthetics, and invasive therapies such as botulinum toxin injections and stellate ganglion blocks.³ Although there are case studies of these effective PHN medications partially relieving PHI, there are no current specific treatments for PHI, and it may prove to be more difficult to manage than PHN-associated pain. For example, pregabalin is also effective in improving end-stage renal disease–associated



Fig 3. Photograph from March 2021 displayed a resolved, epithelialized ulcer. The medication regimen at that time included risperidone 4 mg nightly for 7 months at the current dose, topical lidocaine twice daily for 14 months, and intranasal butorphanol 1 mg daily for 5 months.

pruritus,⁴ and its ineffectiveness to alleviate our patient's pruritus may point to the complexity of her PHI. The successful reduction of PHN-associated pain without concurrent reduction of pruritus may compel the patient to reflexively overscratch the affected area and cause self-induced chronic ulceration in the absence of the deterrent of pain sensation.⁵

Risperidone, a second-generation antipsychotic medication that blocks dopamine in the mesolimbic neural circuit, has been reported to successfully reduce pruritus and scratching behavior in delusional parasitosis, a psychiatric cause of chronic pruritus, yet there are no reports of its successful use in neuropathic pruritus.⁶ We decided to use risperidone to improve our patient's longstanding scratching behavior and nocturnal pruritus. Risperidone may be started at a dose of 0.5 mg before bedtime and increased weekly until reaches a maximum dose of 4 mg/d.⁷ The most common adverse events reported are sedation and

Table 1. Timeline of daily medications, ulcer size, and peak pruritus numerical rating scale

Treatments and ulcer characteristics	Before January 2020	January 2020	February 2020	July 2020	October 2020	March 2021
Daily medications	Pregabalin 50 mg qd for 1 year, mirtazapine 15 mg qhs for 8 months, cyclosporine 100 mg bid for 1 month, and oxycodone 30 mg qd for 1 month	Risperidone 0.5 mg qhs and topical lidocaine bid	Risperidone 1 mg qhs and topical lidocaine bid	Risperidone 2 mg qhs and topical lidocaine bid	Risperidone 4 mg qhs, topical lidocaine bid, and intranasal butorphanol 1 mg qd	Risperidone 4 mg qhs, topical lidocaine bid, and intranasal butorphanol 1 mg qd
Ulcer size	7 × 3 cm	7 × 3 cm	7 × 3 cm	7 × 3 cm	6 × 1 cm	Resolved
PP-NRS (0-10)	10	10	8	7	6	0

bid, Twice a day; PP-NRS, peak pruritus numerical rating scale; qd, every day; qhs, every night.

hyperprolactinemia. Risperidone should be used with caution in patients with a history of an abnormal electrocardiogram as it may prolong the corrected QT interval.⁷

After 7 months of treatment with risperidone, our patient's urge to scratch decreased as well as her ulcer size; therefore, we decided to add intranasal butorphanol, a κ -opioid receptor agonist and μ -opioid receptor antagonist, to target the pruritus that our patient was still experiencing. A recent case series of 16 patients with refractory chronic pruritus treated with intranasal butorphanol found a significant improvement of pruritus in 81% of subjects.⁸ The most common adverse events are sleep disturbances, sedation, psychomotor impairment, and nausea and vomiting.⁹

Our patient's improvement in pruritus and scratching behavior with intranasal butorphanol and risperidone is uncommon in the current literature and may provide insight into the poorly understood pathogenesis of PHI. Simultaneous activation of the κ -opioid receptor system and inhibition of the μ -opioid receptor system within the mesolimbic circuit act to decrease dopaminergic activity, resulting in an "antireward" effect on addiction and itching behavior.¹⁰ Therefore, the successful use of these medications, along with the worsening of pruritus that occurred following treatment with oxycodone, a μ -opioid receptor agonist, may represent a central component of PHN pathogenesis that drives both pruritus and scratching behavior.

Conflicts of interest

Dr Yosipovitch is a consultant for Pfizer, Galderma, Sanofi Regeneron, Kiniksa, Trevi, Eli Lilly, Novartis, GSK,

Leo, and Bellus and has received grant/research support from Leo Pharma, Pfizer, Novartis and Kiniksa, and Sanofi Regeneron. Author Ingrasci and Drs Arbrouk, Haitz, and Kirsner have no conflicts of interest to declare.

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