# UCLA Proceedings of UCLA Health

## Title

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**Permalink** <u>https://escholarship.org/uc/item/0br9x5fd</u>

**Journal** Proceedings of UCLA Health, 23(1)

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# **Publication Date**

2019-03-08

# Empiric Antiviral Treatment during Suspected Prodrome of Herpes Zoster

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#### Case 1

A 50-year-old female presented to the office with 5 days of left lower abdominal quadrant pain, and bloating. Rotation of the torso aggravated symptoms and but overall, the pain was constant and unremitting in nature. There were no associated fevers or changes in bowel or bladder activity. Her examination was notable for a left sided lower thoracic dermatomal distributional pain in response to stroking the skin lightlymechanical allodynia, but deeper abdominal exam was unremarkable. A CT scan of the abdomen and pelvis was unremarkable, urine and serologic markers of inflammation were normal. The pain escalated, and so empiric treatment with valacyclovir for viral prodrome of left sided T11-12 zoster was felt safe to initiate with a history of recent normal kidney functions studies. Six days later, the pain had resolved and there have been no recurrences in two-year follow-up.

### Case 2

A 48-year-old female with a history of quiescent relapsing remitting Multiple Sclerosis presented to her local emergency room after three days of escalating left sided chest pain. She was evaluated and subsequently ruled out for pulmonary embolism with a normal CT pulmonary angiogram. She was ruled out for a myocardial infarction and other routine lab work was unremarkable. She was discharged with a short course of NSAIDS and breakthrough opiates. She presented in follow up on the following day and her examination was unremarkable. She described an area of deep constant pain that was not associated with movement. There were no constitutional symptoms. The pain distribution followed the left T5 dermatome but there was no rash or hyperesthesia. Her pain had been escalating through her discharge medications. An empiric treatment of the suspected neuralgia with initiation of 50 mg bid pregabalin and empiric treatment for a left T5 herpes zoster prodrome with valacyclovir 1000 mg every 8 hours for a week was initiated. The pain was reported as more manageable over electronic communications in the next 2 days and all symptoms had resolved by the end of the week of treatment.

### Case 3

A 52-year-old female presented to the office with leg pain. The pain started approximately two weeks earlier, as a constant dull ache in the left medial thigh not affected by weight bearing. There were no associated rashes, fevers, and no recent mechanical injuries. Hyperesthesia was noted on examination of the left leg, along the L3 dermatome. Her neurologic, musculoskeletal, and vascular examinations were otherwise unremarkable. The remainder of her clinical examination was normal. The differential was broadened to consider the viral prodrome of an L3 dermatomal based Herpes Zoster, and antiviral treatment with valacyclovir was initiated at 1000 mg every eight hours. Within the week, the patient reported complete resolution of all pain and there have been no recurrences of symptoms reported in annual follow up examinations.

#### Discussion

Timeliness in the diagnosis and treatment of Herpes Zoster and the resultant reduced incidence and duration of post herpetic neuralgia is well documented.<sup>1</sup> Overall, the sooner treatment is initiated, the sooner the resolution of zoster based neuralgia is achieved.<sup>2</sup> VZV viral load elevations have been demonstrated by PCR in acute zoster, and the prodromal pain is associated with higher baseline viral loads. The viral load levels themselves however did not predict the development or persistence of post herpetic neuralgia.<sup>3</sup>

Identification of the viral prodrome phase of herpes zoster and immediate treatment with viral suppression may provide the optimal means of reducing morbidity of post herpetic neuralgia. While the typical duration of this prodromal phase is 1-5 days, case reports have demonstrated prodromal phases up to 18 days prior to the development of rash. In all of these studies however, treatment was not initiated until a rash had been confirmed.<sup>4,5</sup>

VZV resides in the sensory ganglia after recovery from chickenpox. During reactivation, in the Herpes Zoster phase, it travels along the affected sensory ganglia and reproduces in the epidermis.<sup>6</sup> The neuropathic pain is thought to be triggered by VZV replication. Inhibition of further viral replication as soon as possible with antivirals is essential for effective relief of symptoms.<sup>7</sup>

In the three cases presented, each patient had prolonged unilateral pain syndromes where etiologies that are more common were ruled out. Because the characteristic pain persisted, the differential diagnosis was broadened to consider the prodrome of Herpes Zoster. Antiviral therapy risks in patients without impaired renal function were felt to be outweighed by the potential benefits of immediate treatment and varicella zoster viral suppression. In each case described, rapid initiation before evidence of a vesicular eruption was followed by a complete resolution of symptoms within one week of treatment. No vesicular eruptions occurred through treatment in any of the cases presented.

There are no case reports in the literature of pretreatment in suspected viral prodromes of Herpes Zoster. This type of treatment is best characterized as empiric, based on clinical suspicion that the opportunity to treat more acute illnesses were adequately ruled out, and that the quality and character of the persistent symptoms followed a typical unilateral dermatomal pattern commonly found in herpes zoster.

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Submitted February 7, 2019