CASE REPORT

A case of zoster sine herpete presenting with thoracic radicular pain diagnosed by polymerase chain reaction in skin exudate

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A B S T R A C T

Varicella zoster virus (VZV) can cause radicular pain in the absence of skin lesions; such cases are referred to as zoster sine herpete (ZSH) and are usually diagnosed by using serological assays or polymerase chain reaction (PCR). An effort is underway to detect VZV DNA in novel specimens rather than conventional samples (e.g., blood or cerebrospinal fluid) for PCR. There are two reports that PCR analysis in the exudate of the auricular skin can be a useful diagnostic tool for the diagnosis of ZSH in patients presenting with cranial nerve paralysis without herpetic eruptions. Here, we report a case of ZSH diagnosed by using PCR analysis of skin exudates in a patient who developed thoracic radicular pain. This is believed to be the first case of ZSH diagnosed using PCR analysis of skin exudate in a patient in whom the cranial nerve was not involved.

Introduction

Herpes zoster is characterized by pain and vesicular eruption on an erythematous base in 1–3 dermatomes. However, varicella zoster virus (VZV) reactivation can produce radicular pain without a rash (zoster sine herpete, ZSH), making the diagnosis more difficult for physicians. In cases in which ZSH is suspected, virological confirmation is needed. The conventional methods that use vesicle samples (e.g., Tzanck smear, punch biopsy, and cell culture) are not available for the diagnosis of ZSH. In addition, serological methods that have been used to confirm the diagnosis of herpes zoster are not useful for an early diagnosis, because immunoglobulin (Ig)M and IgA antibodies specific for acute VZV infection are only detected in about 60% of cases.1 Also, cross-reactions to herpes simplex virus have been reported.1 Currently, when ZSH is suspected, blood and cerebrospinal fluid (CSF) examination for VZV DNA and anti-VZV IgM and/or IgG antibody are available to confirm the etiological agent.4 However, CSF examination is too difficult to perform in the outpatient clinic, and VZV DNA has been detected in peripheral blood mononuclear cells (PBMCs) in 16–20% of patients with herpes zoster.3,6 In addition, it has been revealed that VZV DNA was not detected in PBMCs from patients with ZSH.7 As a result, other methods to diagnose ZSH have been attempted. Here, we report a case of ZSH diagnosed by performing polymerase chain reaction (PCR) analysis of skin exudate in a patient who developed thoracic dermatomal distribution pain that had not been reported.

Case report

A 37-year-old woman was transferred to our dermatology department from the orthopedic department because the orthopedist could not find the cause of her pain, even after analysis of thoracic magnetic resonance imaging, and symptomatic treatment with a painkiller was not effective. The patient complained of burning pain that developed 2 weeks previously on her right trunk and back. Concomitantly, she presented with cutaneous lesions that developed on the right side of the back while using the pain relief patch 5 days previously. Past history and family history were unremarkable. On physical examination, several pinhead-sized papules and pustules were localized to the application site of the pain relief patch on the right side of the back (Figure 1). The patient’s pain radiated to the right T7–8 dermatomes. To rule out medical disease that may be the cause of the trunk and back pain, laboratory studies, including complete blood cell count with
blood mini QIAcube kit (Qiagen Inc., Hilden, Germany) according to the manufacturer’s protocol. VZV DNA was amplified with nested PCR technique using two primer sets derived from the gene 29 encoding the DNA binding protein (1st PCR: 5'-TACGGGTCTTGCGCAGGCTGTAT-3' and 5'-AATGCCGTGGCACACATATAAT-3'; 2nd PCR: 5'-TCTTTTCGAGGCAAACAC-3' and 5'-TCCAAGGGGCTGAGCA-TATCT-3'). Nested amplification product was seen with 2% agarose gel electrophoresis and the expected 161 base pair products were confirmed in the patient’s sample (Figure 3). Finally, ZSH was diagnosed in this patient. Treatment with famciclovir 250 mg three times daily was administered for 7 days. The patient refused analgesics because they had been ineffective previously. After 7 days, there was marked improvement in the patient’s radicular pain. After 2 weeks, the cutaneous lesions and pain had completely subsided without sequelae.

**Discussion**

ZSH refers to a condition in which pain with a dermatomal distribution occurs in the absence of an antecedent rash. Since the original description of “radicular pain without cutaneous rash” observed by Widal, a few cases have been reported in the neurological literature. However, only one case has been reported in our review of the dermatological literature. Although the true incidence of ZSH is not yet known, we have frequently encountered cases in which ZSH was suspected, and our case could offer useful information to other dermatologists.

Although herpes zoster is generally diagnosed on a clinical basis alone, VZV reactivation without rash requires virological confirmation. Laboratory testing (e.g., punch biopsy, Tzanck smear, or viral isolation in cell culture of vesicle samples), which has been used in the diagnosis of herpes zoster, is not useful in the absence of cutaneous lesions. Recently, it has been reported that the appropriate investigations to establish the diagnosis of ZSH are PCR for VZV DNA, as well as anti-VZV IgG in CSF, and examination of PBMCs for VZV DNA. In dermatological practice, blood specimens are more commonly used than CSF for diagnosis. However, VZV DNA has been detected in PBMCs in approximately one-fifth of patients with herpes zoster, and there is a report that VZV DNA was not detected in PBMCs in patients with ZSH. Judging from these findings, PCR for PBMCs does not provide a useful measure of VZV in patients with ZSH. Therefore, the use of other specimens has been attempted, and diagnostic methods using saliva or tear fluid have been reported. In addition to saliva and tear fluid, skin exudate has been used in the diagnosis of ZSH. Murakami et al have reported that PCR analysis in skin exudate of the auricular skin can be a rapid and useful diagnostic tool for identification of VZV infection in acute peripheral facial palsy or dysphagia without herpetic eruption. In that study, skin exudate, blood, and tear fluid were collected in the six patients in whom ZSH was retrospectively diagnosed through elevation of serum antibody titer. VZV genomes were detected in four of the six specimens of the auricular skin exudate (67%), in two of the six PBMC specimens (33%), and in two of the six tear fluid specimens (33%). These results suggest that PCR analysis of VZV DNA in skin exudate can be more useful than other specimens for diagnosis of ZSH. Once latent VZV reactivates in the ganglia, it migrates via the sensory nerves, and is released from the nerve endings in the skin, forming a zosteriform rash. Thus, VZV might be present in the nerve endings of skin epithelial cells, and identified in skin exudates as in our case.

In the current case, famciclovir was prescribed and illness progression was observed. During the patient’s next visit, pain was dramatically improved although no analgesic was given. Apart from her dermatomal pain and PCR result, the patient’s response to antiviral drug therapy was suggestive of herpes zoster. Randomized
clinical context, particularly when there is a history of chronic radicular pain unresponsive to previous treatment. We conclude that PCR analysis of VZV DNA in skin exudate can be more valuable than PCR for other specimens in the diagnosis of ZSH, but in order to assess diagnostic usefulness of PCR analysis of VZV DNA in skin exudate of patients presenting with radicular pain, a large anterograde study is mandatory.

References