

Zoster ... “almost” ... *sine herpete*: diagnostic utility of real time-polymerase chain reaction

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SUMMARY

Zoster sine herpete is a particular form of varicella zoster virus (VZV) infection characterized by segmental pain and dysesthesia, without any cutaneous lesions ever becoming perceptible. This report describes the case of a female patient, presenting with intercostal pain associated with a single papulo-vesicular lesion localized within the same area. Thanks to such a lesion, real time-polymerase chain reaction (PCR) analysis on vesicle fluid swab was possible, thus revealing a significant number of VZV genome copies. This innovative tool has proven essential to diagnose this abortive form of herpes zoster, which would otherwise have remained unidentified.

KEY WORDS: Herpes zoster virus, Polymerase chain reaction, *Zoster sine herpete*

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A 53-year-old woman came to our outpatient unit presenting with a small oval pigmented nodule in the right sub-mammary fold, which was diagnosed as a suspected atypical melanocytic lesion by her primary care physician. The lesion had gradually undergone significant changes in size and morphology, and became eroded and inflamed during the last two weeks. Concomitantly, the patient also complained of severe burning pain in the same region involving the entire intercostal space up to the right paravertebral region. She was treated with nonsteroidal anti-inflammatory drugs without any benefit. Clinical and dermoscopic assessments revealed that the pigmented nodule was a seborrheic keratosis, thus relieving patient's concerns about the malignant nature of the lesion and the possible relationship with neuralgia. On physical examination, an isolated papulovesicular lesion was not-

ed in the paravertebral region within the same dermatome affected by pain. The metameric neuralgia led us to suspect herpes zoster. Routine hematochemical tests were normal; serology for herpes viruses disclosed the presence of IgG antibodies for herpes simplex virus 1 and varicella zoster virus (VZV). Real time-polymerase chain reaction (PCR) on vesicle fluid was performed, showing a high positive title for VZV of 17984 vg/ml. Treatment with famciclovir 250 mg three times daily was given for 7 days. Further cutaneous lesions did not develop and neuralgia gradually disappeared within 2 months of treatment with analgesics.

Herpes zoster is a localised sporadic infectious disease caused by the endogenous reactivation of VZV which, after primary infection, persists in a latent form in dorsal root ganglia. In the event of reactivation, which commonly occurs in the elderly, VZV may clinically emerge to cause a vesicular eruption with dermatomal distribution (shingles) associated with unilateral radicular pain and/or dysesthesia (Sampathkumar *et al.*, 2009). Nerve involvement without cutaneous rash is a condition first observed in the early 20th century and was initially termed “*zona frusta*” by Widal and later “*zoster sine herpete*” by Weber (Gilden *et*

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al., 1994). Due to the absence of the pathognomonic skin lesions, the clinical diagnosis of "zoster sine herpette" may be only suspected in case of metameric neuralgia, and has been also hypothesized in a wide array of unilateral neurological symptoms, such as otalgia, acute labyrinthitis, ophthalmic neuralgia and muscular palsy.

VZV infection is usually diagnosed on a clinical basis only. In doubtful cases, confirmatory laboratory tests (e.g., serological assays and the replication of the virus in cell culture) may be required (Cohen, 1994). Today, however, this infection can be more rapidly and efficiently diagnosed by new techniques like PCR methods. In particular, real time-PCR represents an advanced PCR subtype which is faster than conventional PCR methods and provides the highest test specificity and sensibility currently available. Stained Tzanck smears, saliva, vesicle fluid swabs, dried crusts, cerebrospinal fluid and skin biopsies are all eligible specimens for VZV DNA detection (Stránská *et al.*, 2004). In our patient, who had an intercostal neuralgia and only one small skin lesion

in the same dermatome, we were able to confirm herpes zoster diagnosis by PCR analysis on the vesicle fluid, without performing any invasive procedure such as biopsy. Therefore, DNA analysis by real time-PCR might be a valid diagnostic tool in the presence of abortive forms of herpes zoster, with very few cutaneous lesions as in our case.

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