

Zosteriform herpes simplex

Koh M J A, Seah P P, Teo R Y L

ABSTRACT

Herpes simplex virus (HSV) infection, though most commonly seen in the oral, perioral and genital areas, can occur anywhere on the body. After primary infection, HSV then establishes latency in sensory nerve ganglia and reactivates intermittently, precipitated by various factors. These reactivations may be recurrent and appear in a dermatomal distribution, mimicking herpes zoster, often leading to misdiagnosis if no confirmatory laboratory tests are carried out. We report a 65-year-old man who presented with recurrent episodes of a “zosteriform eruption”, who was initially clinically diagnosed and treated as for recurrent herpes zoster, but was subsequently found to have recurrent herpes simplex virus type 2 after laboratory investigations.

Keywords: herpes simplex, herpes zoster, skin infection, viral infection, zosteriform herpes simplex

Singapore Med J 2008;49(2):e59-e60

INTRODUCTION

Recurrent herpes simplex virus (HSV) infection can mimic herpes zoster if it occurs in a dermatomal distribution. This similarity can lead to incorrect diagnosis and treatment if no confirmatory laboratory tests are carried out. In fact, recurrent zoster remains an unproven entity, as many reports in the literature have not been accompanied by confirmatory laboratory methods.⁽¹⁾ We present a case of recurrent “zosteriform” HSV infection.

CASE REPORT

A 65-year-old man first presented for a mildly pruritic rash, on his left thigh, of five days duration. He had a history of hypertension and diabetes mellitus. He also gave a history of childhood chicken-pox infection. On examination, there were grouped blisters and erosions in a “zosteriform” distribution over his left thigh, corresponding to L2 dermatome. A diagnosis of herpes zoster was made clinically, and the patient was treated with five days of oral acyclovir 800 mg five times a day. Over the next three years, the patient experienced recurrent episodes of this similar eruption every 2–3 months, initially over L2 dermatome on the left thigh, then subsequently, over L1 dermatome on the right lumbar region. During each recurrence, he responded to treatment with oral acyclovir 800 mg five times a day for five days prescribed by his general practitioner. There was no complaint

of post-herpetic neuralgia after each episode. During the last recurrence in January 2006, he was seen at our dermatology department and fluid from the vesicles was sent for HSV and varicella zoster virus (VZV) isolation. Results returned positive for HSV 2 and negative for VZV. The patient declined investigations to exclude human immunodeficiency virus (HIV) infection. As the patient experienced frequent symptomatic recurrences, he was started on prophylactic oral acyclovir 400 mg bid and has remained well since.

DISCUSSION

HSV infection is one of the most common viral infections of the skin and mucous membranes. There are two major antigenic types: HSV-1 commonly causing orolabial lesions and HSV-2 typically causing genital lesions, although there can be considerable overlap of clinical manifestations. Apart from these typical sites of infection, HSV can affect other areas of the body e.g. herpetic whitlow and herpes gladiatorum. HSV persists in sensory nerve ganglia after the primary infection. After a period of latency, it can cause recurrent disease, which typically is less severe than the primary HSV infection in an immunocompetent host. However, in immunocompromised patients, recurrent herpetic infections may occur with increased incidences and severity, and may run a prolonged or atypical course.^(2,3)

Recurrences are also more frequent after HSV-2 genital infections, compared to after HSV-1 oral infections.⁽⁴⁾ Though in most cases, a trigger cannot be accurately identified, recurrences may be caused by minor trauma, ultraviolet radiation exposure, infections such as upper respiratory tract infections, surgery, and emotional stress.⁽⁵⁻⁷⁾ Vesicles typically appear on an erythematous base a few hours to days after preceding symptoms of itching or burning over the site. The vesicles soon become crusted and heal without scarring after 7–10 days. Though most common on the face, especially around the mouth, they can be situated anywhere on the body. They tend to recur in the same region but not always at the same site, and although they usually form an irregular cluster, they may be arranged in a line or in a “zosteriform” distribution, especially when located in the lumbar or lower thoracic region.

This form of presentation of recurrent HSV infection mimics the evolution and morphology of herpes zoster and can lead to misdiagnosis.^(1,8) Although there have been numerous reports over the years documenting the occurrence of recurrent herpes zoster, they have not been substantiated by laboratory confirmation.⁽¹⁾ Conversely, several more recent reports have emphasised the use of

Department of
Dermatology,
Changi General
Hospital,
2 Simei Street 3,
Singapore 529889

Koh MJA, MBBS,
MRCPCH
Registrar

Seah PP, MBBS,
MRCP, FAMS
Senior Consultant

Teo RYL, MBBS,
MRCP, MMed
Registrar

Correspondence to:
Dr Mark JA Koh
Tel: (65) 8121 1496
Fax: (65) 6788 0933
Email: docmark@
pacific.net.sg

laboratory investigations to confirm the diagnosis, as the differentiation between HSV and VZV as the cause of recurrent zosteriform eruptions cannot be reliably distinguished simply based on clinical grounds.^(1,8-10) Presence of multinucleated giant cells in scrapings or swabs from the base of lesions (Tzanck smears), which is characteristic of infections caused by herpes viruses, cannot be used to differentiate between HSV and VZV infections. Confirmation would therefore require the use of viral cultures, antigen detection, serology and molecular techniques, e.g. polymerase chain reaction (PCR). Viral culture is the preferred test to differentiate HSV and VZV, as it is both sensitive and specific. It also allows for HSV typing. However, sensitivity is lower for recurrent lesions and declines as lesions begin to heal. PCR assays for HSV DNA have the highest sensitivity and viral typing is possible.^(11,12)

With the advent of real-time nested multiplex PCR, a single specimen from a patient can be tested for HSV-1, -2 and VZV, with even faster turnaround time, increased sensitivity and greater convenience.⁽¹³⁾ Antigen detection yields quick results, but is less sensitive and typing is not possible. Accurate type-specific HSV serological tests are based on the HSV-specific glycoprotein G1 (HSV-1) and glycoprotein G2 (HSV-2). They have good specificity and sensitivity and may be useful in certain situations, e.g. recurrent symptoms or atypical symptoms with negative HSV cultures, counselling of sexual partners of patients, detection of unrecognised infection, and for epidemiological studies. VZV serology is diagnostic of herpes zoster if the convalescent serum shows a fourfold increase in titres relative to acute specimens. Therefore, it is only useful retrospectively. Patients who present with recurrent herpes simplex infection in a "zosteriform" pattern should ideally be further investigated for immunosuppression, in particular for HIV infection.

It is important to make the distinction between HSV and VZV infections. One reason is that although VZV and HSV respond to similar anti-viral medications, e.g. acyclovir, famciclovir and valacyclovir, the sensitivities of these two viruses to these antiviral drugs can vary significantly. Proper diagnosis will lead to more precise anti-viral therapy. As the concentration of acyclovir that inhibits VZV is ten times more than is needed to inhibit HSV, the current treatment of uncomplicated herpes zoster is systemic acyclovir 800 mg five times a day, whereas for herpes simplex, treatment with the same drug is at 400 mg three times a day.^(14,15) This fact may become more relevant in the future, with the advent of newer and more precise anti-viral treatments, as the choice of anti-viral drug may depend on whether the infection is caused by HSV or VZV. Another reason for proper diagnosis is the risk of instituting improper treatment, which can cause complications. For example, VZV infections of the eye are frequently treated with corticosteroids, but if given to patients with HSV eye infection, it can lead to detrimental results.⁽¹⁾

There is also good evidence that early treatment of herpes zoster with anti-viral agents at anti-zoster dosages will reduce the development of post-herpetic neuralgia.⁽¹⁶⁾ A third reason for proper diagnosis is the need for institution of proper isolation procedures. A hospitalised patient with VZV infection would require more stringent isolation protocols, as compared to an inpatient with HSV infection. Similarly, patients with VZV infections, when given outpatient treatments, are provided with longer medical leave compared to patients with HSV infections. Incorrect diagnosis of HSV infection as VZV infection will therefore eventually lead to increased inconvenience, cost and time incurred by both patients, hospitals and employers.⁽⁸⁾ In conclusion, as demonstrated in this case report, recurrent "zosteriform" eruptions caused by HSV infection can mimic herpes zoster infection. We recommend the use of laboratory test for accurate diagnosis, in order for proper treatment and isolation protocols to be instituted.

REFERENCES

- Heskel NS, Hanifin JM. "Recurrent herpes zoster": an unproved entity? *J Am Acad Dermatol* 1984; 10:486-90.
- Corey L, Spear PG. Infections with herpes simplex viruses. *N Engl J Med* 1986; 314:686-91, 749-57.
- Jarratt M. Herpes simplex infection. *Arch Dermatol* 1983; 119:99-103.
- Corey L. First-episode, recurrent and asymptomatic herpes simplex infections. *J Am Acad Dermatol* 1988; 18(1 Pt 2):169-72.
- Perna JJ, Mannix ML, Rooney JF, Notkins AL, Straus SE. Reactivation of latent herpes simplex virus infection by ultraviolet light: a human model. *J Am Acad Dermatol* 1987; 17:473-8.
- Haverkos HW, Pazin GJ, Ho M, Nelson PB. Reactivation of type 2 herpes simplex virus by thoracolumbar neurosurgery. *Ann Intern Med* 1984; 101:503-4.
- Schmidt DD, Schmidt PM, Crabtree BF, et al. The temporal relationship of psychosocial stress to cellular immunity and herpes labialis recurrences. *Fam Med* 1991; 23:594-9.
- Kalman CM, Laskin OL. Herpes zoster and zosteriform herpes simplex virus infections in immunocompetent adults. *Am J Med* 1986; 81:775-8.
- Rübben A, Baron JM, Grussendorf-Conen EI. Routine detection of herpes simplex virus and varicella virus by polymerase chain reaction reveals that initial herpes zoster is frequently misdiagnosed as herpes simplex. *Br J Dermatol* 1997; 137:259-61.
- Nahass GT, Mandel MJ, Cook S, Fan W, Leonardi CL. Detection of herpes simplex and varicella-zoster infection from cutaneous lesions in different clinical stages with the polymerase chain reaction. *J Am Acad Dermatol* 1995; 32(5 Pt 1):730-3.
- Nahass GT, Goldstein BA, Zhu WY, et al. Comparison of Tzanck smear, viral culture, and DNA diagnostic methods in detection of herpes simplex and varicella-zoster infection. *JAMA* 1992; 268:2541-4.
- Stránská R, Schuurman R, de Vos M, van Loon AM. Routine use of a highly automated and internally controlled real-time PCR assay for the diagnosis of herpes simplex and varicella-zoster virus infections. *J Clin Virol* 2004; 30:39-44.
- O'Neill HJ, Wyatt DE, Coyle PV, McCaughey C, Mitchell F. Real-time nested multiplex PCR for the detection of herpes simplex virus types 1 and 2 and varicella-zoster virus. *J Med Virol* 2003; 71:557-60.
- Kleymann G. Antiviral treatment. In: Studahl M, Cinque P, Bergstrom T, eds. *Herpes Simplex Viruses*. New York: Taylor & Francis Group, 2006: 153-176.
- Wagstaff AJ, Faulds D, Goa KL. Aciclovir. A reappraisal of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. *Drugs* 1994; 47:153-205.
- Jackson JL, Gibbons R, Meyer G, Inouye L. The effect of treating herpes zoster with oral acyclovir in preventing postherpetic neuralgia: a meta-analysis. *Arch Intern Med* 1997; 157:909-12.