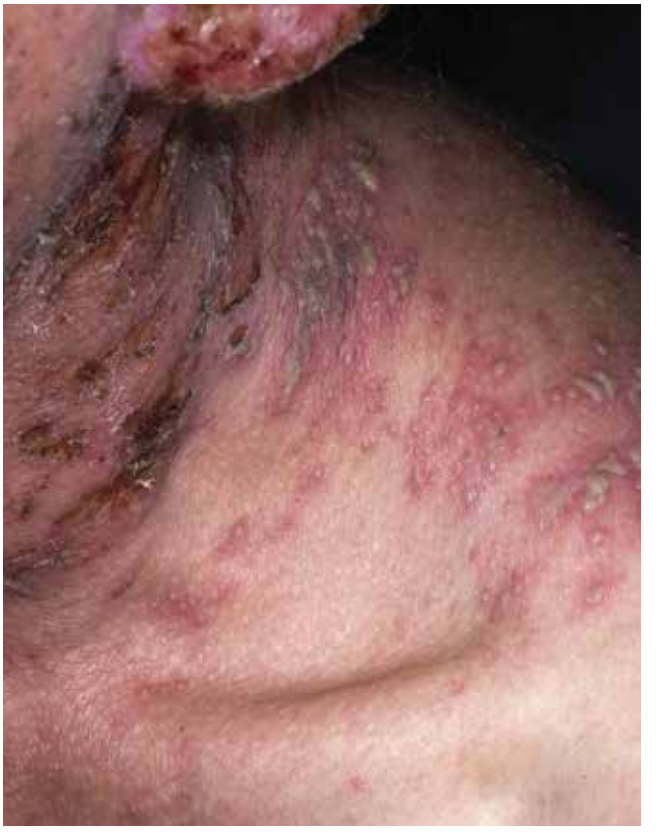
An elderly woman with recurrent zosteriform eruptions



Commentary by:

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A 73-year-old woman has recurrent zoster-like blistering on her face and persistent pain after having shingles three years ago. Would an antiviral agent and zoster vaccination be appropriate?

Case scenario

Barbara is 73 years of age and has endured ongoing pain and relapses of blistering after a herpes zoster (shingles) outbreak in the ophthalmic branch of the trigeminal nerve (C5) three years ago. At the time she had a protracted stay in the intensive care unit, requiring a ketamine infusion due to the severity of her herpetic neuralgia, before being discharged home on analgesia. Since then she has used pregabalin, narcotics and amitriptyline but finds nothing really helps and so is on minimal medication. The blistering is recurring in the same region each time.

- Would a prophylactic antiviral agent be indicated for this patient?
- Would she benefit from a zoster vaccination?

Commentary

It is interesting to note that in this 73-year-old woman the relapses are frequent, which is unusual in herpes zoster. The literature reports cases of recurrence occurring usually over a period of 12 to 15 months in immunocompetent individuals, and a few cases of more frequent recurrence in immunocompromised individuals. Very rarely a recurrence for the third time has been reported in immunocompetent individuals.

There are reports of recurrent herpes zoster in a 67-year-old woman with a four-year history of actinic reticuloid (also known as chronic actinic dermatitis) treated intermittently with oral prednisone over that time period. The patient developed three separate episodes of a vesicular eruption over a five-month period, which resolved with valaciclovir therapy.

Prednisone is a well-recognised risk factor for herpes zoster, as varicella-zoster virus reactivation is related in part to host cell-mediated immunity.[1] Despite the large number of patients taking immunosuppressive medications, there are few reports documenting increased risk of recurrent or persistent herpes zoster in this population, as there is with the HIV population. Although patients with haematological malignancies exhibit higher rates of herpes zoster, increased rates of recurrent herpes zoster are not frequently reported in this population either.

A case was reported in 2004 of a 5-year-old boy with two episodes of herpes zoster occurring 15 months apart in separate dermatomes (S2 to 3, then C6), with both outbreaks confirmed on laboratory testing.[2] There are few other laboratory-confirmed cases of cutaneous zoster recurrence in immunocompetent individuals.

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Zosteriform herpes simplex or herpes zoster?

The relapses with blistering in the same region occurring periodically in this 73-year-old woman could be due to varicella-zoster virus if she were severely immunocompromised. An alternative diagnosis is a distinct type of cutaneous herpes called 'zosteriform herpes simplex', a rare presentation of herpes simplex virus infection where lesions appear in a dermatomal distribution similar to herpes zoster. These reactivations may be recurrent and appear in a dermatomal distribution, mimicking herpes zoster, often leading to misdiagnosis unless confirmatory laboratory tests are carried out. There are reports of patients who were originally misdiagnosed to have recurrent herpes zoster skin infections later correctly identified as herpes simplex virus following culture of virus from their vesicles. Herpes simplex infection tends to produce a shorter and milder prodrome, followed by skin vesicles that are more uniform, smaller and closely clustered. Herpes simplex virus infection is also more likely to be recurrent with multidermatomal involvement in immunocompromised individuals.

Articles dating back to 1900 purport cases of recurrent zoster, but most of these reports predated routine laboratory testing for varicella-zoster virus, which was first cultured from herpes zoster lesions in 1952.[1] In 1965, a review was published of 192 cases of herpes zoster seen in a 16-year period in Cirencester, England, classifying eight as second-attacks and one as a third attack.[3] However, reports as early as 1950 noted that herpes simplex virus infection could clinically imitate herpes zoster. Ironically, there are actually more laboratory-confirmed cases of misdiagnosed recurrent zoster in the literature than there are of actual recurrent zoster in immunocompetent patients. A report described three patients initially diagnosed with recurrent herpes zoster but all with herpes simplex virus by culture, again raising the question as to whether earlier cases of recurrent zoster represent instead misdiagnosed cases of herpes simplex virus infection.[4]

Viral culture or examination of vesicle contents using nucleic acid tests such as polymerase chain reaction (PCR) or much less frequently by indirect immunofluorescent techniques or virus isolation provide definitive diagnosis of the aetiology of a zosteriform eruption. With the advent of real-time nested multiplex PCR, a single specimen from a patient can be tested for herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) and varicella-zoster virus, with even faster turnaround time, increased sensitivity and specificity and greater convenience.[5,6] Type-specific herpes simplex virus serological tests are based on the herpes simplex virus-specific glycoproteins G1 (in HSV-1) and G2 (in HSV-2). These tests are useful in cases where nucleic acid testing is unavailable due to lack of appropriate lesions at the time of consultations, where recurrent symptoms or atypical symptoms are present with negative herpes simplex virus cultures, to aid in counselling of sexual partners, in the detection of unrecognised infection and for epidemiological studies. These serological assays have good specificity and sensitivity and are useful retrospectively.[6]

Antiviral treatment

It is important to make the distinction between herpes simplex virus infection and varicella-zoster virus infection. Although herpes simplex virus and varicella-zoster virus respond to the antiviral medications aciclovir, famciclovir and valaciclovir, the virus susceptibility to these antiviral drugs differs; for example, the concentration of aciclovir that inhibits varicella-zoster virus is more than is needed to inhibit herpes simplex virus.[6] Valaciclovir or famciclovir are used for oral treatment, and intravenous aciclovir if intravenous therapy is needed for hospitalised patients.

Proper diagnosis reduces the risk of instituting improper treatment, which can cause complications.[6] There is also emerging evidence that early treatment of herpes zoster with antiviral agents at dosages effective against varicella-zoster virus will reduce the development of postherpetic neuralgia.[6]

Use of aciclovir, famciclovir or valaciclovir usually alleviates acute pain and reduces the risk of long-term pain in patients with herpes zoster; however, it is unclear to what extent these antiviral agents reduce the incidence of prolonged postherpetic neuralgia.[7] By inhibiting replication of varicella-zoster virus, these drugs attenuate the severity of zoster – specifically, the duration of viral shedding is decreased, rash healing is hastened and the severity and duration of acute pain are reduced. Elderly patients with herpes zoster should be treated with antiviral agents if they have presented less than 72 hours from rash onset as they will still derive benefit.

Vaccination of people with a history of herpes zoster

It is recommended that adults who are aged 60 years and older and not immunocompromised should receive a single dose of the zoster vaccine.[8]

People over 60 years of age with a clinical history of herpes zoster should also receive the vaccine.[8] This recommendation is based on the difficulty in predicting when a repeat episode may occur, and that the patient may have inaccurately recalled previous shingles or the illness may have been misdiagnosed. The zoster vaccine is, however, not indicated for use during an acute herpes zoster episode or for the treatment of patients with postherpetic neuralgia.

Zoster vaccine has not been shown to prevent recurrent episodes of herpes zoster and there are few studies to inform this. A US retrospective cohort study did not show any effect of the vaccine on recurrent zoster in adults with recent acute zoster.[9] Leaving a gap of at least 12 months between recent zoster and vaccination is recommended, although there is little

evidence to inform this decision. The vaccine has a similar safety profile in immunocompetent adults with recent herpes zoster as in those with no history of herpes zoster.[8]

Conclusion

Many recurrent zosteriform eruptions are caused by herpes simplex virus rather than being due to varicella-zoster virus (i.e. recurrent herpes zoster), as illustrated by the presented case of an elderly woman with recurrent zoster-like blistering on her face.

The cause of recurrent zosteriform eruptions should be confirmed microbiologically, and if true recurrent varicella-zoster virus infection is documented then possible underlying immunosuppression should be investigated. Depending on the frequency and severity of the recurrences, long-term prophylactic antiviral therapy should be considered. MT

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