Shingles
an update on treatment

Shingles is often a painful and debilitating condition. This article will review its clinical features and give an update on the options available for treatment.

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Varicella–zoster virus (VZV) infection is an almost universal infection in humans, usually acquired in childhood. Shingles, or herpes zoster, is the manifestation of recurrent VZV infection. As we age, zoster becomes increasingly common, with about 10% of people having an attack by 50 years of age and 40% or more of people who reach 90 years.

The condition is self-limiting and, to the observer, can appear mild. However, the patient's perspective is quite different, and the condition is often painful and debilitating, particularly in those unlucky enough to suffer persisting pain.[1]

Varicella–zoster virus

VZV is a highly contagious virus (Figure 1), which infects over 80% of susceptible household contacts of chickenpox (varicella). It will have infected 95% of us by the time we have reached adulthood.

After the primary infection, VZV establishes latent infection in ganglia, from where it reactivates in some people to cause zoster. When the virus reactivates it causes extensive inflammation and damage within the ganglion and involves many neurons. This probably explains why the pain from acute zoster may be so severe.

IN SUMMARY

- **Laboratory confirmation of shingles should be done when there is significant doubt, in complicated disease, in immunocompromised patients and when the infection poses a serious risk to contacts.**
- **The diagnosis is best achieved by detection of the virus in samples from the skin lesions. Try to swab areas of recent onset: vesicles are a better source than papules or crusted lesions.**
- **Skin lesions on the nose are predictive of corneal involvement. All patients with lesions around the eye should be treated promptly, and urgent ophthalmologic review should be sought if there is any suspicion of direct ocular involvement.**
- **In general, the benefits of antiviral therapy on acute zoster and chronic pain are confined to patients treated within 72 hours of onset of rash. The exception is zoster ophthalmicus where treatment up to seven days after onset reduces ocular complications.**
- **Valaciclovir and famciclovir are equivalent, and both are superior to aciclovir, for treating shingles.**
- **Severe pain in the acute phase seems to increase the risk of postherpetic neuralgia. Therefore, pain should be monitored closely and adequate pain relief should be provided, up to and including opiates.**
- **Postherpetic neuralgia is usually described as a boring, aching, burning or stabbing pain. It is also characterised by abnormal sensation and may be triggered by minor stimuli.**

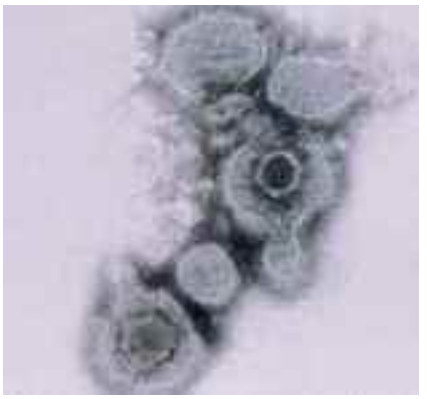

Figure 1. Electron micrograph of varicella–zoster virus obtained from a shingles vesicle.

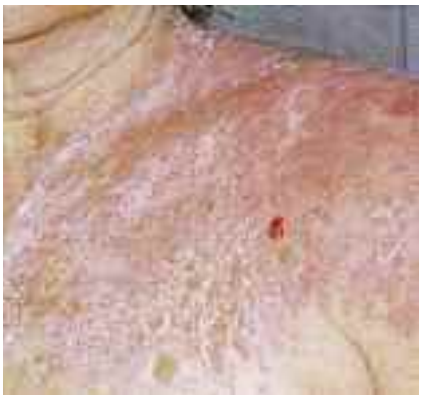

Figure 2. Classic shingles in an elderly woman.

Figure 3. Vesicular lesions on the patient shown in Figure 2.

FIGURES 1 TO 3 COURTESY OF DR LIAM O'CONNOR, PERTH

It is not known what triggers VZV reactivation – though declining immunity with age or immunosuppression is an important factor. Also, it is not known why reactivation preferentially involves a single dermatome.

The classic presentation of shingles

With reactivation, the virus travels back down the sensory nerve to the skin to produce the skin lesions. Pain in the involved dermatome is the most common initial manifestation and may precede the rash by several days. The rash initially appears as red blotches or papules that form small vesicles then larger blisters, which coalesce (Figures 2 and 3). These lesions crust and eventually heal. The period from onset of rash to a dry crusted lesion is usually four to five days.

Typically the lesions appear in only one area of one dermatome, though discrete patches throughout the dermatome are not uncommon. Dermatomes adjacent to the affected one may also be involved, and the lesions can cross a little way over the midline, following the patterns of cutaneous innervation. Thoracic dermatomes are involved in about half of the cases, and a further 20% of cases involve the face.

These features are accompanied by general malaise and lethargy, but fever occurs in only a minority of cases. Usually only one set of vesicles appears and resolves over about a week; however, complete healing may take much longer.

In unusual cases there can be VZV infection and pain but no rash. This condition is called zoster sine herpete.

Diagnosis

Because of its classic features, the clinical diagnosis of shingles in immunocompetent patients is usually straightforward.

Zosteriform herpes simplex should be considered as a differential diagnosis, particularly if there is a localised crop of vesicles in the genital or adjacent areas (Figure 4). Early cutaneous lesions can be quite uncharacteristic and may resemble a number of other conditions, including staphylococcal furunculosis. The presence of pain in a nerve root distribution is helpful; however, this type of pain can be mimicked by other causes of nerve root irritation or by musculoskeletal pain.

Laboratory confirmation of the diagnosis should be done when there is significant doubt, in complicated disease, in immunocompromised patients and when the infection poses a serious risk to contacts. The last group includes patients who have close contact with neonates or with immunocompromised people (e.g. when the patient is a health care worker).

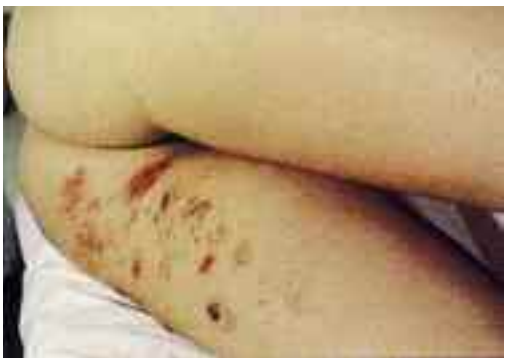

Figure 4. Zoster involving sacral dermatomes in a young woman. (If there is only a small area of lesions, sacral shingles can be mistaken for genital herpes.)

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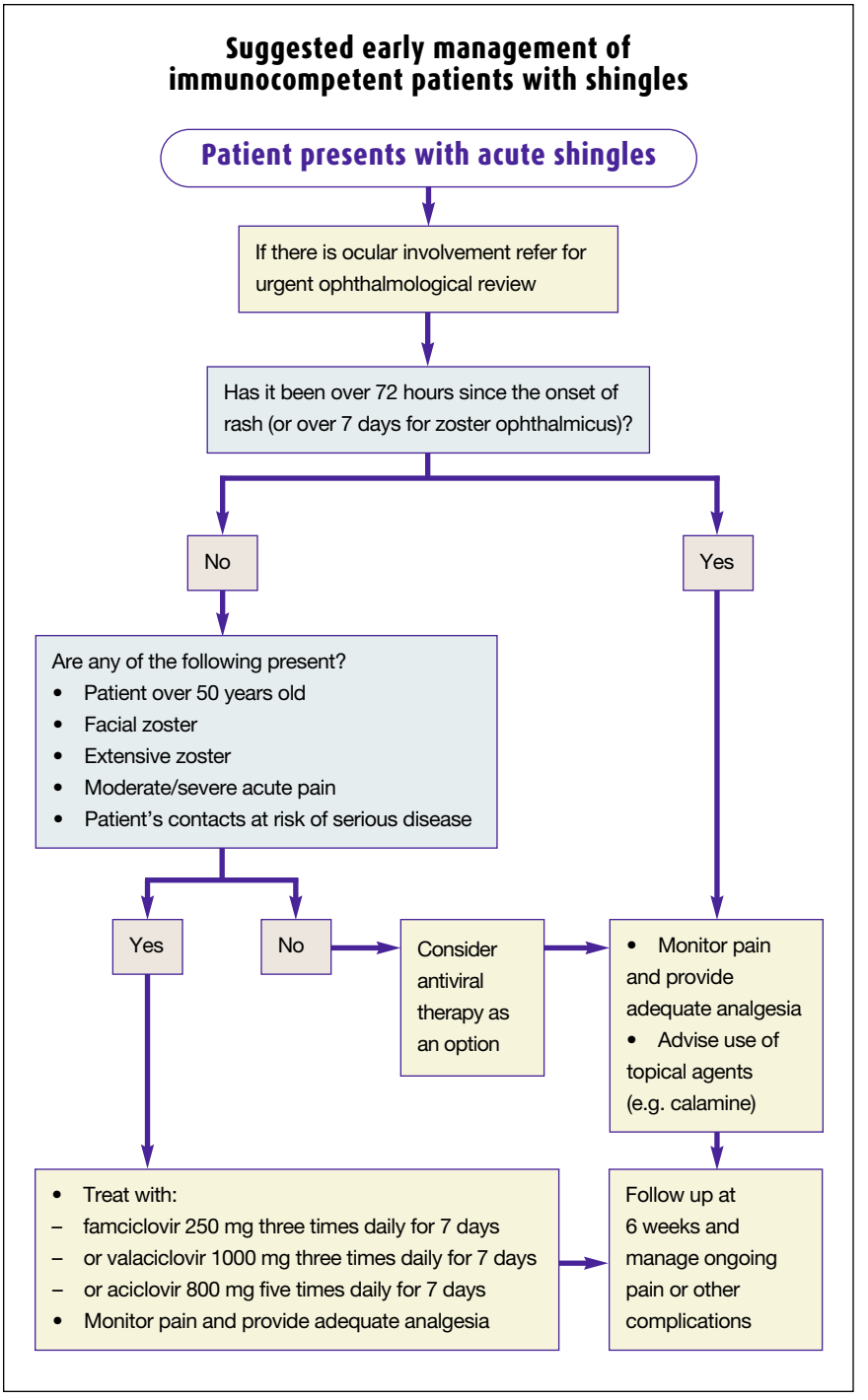

The diagnosis is best achieved by detection of VZV in samples from the skin lesions. Try to select areas of recent onset: vesicles are a better source than papules or crusted lesions. A cotton or dacron swab can be used to collect vesicle fluid or to swab firmly under the crust.

Detection of viral DNA by polymerase chain reaction (PCR) is the most sensitive test for detecting VZV, particularly in very early or late lesions. However, this test is available in only a small number of laboratories. PCR has proved to be useful in situations such as detection of the virus in cerebrospinal fluid in VZV meningitis or encephalitis.

Culture can be performed if the swab is placed in viral transport medium, stored at 4°C and transported to the laboratory as soon as possible. Current culture methods yield results in two to three days, but the virus can be troublesome to grow and therefore a negative result cannot exclude the diagnosis. VZV can also be detected by firmly swabbing the base of an ulcer, rolling this onto a slide and sending for immunofluorescent staining. This is quick, but it may miss some cases.

Techniques such as electron microscopy of vesicle fluid and Tzanck smears are insensitive and cannot distinguish between VZV and herpes simplex virus. So they are not usually helpful.

When samples for virus detection cannot be obtained, serology can sometimes be helpful. It may be possible to demonstrate a rise in IgG levels between acute and convalescent sera if these are available. Specific IgM may be detected in patients with shingles, but it is not reliable.

Risk of transmission to contacts

Although shingles is much less contagious than chickenpox, it is important to remember that shingles patients will shed VZV for several days until the lesions are dry and crusted. Transmission is particularly a risk when the lesions are on exposed parts of the body and are unable to be covered. During shingles attacks, patients should be advised to avoid contact with:

- children and adults who do not have a definite history of previous chickenpox
- pregnant women
- people with immunosuppressive diseases or receiving treatment that

depresses the immune system.

Patients in the latter two groups who have a significant contact with shingles should be managed like a chickenpox exposure and the use of zoster immuno - globulin should be considered.

Complications of zoster

The complications of zoster can be divided into three groups:[2,3]

- pain
- effects of local disease
- disseminated disease.

Pain is the most common debilitating consequence of zoster. It is discussed in detail in the next section.

Local zoster can cause serious tissue damage. If zoster involves the eye, corneal ulceration may develop as well as uveitis and conjunctivitis. Skin lesions on the nose are predictive of corneal involvement because both areas are supplied by the nasociliary nerve. All patients with lesions around the eye should be treated promptly, and if there is any suspicion of direct ocular involvement an urgent ophthalmologic review should be sought. Zoster elsewhere is occasionally complicated by skin lesions and scarring, which is much more common than with herpes simplex virus. Ramsey–Hunt syndrome is a classic complication of zoster involving the geniculate ganglion of the seventh cranial nerve, causing vesicles within the external auditory canal, facial nerve palsy, vertigo and anaesthesia of the anterior two-thirds of the tongue on that side. Rarer complications of facial zoster include ocular muscle palsies and granulomatous arteritis causing stroke.

VZV may not remain confined to its primary dermatome. Neural spread can cause myelitis, meningitis or encephalitis. A variety of motor nerve palsies are seen in rare cases. More widespread dissemination via the bloodstream occurs in up to 2% of immunocompetent patients but is much more common in patients who are immunocompromised. Most often this is just cutaneous dissemination, but it may also involve internal organs such as the liver, lungs and brain.

Pain arising from zoster

Pain arising from zoster can be divided into two phases – acute and chronic – with the chronic phase corresponding to what most of us understand as postherpetic neuralgia. Definitions of chronic pain vary, but the usual definition is pain persisting more than one month (30 days) after the onset of the rash.

Acute pain

Acute pain is very common, occurring in up to 90% of patients with zoster. It varies markedly with age, ranging from affecting 17% of those under 20 years old to 85% of those over 50 years old. The pain is thought to be due to direct sensory neuron damage secondary to viral infection. It occurs within involved dermatomes but may precede the onset of rash by up to several days. The severity of pain varies, it may be constant or intermittent, and its character may be sharp, shooting, throbbing, boring, aching, tender and sometimes burning.

Chronic pain

Postherpetic neuralgia is pain occurring within the area of rash that persists more than 30 days after the onset of rash. It is highly age dependent: it is rare under 50 years of age, rises to 20% in the 50 to 60 years age group but is short-lived, and in those older than 60 it rises to 50% and is often prolonged. The risk of postherpetic neuralgia also increases with the severity of the rash and the amount of acute pain.[4]

The pain persists for three months in about 30 to 50% of patients and for over one year in 20 to 30%. Postherpetic neuralgia is usually described as a boring, aching or burning pain, or as a stabbing pain. It is also characterised by abnormal sensations (dysaesthesia and hyperaesthesia) and may be triggered by minor stimuli (allodynia). It is extremely debilitating, and many patients will have depression.

There has been much speculation regarding the pathogenesis of postherpetic neuralgia, though we still do not have a clear answer. One pathogenic component appears to be a failure to 'reset' the hyperexcitability of spinal cord neurons induced by pain receptor stimulation during acute zoster. Therefore, adequate pain relief in the acute illness should reduce the risk of postherpetic neuralgia.[5]

Treatment

The flowchart on page 52 outlines a suggested protocol for the early management of immunocompetent patients who have zoster. If the infection is in an immunocompromised patient the treatment should be discussed with an appropriate specialist because of the risk of serious complications, such as pneumonia, encephalitis or disseminated infection.

Antiviral therapy of zoster in immunocompetent patients

In the following cases, antiviral treatment is recommended, provided that it can be commenced within 72 hours of onset of rash (or within seven days for zoster ophthalmicus). Depending on clinical circumstances, it may be appropriate in other patients also.

- Facial zoster – treatment will reduce acute and chronic pain and complications
- Patients over 50 years old – treatment will reduce acute and chronic pain
- Moderate to severe acute pain – treatment will reduce acute and chronic pain
- Extensive zoster – treatment will reduce the acute illness and chronic pain
- When contacts are at risk of serious infection – early treatment will reduce infectivity

Antiviral therapy

Antiviral therapy is now a well accepted part of the management of zoster, following the studies that showed that aciclovir at a dose of 800 mg five times a day reduced the severity and duration of rash and acute pain. The duration of pain was reduced by over 50%, and a similar reduction was seen in the number of patients with pain persisting for more than six months.[6]

In general, the benefits of antiviral therapy on acute zoster and chronic pain are confined to patients treated within 72 hours of onset of rash. The exception is zoster ophthalmicus, where treatment up to seven days after onset reduces ocular complications.

Valaciclovir (Valtrex) is a prodrug of aciclovir with much better oral absorption than aciclovir, and therefore it needs only to be given three times daily. It has also been shown to be superior to aciclovir in reducing the severity and duration of pain and the incidence of postherpetic neuralgia, with an additional 25% reduction of symptoms. Famciclovir (Famvir) is a well absorbed prodrug of the active agent penciclovir. Penciclovir has a mode of action similar but not identical to aciclovir. Famciclovir is superior to aciclovir and equivalent to valaciclovir for treating shingles.[7] It is given as 250 mg three times a day for seven days, but, like aciclovir and valaciclovir, it should be commenced within 72 hours of onset of rash.

Antiviral therapy should be considered in all patients presenting with shingles within the first 72 hours of onset of rash. Suggested indications for use of antiviral agents are listed in the box on page 55.

Data are beginning to emerge on the use of antivirals for complicated herpes zoster and it is likely that they will be useful for most, if not all, of the acute complications of shingles. However, while antiviral therapy is useful in preventing postherpetic neuralgia, it has no role in treating the condition once established.

There are still other drugs under evaluation that will expand the range of choices for treatment of zoster. None are likely to be dramatically better than existing agents, and there is, as yet, no likelihood of cure.

Corticosteroids

Good studies have now been conducted on the use of corticosteroids in acute zoster and they do not show any major benefit. While there may be a slight reduction in acute pain, no effect was shown on chronic pain. Therefore, corticosteroids should not be used routinely in the management of zoster.

In one study, there was an accelerated rate of return to normal sleep and daily activities in otherwise healthy adults over 60 years old.[8] Therefore, some practitioners do use corticosteroids in this group of patients provided they have moderate to severe pain and no contraindications.

Pain relief

Early aggressive pain relief is important in relieving the acute pain of zoster. Also, severe pain in the acute phase seems to increase the risk of postherpetic neuralgia. Therefore, pain should be monitored closely and adequate pain relief should be provided, up to and including opiates.

A recent small study suggested that the use of amitriptyline in acute shingles reduced the incidence of postherpetic neuralgia.[9] Unfortunately, amitriptyline is relatively toxic in the groups of patients who are at high risk of postherpetic neuralgia, and it would be prudent to await more data before using it routinely for prevention of postherpetic neuralgia.

For established postherpetic neuralgia,[3] simple advice to avoid tight clothing and to use cold packs will help reduce pain. The mainstay of drug therapy is tricyclic antidepressants, particularly amitriptyline (Endep, Tryptanol) or nortriptyline (Allegron), starting at low doses and increasing until pain relief is achieved or side effects are unacceptable. Nortriptyline is preferred because of its better tolerability. If this fails, the anticonvulsant gabapentin (Gantin, Neurontin) may be effective. Analgesia is important and may require the use of opioids. Topical analgesics help, but the preparations currently available are messy and difficult to use for long periods. A lignocaine patch now available overseas can be successfully used for prolonged periods for postherpetic neuralgia. Capsaicin (Zostrix) is a derivative of red chilli peppers and causes a selective depletion of the pain receptor neurotransmitter. Topical application appears to reduce postherpetic neuralgia – though a temporary sensation of burning follows application. If these treatments fail to relieve postherpetic neuralgia, then a referral to a pain specialist is appropriate.

Adequate pain relief in the acute illness should reduce the risk of postherpetic neuralgia.

Varicella vaccine

In recent years effective live-attenuated vaccines have become available for prevention of chickenpox, and there has been interest in whether vaccines in adults may boost immunity sufficiently to prevent shingles. There are some encouraging early results, but further data are awaited.

There are rare cases of shingles due to the vaccine strain. These can be effectively treated with antiviral agents.

Conclusion

Although shingles is usually a self-limiting condition, the acute illness is often painful and debilitating with occasional serious complications, and chronic pain is common in older patients. Early diagnosis and instigation of antiviral therapy and adequate pain relief will reduce the severity of both the acute and chronic illness. MT

A list of references is available on request to the editorial office.

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