Topics in Primary Care Medicine

Clinical Aspects of Herpes Zoster

RICHARD B. GLASER, MD, *San Francisco*

"Topics in Primary Care Medicine" presents articles on common diagnostic or therapeutic problems encountered in primary care practice. Physicians interested in contributing to the series are encouraged to contact the series' editors.

BERNARD LO, MD
STEPHEN J. McPHEE, MD
Series' Editors

Herpes zoster is a frequent, occasionally incapacitating and rarely fatal infection with *Herpesvirus varicellae* (varicella-zoster virus).

Zoster results from the reactivation of latent varicella-zoster virus in persons who at a younger age had suffered a primary varicella (chickenpox) infection. According to the widely accepted Hope-Simpson theory, based on epidemiologic and pathologic observations, the varicella-zoster virus enters cutaneous nerves during the primary varicella infection and migrates to the dorsal root or trigeminal ganglion where it remains dormant. If this homeostasis is somehow upset and the virus is able to replicate, herpes zoster develops. The efficacy of the host response then determines whether the infection remains localized to the dermatome innervated by the ganglion or becomes more widespread, involving other dermatomes, anterior horn cells or even viscera.

Predisposing Factors

Table 1 shows the factors predisposing to the development of herpes zoster. The most common factor predisposing for herpes zoster is age. The attack rate climbs with each passing decade and the infection is especially common after age 50. In 3,534 patients followed in England for 15 years, the overall incidence of zoster was 5.4%, rising to 16.2% for people in their ninth decade.

While it is true that certain neoplasms, especially lymphoproliferative disorders, do predispose to zoster, the converse is not true. People who have zoster are not significantly more likely to have a neoplasm than are age-matched controls. Hodgkin's disease is associated with an especially high incidence of herpes zoster, which has been reported to occur in 4.2% to 25% of patients with Hodgkin's. The higher incidence may reflect the effect of more aggressive therapy for this lymphoma in recent years. A strong association has been noted between therapeutic x-irradiation and zoster, and a recent study suggested that x-irradiation followed by chemotherapy posed the greatest risk to a patient with Hodgkin's disease. Other factors predisposing to zoster include local trauma, surgical procedures, spinal cord tumors and heavy metal poisoning. The findings of several studies indicate an increased incidence in patients treated with systemic corticosteroids or cytotoxic agents, but the magnitude of increased risk seems small in the absence of other risk factors such as irradiation or neoplasia.

Clinical Manifestations

The lesions of zoster begin as erythematous macules that usually evolve over 24 to 72 hours to form grouped vesicles. The rash usually begins posteriorly and moves anteriorly. New crops of lesions appear over one to four days and form crusts that last from two to four weeks. The severity of the eruption can vary from two to three vesicles to large confluent patches. Thoracic dermatomes are involved in about 50% of cases, the remainder being evenly divided between cervical, facial and lumbar dermatomes. About 20% of cases overlap adjacent dermatomes. In general, lesions do not cross the midline. While the major eruption is usually confined to one or two unilateral dermatomes, it is not uncommon to see as many as 10 to 20 vesicles in widespread, nonadjacent sites. This does not indicate dissemination. The rash is frequently preceded by a prodrome of four to five days' duration, characterized by neuralgia, pruritus and paresthesias. Pain in the absence of rash can be confused with myocardial

Refer to: Glaser RB: Clinical aspects of herpes zoster (Topics in Primary Care Medicine). West J Med 1983 Nov; 139:718-720.
From the Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, School of Medicine.
Reprint requests to Richard B. Glaser, MD, 400 Parnassus, 405A, University of California, San Francisco, San Francisco, CA 94143.

TABLE 1.—*Predisposing Factors for Herpes Zoster*

Increasing age
Local irradiation
Surgical procedure
Hematologic neoplasms and lymphomas
Rheumatologic disorders, such as systemic lupus erythematosus, rheumatoid arthritis
Cytotoxic chemotherapy

ischemia, peptic ulcer or biliary or renal disease. Rarely, the pain will not be followed by a rash *(zoster sine herpete)* As with varicella, the rash can cause significant scarring. Motor dysfunction caused by involvement of anterior horn cells occurs in about 1% of patients. The distribution of weakness almost always coincides with the involved sensory dermatome. Functional recovery occurs in 75% of affected persons. It is important to keep in mind the possibility of spinal tumors when motor paralysis complicates zoster, because tumors may be associated with both zoster and motor dysfunction.

Zoster involvement of the external auditory canal or tympanic membrane may be accompanied by homolateral facial paralysis (Ramsay-Hunt syndrome). This may be associated with loss of taste over the anterior two thirds of the tongue and disturbed lacrimation. Functional recovery is the rule, but occasionally neurologic regeneration is faulty, leading to profuse tearing during mastication (crocodile-tear syndrome).

Zoster involving the eye occurs in about a third of patients who have zoster of the ophthalmic division of the trigeminal nerve. There is close correlation between vesicles at the tip of the nose and eye lesions due to their common innervation by the nasociliary nerve. Anterior uveitis, secondary glaucoma, corneal scarring and postherpetic eye neuralgia may result from eye involvement. Ophthalmoplegia and ptosis may also occur and may precede the eruption.

Zoster encephalomyelitis is an uncommon manifestation of varicella-zoster infection, occurring from one week before to eight weeks after the cutaneous eruption. The onset is abrupt, with seizures, headache and a change in sensorium. Ataxia and cerebellar signs are frequent, and transverse myelitis may occur. A third of patients have a distinct syndrome of ophthalmic zoster and contralateral hemiplegia. Death is less common than with herpes simplex encephalitis, occurring about 25% of the time in untreated patients.

Zoster in an Immunocompromised Host

Patients who have disorders affecting humoral antibody responses, cell-based immunity or phagocytosis all seem to be at a greater risk for zoster developing. The disease is also more likely to take an aggressive form in such patients. In about 2% of otherwise healthy patients, and in up to 30% of immunocompromised hosts (almost invariably anergic), the disease disseminates widely. There may be involvement of the viscera as well as widespread cutaneous lesions. Symptomatic involvement of lungs, heart, central nervous system, gastrointestinal tract and serosa may occur. Such dissemination typically occurs from 4 to 11 days after the onset of localized lesions. Disseminated zoster in an immunocompromised host resembles varicella, with very low mortality. When there is serious underlying disease, mortality may reach 30% to 40%.

Children with no history of varicella, who are immunosuppressed or have widespread eczema, have fewer and less severe infections when treated prophylactically with zoster immune globulin after exposure. Interferon ameliorates the consequences of varicella-zoster infection in patients who have cancer. Whereas there seems to be considerable variability in *H varicellae* susceptibility to acyclovir, there are several anecdotal reports of its efficacy in disseminated zoster. There are as yet no controlled studies documenting the value of acyclovir in such situations.

Postherpetic Neuralgia

Postherpetic neuralgia is usually defined as pain lasting for two or more months after the resolution of cutaneous lesions. As many as 5% of patients with postherpetic neuralgia will have pain that persists indefinitely. Postherpetic neuralgia is unusual before age 40, but reaches an incidence of over 50% after age 60. Severe pain preceding or accompanying the eruption is associated with a greater likelihood of persistent pain following resolution of the rash.

In patients younger than 60 years, analgesics of sufficient strength should be used to make them comfortable. Patients older than 60 years should be considered for prophylaxis to prevent postherpetic neuralgia in addition to management of pain with analgesics. Corticosteroids, when administered soon after the onset of skin lesions, diminish the incidence of postherpetic neuralgia. In a controlled study, 73% of a control group and 30% of a corticosteroid-treated group had postherpetic neuralgia. The healing time of the skin was comparable in both groups, and there was no evidence of lesion dissemination in any of the steroid-treated patients. Prednisone is given in divided doses, 60 mg a day for one week, followed by 30 mg a day for one week and 15 mg a day for one week. Comparable corticosteroids may be used. Administration should be based on an analysis of the attendant risks as well as the benefits. For patients who have diabetes, hypertension, peptic ulcer disease, congestive heart failure or other infectious diseases, the relative risk may be too great to warrant using steroids.

For patients who have severe pain or a high risk of postherpetic neuralgia in whom corticosteroids are contraindicated, other less proved but potentially effective therapies are available (Table 2).

A 40% solution of idoxuridine in dimethylsulphoxide (DMSO)* applied continuously with a wet dressing to the affected dermatome for four days is used in Europe.

Levodopa, 100 mg given three times a day, in con-

*DMSO has not been approved by the Food and Drug Administration for this use in the United States.

TABLE 2.—*Treatment of Postherpetic Neuralgia*

Indications and Effect	*Drug*	*Treatment Schedule*
Prophylaxis		
Effective	Prednisone	60 mg a day for 1 week in divided doses 40 mg a day for 1 week in divided doses 20 mg a day for 1 week in divided doses
	Idoxuridine	40% in dimethylsulfoxide applied continuously to dermatome for 4 days
Possibly effective ...	Levodopa	100 mg, and benserazide, 25 mg 3 times a day, until pain subsides
	Dehydroemetine dihydrochloride	60 mg a day by injection until pain resolves (maximum 10 injections)
Treatment of Established Pain		
Possibly effective ...	Amitriptyline and substituted phenothiazine in therapeutic doses	
	Adrenocorticotropic hormone, 60 units given intramuscularly; repeat only if pain recurs after initial response	
	Chlorprothixene	50-100 mg given intramuscularly, then 50 mg by mouth every 6 hours for 7-10 days, or 50 mg by mouth every 6 hours for milder cases
	Transcutaneous nerve stimulation	

junction with benserazide, a peripheral decarboxylase inhibitor, 25 mg given three times a day, appears to abruptly alleviate symptoms and to possibly decrease the incidence of postherpetic neuralgia. In a group of 20 patients older than 60 years given dehydroemetine dihydrochloride, 60 mg daily intramuscularly, all had excellent relief of pain within nine days.

Established pain may be effectively treated using psychotropic drugs. Chlorprothixene (Taractan), 50 to 100 mg given intramuscularly in severe cases, followed by 50 mg by mouth every six hours for seven to ten days, was shown in one study to afford relief to 29 of 30 patients within 72 hours. Amitriptyline, 75 to 100 mg at bedtime, plus a substituted phenothiazine (such as perphenazine, 4 mg three times a day; thioridazine hydrochloride, 25 mg four times a day) is also effective. Transcutaneous electric nerve stimulators have worked in patients who have been refractory to other therapies.

GENERAL REFERENCES

Dolin R, Reichman RC, Mazur MH, et al: Herpes zoster-varicella infections in immunosuppressed patients. Ann Intern Med 1978 Sep; 89: 375-388

March SM, Kibrick S: Varicella and herpes zoster, chap 89, *In* Hoeprich PD (Ed): Infectious Diseases, 2nd Ed. Hagertown, Md, Harper & Row, 1977, pp 744-757

Mazur MH, Dolin R: Herpes zoster at the NIH: A 20-year experience. Am J Med 1978 Nov; 65:738-744

Merselis JG, Kaye D, Hook EW: Disseminated herpes zoster. Arch Intern Med 1964 May; 113:679-686

Shingles: A belt of roses from Hell (Editorial). Br Med J 1979 Jan 6; 1:5