HERPES ZOSTER INFECTION

Definition

Varicella-zoster virus (VZV), also known as Human Herpes Virus III (HHVIII), is a member of the herpes virus group. As all the other viruses from this group, VZV can manifests itself as a recurrent infection. After entering the body and causing primary infection, varicella-zoster virus remains latent in the neurons of sensory ganglion, especially dorsal roots of ganglion of the spinal nerves and extramedullar ganglion of the cranial nerves. Reactivation of the VZV infection is easily triggered by immune suppression. VZV infection is common in elder persons, immunocompromised or HIV positive individuals, and patients affected by malignant blood dyscrasias, malignant tumours, or undergoing immunosupressive therapy and radiotherapy.

Epidemiology

Varicella (chickenpox) is the primary infection of VZV and it is very common among children of both sexes. Herpes zoster (shingles) is the recurrent form of infection and occurs in the 3-5% of population, mainly among older individuals and immunocompromised. One percent of the persons who are 80 years old may have an infection during the period of one year. In 10% of HIV positive patients, HIV disease starts with herpes zoster infection in the oral cavity as an oral opportunistic infection. Reactivation of infection is infrequent in younger people and children. Postherpetic neuralgia, a significant pain or dysaesthesia present 3 or more months after herpes zoster, approximately 10–20% of zoster patients of all ages are affected, but frequency increases with age.

Clinical manifestations

Herpes zoster (HZ) in the oral cavity results from the involvement of second and third branch of the trigeminal nerve.

HZ develops 2-4 days after prodromal period, manifesting itself with general symptoms, such as fever, weakness, fatigue, and neck stiffness. Paresthesia and burning sensation in the region of the affected nerve are also frequent consequences of the VZV infection. Characteristic sign of oral HZ is the presence of unilateral vesicles that break rapidly, leaving small ulcers. On skin and lips, vesicle rupture can result in erosions covered by pseudomembranes and haemorrhagic crusts. Oral lesions without facial skin involvement are rather infrequent. Crusts and pseudomembranes, developing during the first week of vesicle formation, usually disappear in the second or third week. The patient is contagious from 48 hours

before vesicle formation, until oral lesions heal. It is possible that HZ occurs without lesions ("herpes sine herpete" zoster without eruptions), when only neurological symptoms are present. A frequent complication of HZ infection is postherpetic neuralgia (PHN). PHN, which is not correlated with immune suppression, is characterised by pain, paresthesia, hyposthesia or alodynia and can persist for months and year. Neuralgic pain is frequently associated with sensory loss.

Etiopathogenesis

Following primary infection, the virus is latent in the neurons of the sensory ganglia and reactivates itself as a consequence of immunodefficiency. The inflammation of the ganglion is followed by hemorrhagic necrosis of the nerves together with a partial necrosis of the ganglion. VZV affects neighbouring neurone ganglia and it might affect several branches of the nerve. Viruses spreading through sensory parts of the second and third branch of the trigeminal nerve, lead to the pathological changes in the oral cavity. The viral presence further leads to the acantholysis in the prickle cell of the epithelium and formation of the vesicles. Because of the subtle overlying layer, vesicles rupture rapidly, leaving erosions. VZV damages peripheral nerves through demineralisation, leading to sclerosis and degeneration.

Diagnosis

Diagnosis is made on the basis of clinical manifestations and subjective symptoms, presence of the viral antigens as well as presence of antibodies against VZV. Differential diagnosis of other viral infections is also possible so this infection must be well documented. The best laboratory diagnostics are PCR and direct VZV identification in the cell culture of human fibroblasts. The sample should be taken from vesicle or serum. The presence of VZV is evidenced by direct immunofluorescence of antibodies against VZV from the vesicle and up to 80% of the VZV infections could be detected using this method. Serological findings are helpful in recurrent VZV infections and show increased IgM, ten days after eruptions and increased IgG and IgA four days after the eruptions. Serological tests which reveal antibody titers might be useful in immunocompromised patients.

Treatment

Therapeutic regimens have become more efficient nowadays, especially when they are applied 48-72 hours after the appearance of the oral lesions. Systemic intake of antiviral agents is urgent in the patients who are older than 50 years of age, in immunocompromised, and in all patients with infection of the head and neck region,

especially in those with HZ of the ophthalmic branch. In adult immunocompetent subject of less than 50 years of age, symptomatic treatment is generally sufficient. Acyclovir, valacyclovir, famciclovir or brivudin must be administered systemically. Valacyclovir is proven to be more efficient when compared to the acyclovir. Brivudin showed higher antiviral potential then acyclovir, valacyclovir and famciclovir. Brivudin is also more easily administered (i.e. once a day during 7 days) and has no nephrotoxic properties.

Systemic use of the antiviral drugs shortens the healing period and lessens the pain symptoms together with prevention of other acute and/or chronic complications. Treatment of PHN usually comprises of analgesics together with neuroactive agents as well as with antiviral drugs. Corticosteroids administered systemically during the first two weeks of the disease are helpful in the PHN prevention, but they should not be given when PHN is already present. Some authors suggested combination of the perilesional anesthetic and corticosteroid injections. Reports upon shortening of the period of healing, but not PHN prevention have been documented. While treating neuralgia, analgesics, neuroactive agents and B vitamin complex should be administered. Some trials suggested that tryciclic antidepressants can be effective in alleviating neuropatic pain.

Prognosis and complications

Complications can occur in 10-46% patients with herpes zoster infection. Severe immunodeficiencies which precede HZ infection might predispose viral dissemination in the visceral organs, microbial superinfection and staphylococcal sepsis. Disseminated HZ infection might manifest as pneumonia, meningitis, encephalitis and hepatitis, as well as dermatological diseases. Paresis of facial nerve might develop as a complication when ganglion oticum is affected. When HZ affects the first branch of the trigeminal nerve, serious damage of the eye might occur (zoster ophtalmicus). Oral consequences of HZ might include heavy scarring, pulpal necrosis and internal root resorption. Also, cases of bone necrosis with teeth loss in immunocompromised patients with long term HZ have been described. Finally, patients suffering from recurrent HZ may have increased incidence of malignant diseases.

Further reading

1 Greenberg MS, Glick M, Burket S. Oral Medicine, Diagnosis and Treatment, 10th edition. BC Decker Inc. Philadelphia 2003;pp. 55-57, 330-331.

2 Nurimiko T, Bowsher D. Somatosensory findings in postherpetic neuralgia. J Neurol Neurosurg Psychiatry 1990; 3:135-41.

3 McKenzie CD, Gobetti JP. Diagnosis and treatment of orofacial herpes zoster:report of cases. JADA 1990, 120:679-81.

4 Gross G, Schofer H, Wassilev S, et al. Herpes zoster guideline of the German Dermatology Society (DDG). Am Fam Physician.2003; 67:757-62.

5 Cohen JI, Brunell PA, Straus SE, Krause PR. Recent advances in varicella-zoster virus infection Ann Intern Med 1999; 130:922-32

Links

www.ihmf.org/default.asp International Herpes Management Forum (accessed on 1 July 2004).

www.herpes-foundation.org/ The American Herpes Foundation (accessed on 1 July 2004).