Management of post-herpetic neuralgia

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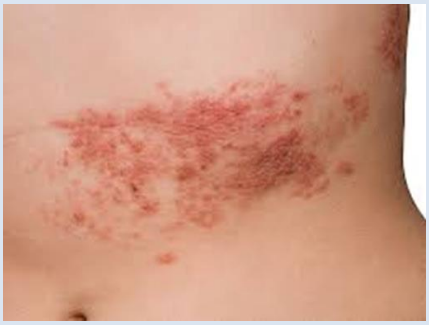


Post-herpetic neuralgia(PHN) is one the most common neuropathic pain which cause suffers in patients, especially in elderly population. The pain is defined as clinically meaningful pain (NRS>3/10), which occurs 3-4 months after onset of herpes zoster rash. The prevalence is around 0.7/ 1000 population with the annual incidence is 40/100000 person-year. The incidence is higher in elderly with age of more than 75, the incidence is 18%. For age between 65-74, incidence is 11% and for age 45-54, incidence is only 4%.

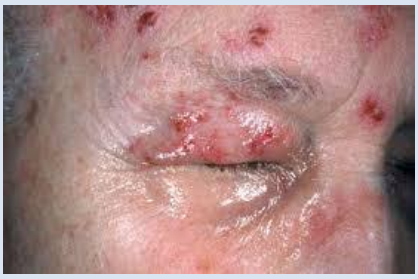
The pain is commonly described as persistent lancinating burning pain or paroxysmal shooting pain. There is also allodynia which usually the last symptom to resolve. In a prospective study of patients older than 50s, 16% of patients suffer from some pain at 6th month and 10% at 4^{th} year. 2% of patients experienced severe pain at 6th months while 0.7% at 4^{th} year. There are some risk factors for developing PHN, for example, age more than 60s, pain > 5 over 10 in acute phrase, presence of prodromal pain or abnormal sensation, extent of rash or inflammation, ophthalmic zoster, female and pre-existing comorbidies.

For the pathophysiology of PHN, varicella zoster virus induces primary infection and becomes latent in dorsal root ganglion. It causes waning of cell-mediated immunity in vulnerable group and replicated by transmission down the nerve axons and to skin, which later forms local infection and results in blisters. It can also travel centrally to meninges and spinal cord, which may cause more serious complication or even mortality. When secondary Inflammation reactivates, it causes widespread neural damage. It will elicit the release of neurotransmitters to some specific receptors and ion channels (TRPV1, TPRM8, Na channel (V1.8/1.9), CB1 and CB2) and induce neuropathic pain.

The presentation of acute infection is usually unilateral vesicular rash in dermatomal pattern, with pustulate and crust in 7 to 10 days. It may take a month to heal and may leads to scars or pigmentation. There is often prodromal pain, pruritus and dysaesthesia. Thoracic nerves, trigeminal nerve (first branch) and cervical region are most commonly affected. In 10-20% patients, herpes zoster opthalmicus occurs and some may result in visual loss. The pain in acute phrase is commonly described as constant deep aching or burning pain. Sometimes also presented with intermittent paroxysmal pain with a lancinating quality or intermittent pain evoked by normally innocuous sensory stimuli such as light touch, cold or hot sensation. The exaggerated pain is resulted from the injury of the peripheral nerves and altered pain threshold at the central nervous system. Besides, axonal regrowth after the injury will also produce nerve sprouts that are prone to unprovoked discharge.

The diagnosis of acute herpes is usually by clinical presentation, but it can be confirmed by viral swabs for immunofluorescence or culture for uncertainty. Differential diagnosis includes zosteriform herpes simplex, contact dermatitis, impetigo, candidiasis, drug eruptions, autoimmune blistering diseases or insect bites. Apart from PHN, other complications are disseminated herpes zoster, keratitis or uveitis, encephalitis, meningitis, myelitis, cranial and peripheral

nerve palsies, vasculitis, stroke, bacterial superinfection and pneumonia.



PHN causes significant physical suffering as well as psychosocial morbidities such as poor sleep, anxiety or depression, social isolation and functional disability. There are also substantial economic burden to society, increased health care use, lost working days and loss of independence in elderly. To alleviate the symptoms and its consequences, it is of paramount importance to limit the duration and severity of the attack, relieve symptoms, and prevent complications in acute phrase. Anti-viral drug should be given within 72 hours after onset of rash to limit the replication and spread of the reactivated virus within the ganglion and to the skin. The drugs of choice are acyclovir, famciclovir or valaciclovir for 7-10 days. Side effects include nausea, headache, diarrhea, and vomiting. However, a Cochrane review in 2009 showed that no evidence for anti-viral treatment can prevent development of PHN.

For management of the acute pain, panadol together with NSAID or tramadol shall be used for mild pain. For severe pain, tricyclic anti-depressant (TCA) such as amitriptyline should be prescribed; it is showed that it can significantly reduce the prevalence of chronic pain at 6 months. Second line drugs for severe acute pain are gabapentin, opioids (oxycodone) or corticosteroids in combination with acyclovir, which did showed some evidence for pain reduction and improved short-term quality of life when compared with placebo.

While for treatment of chronic PHN, there are strong evidence for the use of TCA, gabapentinoids as first line medication, while second line are tramadol, lignocaine and capsacin, Other drugs such as valporate, corticosteroids or iv lignocaine only have weak evidence and are suggested as third line treatment. While combination therapy will have synergism, for instance, gabapentin plus nortriptyline are more efficient than monotherapy. Pain intervention such as sympathetic nerve block, spinal cord or peripheral stimulation are the available option for severe pain, but most evidence are controversial and without long-term benefit. There is uncertain evidence or even no evidence for epidural steriod injection, intrathecal morphine, DREZ, neurectomy, and cordotomy.

Apart from pharmacological approach, non-pharmacological methods such as cold pack, firm garment, desensitization therapy, TENS are available treatment. Psychological interventions such as relaxation exercise, behavior cognitive therapy, biofeedback also have some evidence to reduce pain severity and improve self-management, function and quality of life.

In conclusion, PHN is the most common complication of herpes zoster. It is difficult to resolve with significant physical and psychosocial disability. The best treatment is to prevent with early diagnosis and proper management during acute phrase. Multi-disciplinary approach should be adopted for chronic pain with frequent assessment and early referral.

Reference:

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