《招待講演》

Neurogenic Pain : Diagnosis, Pathophysiology and Treatment

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Definition of Neurogenic Pain

The IASP has defined neurogenic pain as "Pain initiated or caused by a primary lesion, dysfunction, or transient perturbation in the peripheral or central nervous system." Neuropathic pain does not include transitory conditions.

A Neurological Disease

Neurogenic pain is part of the neurological disease spectrum and may be an expression of severe medical pathology. Apart from traumatic nerve damage a number of diseases may be accompanied by neurogenic pain, e.g., stroke, multiple sclerosis, syringomyelia/bulbia, herpes zoster, etc. Neurogenic pain has multiple disguises and may in addition be mimicked by non-neurological pain conditions. For differential diagnosis and specific treatment, it is important for patients with established or suspected pain of neurological origin to see a neurologist early on to confirm, establish or exclude a diagnosis of neurogenic pain.

Diagnostic Criteria

Pain due to neuropathy is projected and, with

few exceptions, confined to the innervation territory of the damaged peripheral nerve, root or central pathway. Therefore, it is mandatory to meticulously survey the distribution of pain, preferably by including a pain drawing made by the patient. A thorough history regarding, e.g., start of pain, the temporal pattern of pain, aggravating factors, and earlier treatment outcomes is important. Pain descriptors are generally of low diagnostic value since there is considerable overlap between descriptors used in neurogenic and nociceptive pain states.

Since pain in neuropathy is due to lesion or dysfunction of the somatosensory system it is reasonable to look for signs of altered sensibility. A careful bedside examination of somatosensory functions, using an array of instruments to explore the entire spectrum range of fibres/pathways is crucial since sensory aberrations may be confined to single modalities. The screening should include tools to test the sensation of touch, cold, warmth and pain. To avoid a chaotic exploration of somatosensory functions, a tentative diagnosis should guide the sensibility examination. Therefore, this procedure should optimally be performed as the final part of the diagnostic work up when collected information up to this point has been evaluated. The result is often valid for adequate diagnosis and clinical management. If necessary, quanti-

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tative sensory testing techniques may also be added to further characterize the somatosensory status. The outcome of the diagnostic work up must be critically evaluated and a reasonable history as well as findings compatible with neuropathy should underly the diagnosis of neuropathic pain.

Importantly, somatosensory aberrations are found also in a subgroup of patients with nociceptive pain, possibly due to intermodality interaction in the central nervous system set up by activity in the nociceptive system, and may be a source of confusion. The diagnostic work up must be evaluated with this alternative in mind.

Pathophysiology

1) Peripheral neurogenic pain

A flora of peripheral and central mechanisms has to be considered as contributors to spontaneous pain and stimulus evoked abnormalities in neurogenic pain. Excessive expression of sodium channels after axotomy and/or demyelination seems to be an important source of ectopic discharge in sensory neurons. Such channels are reasonable targets for treatment efforts aiming at reducing ongoing as well as stimulus-evoked pain. Tactile allodynia is a protruding signature of some neuropathic pain states and may seriously affect the quality of life of the patient. In spots of restricted tactile allodynia neuroma formation may be suspected, containing nociceptive fibres with a lowered activation threshold or such fibres activated by way of ephaptic transmission from neighbouring mechanoreceptive afferents. Larger allodynic areas point to disorganization in the CNS with activity in mechanoreceptive afferents being converted to the nociceptive system. Such a scenario may include the awakening of silent synaptic contacts between low threshold mechanoreceptive fibres and the nociceptive system in, e.g., the dorsal horn of the spinal cord. Alternatively, formation of

new synaptic contacts between collateral sprouts of mechanoreceptive afferents and nociceptive neurons may take place. The cerebral activation pattern in patients with peripheral neurogenic pain has recently been studied in our laboratory using positron emission tomography (PET). Ongoing neurogenic pain resulted in bilateral activation of anterior insula, posterior parietal, lateral inferior prefrontal, and posterior cingulate cortices as well as the posterior sector of the right anterior cingulate cortex. No significant change in activation was found in SI and SII.

2) Central neurogenic pain

From thalamic recording studies in humans with spinal cord injuries spontaneously firing neurons have been demonstrated. Results from animal models of central pain after spinal cord injury point to neuronal abnormalities in the spinal cord, e.g., loss of inhibition, as a potential mechanism underlying the pain. In patients with central post stroke pain (CPSP) a common denominator is the finding of dysfunction in the lateral spino-thalamo-cortical pathway, conveying information ultimately experienced as temperature or pain. The details of the neurophysiological, neurochemical and morphological alterations underlying mechanisms of central neurogenic pain are still to be elucidated.

3) Treatment aspects

First line treatment for the classical neuralgias of the face and oral cavity/pharynx is carbamazepine. About 70-80% of the patients will respond favorably. If unsuccessful, baclofen or phenytoin (and perhaps lamotrigine) should be tried. Neurosurgical interventions such as microvascular decompression of an impinged root or glycerol injection into the cistern surrounding the trigeminal ganglion may be considered in cases resistant to pharmacological treatment. Thermal rizotomy is a further option.

For other peripheral neurogenic pain conditions an array of treatment alternatives could

be suggested based on scientific evidence and/or clinical experience. Alternatives are TENS, spinal cord stimulation, stimulation of the Gasserian ganglion (for trigeminal neuropathy), motor cortex stimulation, amitriptyline and other antidepressants, carbamazepine, phenytoin, baclofen, gabapentin, mexiletine, and adenosine. Central neurogenic pain conditions have been less well studied. The first treatment of choice in CPSP is amitriptyline. Similar pharmacological treatments as suggested for peripheral neurogenic pain may also be tried in central pain. Neurosurgical procedures such as stimulation techniques and ablation, are only exceptionally successful.

Disappointingly, only about 50% of the patients will report substantial relief even if all options are tried.

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