MAYO CLINIC

Central Neuropathic Pain Syndromes

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CME Activity

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Statement of Need: General internists and primary care physicians must maintain an extensive knowledge base on a wide variety of topics covering all body systems as well as common and uncommon disorders. *Mayo Clinic Proceedings* aims to leverage the expertise of its authors to help physicians understand best practices in diagnosis and management of conditions encountered in the clinical setting.

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Learning Objectives: On completion of this article, you should be able to (1) recognize clinical features that differentiate central neuropathic pain from other pain types seen as sequelae of chronic neurologic impairment; (2) define the typical temporal profile of the onset of central neuropathic pain syndromes; and (3) differentiate the roles of various pharmacological, surgical, and neuromodulatory techniques in the treatment of specific central pain syndromes.

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Drs Watson and Sandroni discuss off-label use of various medications as well as spinal cord stimulation, deep brain stimulation for central pain treatment, rTMS, and motor cortex stimulation.

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Abstract

Chronic pain is common in patients with neurologic complications of a central nervous system insult such as stroke. The pain is most commonly musculoskeletal or related to obligatory overuse of neurologically unaffected limbs. However, neuropathic pain can result directly from the central nervous system injury. Impaired sensory discrimination can make it challenging to differentiate central neuropathic pain from other pain types or spasticity. Central neuropathic pain may also begin months to years after the injury, further obscuring recognition of its association with a past neurologic injury. This review focuses on unique clinical features that help distinguish central neuropathic pain. The most common clinical central pain syndromes—central poststroke pain, multiple sclerosis–related pain, and spinal cord injury–related pain—are reviewed in detail. Recent progress in understanding of the pathogenesis of central neuropathic pain is reviewed, and pharmacological, surgical, and neuromodulatory treatments of this notoriously difficult to treat pain syndrome are discussed.

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The International Association for the Study of Pain defines neuropathic pain as pain originating from a lesion or disease of the somatosensory nervous system.[1] Clinicians most commonly encounter neuropathic pain stemming from impairment within peripheral nervous system pathways (eg, painful peripheral neuropathy, radiculopathy, complex regional pain syndrome, postherpetic neuralgia). Less commonly, neuropathic pain can develop from disease affecting the brain, brainstem, or spinal cord. This disorder is termed *central*

neuropathic pain. Central neuropathic pain can result from any type of injury to the central nervous system (CNS) including vascular (ischemic or hemorrhagic), infectious (abscess, encephalitis, myelitis), demyelinating, traumatic (brain or spinal cord), or neoplastic disorders. It can also result from syrinx formation in the spinal cord or brainstem. However, central neuropathic pain is most commonly a sequela of stroke (central poststroke pain [CPSP]), multiple sclerosis (MS), or spinal cord injury (SCI).

There are unique challenges in distinguishing central neuropathic pain from musculoskeletal or peripheral neuropathic pain in patients who are neurologically impaired. Additionally, central neuropathic pain often occurs months or years after the original CNS insult and at a time when a patient's medical care may have transitioned back to their primary care physician and away from specialty care. Finally, central pain is very challenging to treat and may not respond to pharmacological agents routinely used for peripheral neuropathic pain. As such, it is important for primary care physicians, as well as specialists, to be familiar with the distinguishing features of central neuropathic pain and its unique treatment options.

DISTINCTION BETWEEN CENTRAL NEUROPATHIC PAIN AND CENTRAL SENSITIZATION

Central neuropathic pain syndromes should not be confused with central sensitization, which is a sequela of chronic pain. Central sensitization refers to a situation in which chronic nociceptive afferent input from a peripheral pain generator causes reversible ("plastic") changes of central nociceptive pathways (up-regulation or "wind-up") such that nonpainful peripheral stimuli are interpreted as painful (allodynia) and painful peripheral stimuli (eg, pinprick) are interpreted as overly painful (hyperalgesia). In contradistinction, central neuropathic pain refers only to pain that results directly from the CNS injury. Central sensitization from chronic peripheral neuropathic pain generators should not be labeled as central pain syndrome.

PAIN IN NEUROLOGICALLY IMPAIRED PATIENTS

Pain is common in patients who are neurologically impaired, but it is usually not central neuropathic pain. For example, after a stroke, 11% to 55% of patients will experience chronic pain, but it is frequently musculoskeletal nociceptive pain as a consequence of impaired mobility putting a greater burden on nonimpaired limbs.[2] Musculoskeletal shoulder pain in patients with arm paresis is particularly common (30%-40% of patients) following stroke.[3,4] Patients with gait disorders from CNS insults often experience knee, hip, and low back pain from altered mechanics, and patients who are wheelchair bound are at risk for low back pain and upper limb overuse syndromes (up to 75% of patients with SCI).[5] In MS populations with chronic pain, nociceptive pain from low back and musculoskeletal joint pain is common (20%-40% of patients)[6-8] and at least as common as central neuropathic pain.[9] In patients with SCI, musculoskeletal pain is the most common type of pain (50%-70% of those with pain),[9,10] but it is also less severe or limiting than the less prevalent central neuropathic pain.[9] Of course, patients can have multiple pain generators. In SCI cohorts, it has been well recognized that most patients with central neuropathic pain also have superimposed nonneuropathic pain contributors (musculoskeletal or visceral).[9,11] Comorbid noncentral pain types have also been found to be common in CPSP and MS pain cohorts.[8,12,13]

In neurologically intact patients, distinguishing these musculoskeletal pain types from a neuropathic pain etiology may seem straightforward. However, in patients with impaired discriminatory sensation, pain descriptors are frequently vague and localization and pain triggers are poorly defined.[9,14] Further, clinical examination in the office may be challenging in patients who are wheelchair bound or have severe mobility limitations. Ancillary testing and imaging may be necessary if the diagnosis remains in question.

Spasticity (increased tone- and velocity-dependent resistance to movement in the neurologically affected limb) is also a common consequence of CNS lesions and often leads to symptoms of tightness, stiffness, or discomfort in the neurologically affected limb. Central neuropathic pain will have obligatory accompanying sensory deficits that may help distinguish it from spasticity, but when spasticity occurs in a limb with central motor and sensory deficits, the distinction can be difficult. All patients with possible central pain should have the tone of the neurologically affected