Getting to the Root of Central Neuropathic Pain

After stroke or injury, patients are often afflicted with chronic debilitating pain. Here's how to approach some of the most common presentations.

Neurologists are often asked to assess patients with neuropathic pain. Of the neuropathic pain states, central neuropathic pain is probably the hardest to get under control. Consider a 27-year -old male who has developed severe central neuropathic pain after a spinal cord injury or a 35-year-old woman with multiple sclerosis who is experiencing not only painful spasticity but painful dysesthesias and trigeminal neuralgic pain.

In my experience, these have been among the most difficult patients to manage for many reasons including finding an effective regimen as well as one that is well tolerated and that the patient does not become tolerant to. Keep in mind that tolerance is not only an issue with the use of opioids! This column will provide an overview of central pain and the options for treatment.

Clinical Features

Central pain is defined as pain which is associated with lesions of the central nervous system.[1] Most agree that central pain syndromes are among the most difficult and intractable pain syndromes to evaluate and treat successfully. The most commonly cited central pain syndromes are central post-stroke pain (CPSP) and spinal cord injury (SCI) pain; however, one should not overlook the potential for central pain in patients with multiple sclerosis, syringomyelia, a Chiari malformation, neoplasms or other lesions of the spinal cord or brain. Identifying and treating central pain is extremely important, especially in the rehabilitation set-

ting, since impaired pain control may lead to difficulty with rehabilitation program participation.

The most common cause of SCI-related pain is trauma, occurring in 60 to 70 percent of SCI patients. Other causes of SCI pain include post-surgical, neoplastic, inflammatory, vascular, demyelination and congenital abnormalities. There is often a significant delay of several months following the injury before the onset of the SCI-related pain. Almost one-third of patients with SCI-related pain rate their pain as severe. Almost two-thirds of these patients continue to complain of pain for over one year.

SCI pain may be associated with a number of different presentation patterns, including: diffuse pain below the level of the injury; a band-like or dermatomal region of pain; the development following the injury of a cystic lesion in the spinal cord which ultimately results in a syringomyelia. The onset is most delayed in this last pattern. One should keep in mind that non-SCI pain syndromes may co-exist; these may include radiculopathies, secondary overuse syndromes and spasticity to name a few.[2]

The most common central pain syndrome associated with brain injury is that which may occur following a stroke. CPSP was first described in 1906 and is thought to occur in approximately eight percent of patients who have suffered a stroke. The onset of pain can be as early as one to two months following the stroke to as long as one to six years after the stroke. Patients often describe their pain in vague terms, creating ambiguity

that sometimes delays diagnosis.[3]

Nociceptor hyperexcitability has been postulated to be one of the mechanisms of SCI-related pain. This can lead to both spontaneous and evoked pain. When both types of pain are present, both spinal and supraspinal pathways are assumed to be affected. Some have postulated that the spontaneous pain associated with SCI occurs most commonly in those individuals with lesions of the dorsal or dorsolateral aspects of the spinal cord with resulting abnormalities of descending pain inhibitory input to the spinal cord.[4]

CPSP has frequently been termed "thalamic" pain in part because early research has pointed towards the thalamus as a source of the pain. Cortical processing has now been shown to be important as well in the development of CPSP, in addition to any role that the thalamus might play. Spinal thalamic cortical pathways may be injured following an ischemic or hemorrhagic infarct. Thalamic areas most commonly involved include the ventroposterior inferior and ventromedial nuclei of the thalamus. Alterations in thalamic and cortical processing of "normal" nociceptive pathways may lead to sensitization and loss of inhibition resulting in a sub- normal threshold activation of pain pathways.[5]

Very often, the terms which are used by patients experiencing central pain may be vague and downright strange. Their complaints may vary considerably from day to day and may sometimes confuse clinicians. SCI-related pain may be associated with nerve root lesions, partial or segmental cord damage, more com-

> **There is often a significant delay of several months following the injury before the onset of the spinal cord-related pain.**

plete cord injury, secondary visceral involvement through connections via the sympathetic nervous system and injury to the cauda equina.

Patients with SCI pain may complain of band-like muscle pain, described at times as a crushing or aching sensation. Any patient with central pain may complain of abnormal sensations—these are often poorly localized and quite upsetting to the patient. Allodynia (*i.e.*, pain from a normally non-painful stimulus) and hyperalgesia (*i.e.*, more pain than normal following a painful stimulus) are common in central pain. Patients will also commonly complain of lancinating as well as shooting pain, "pins and needles," and sensations of bloating or bladder fullness. Painful micturition is also not uncommon.[6]

Treatment Options

Surprisingly few controlled studies have been completed for patients with central pain. Evidence of pain relief in patients with CPSP has been noted with the use of the tricyclic antidepressant amitriptyline. At doses of 50-75mg/day, significant pain relief compared to placebo was noted in 10 out of 15 patients. One might consider other similar agents with fewer side effects.

As might be expected, anticonvulsant medications have been studied in central pain syndromes as well. Lamotrigine has been shown to be effective in the treatment of both CPSP as well as SCI-related pain in separate studies. Gabapentin has been shown to be effective in the treatment of SCI-related pain. Both topiramate and carbamazepine have been shown to be ineffective in the management of central pain states.

The use of opioids, especially intravenously administered morphine, has been shown to be effective in the management of spontaneous and certain types of evoked pain in patients with CPSP or SCI-related pain. When patients in this trial were switched to oral morphine, however, six out of 15 could not tolerate the oral regimen and discontinued their use of the morphine.[7]

Intravenous lidocaine has been shown to be quite effective in the management of central pain but regrettably needs to be repeated in order to maintain its effect. In a randomized controlled study, the intensity of spontaneous burning pain as well as brush allodynia was reduced compared to placebo in patients who received IV lidocaine. Overall in the same study, 69 percent of patients receiving intravenous lidocaine compared with

38 percent of patients receiving placebo experienced moderate or complete relief. Unfortunately, patients subsequently treated with the oral anti-arrythmic agent mexilitene after the use of intravenous lidocaine were in general not effectively treated.[8]

Direct lesioning of the spinal cord, except in selected cancer pain syndromes, has not been shown to be particularly effective in the management of central pain. When these treatments have been utilized in non-cancer pain there is a 60 to 80 percent recurrence of pain within two years.

Spinal stimulation as well as deep brain stimulation have both shown to be effective in central pain syndromes such as phantom limb pain as well as CPSP. A recent report suggests the potential benefit of botulinum toxin injected subcutaneously for the treatment of SCP pain. The use of intrathecal analgesics including both opioid and non-opioid analgesics can be considered as well in refractory situations.[9] **PN**

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