Pain after stroke

Challenges in assessment and management

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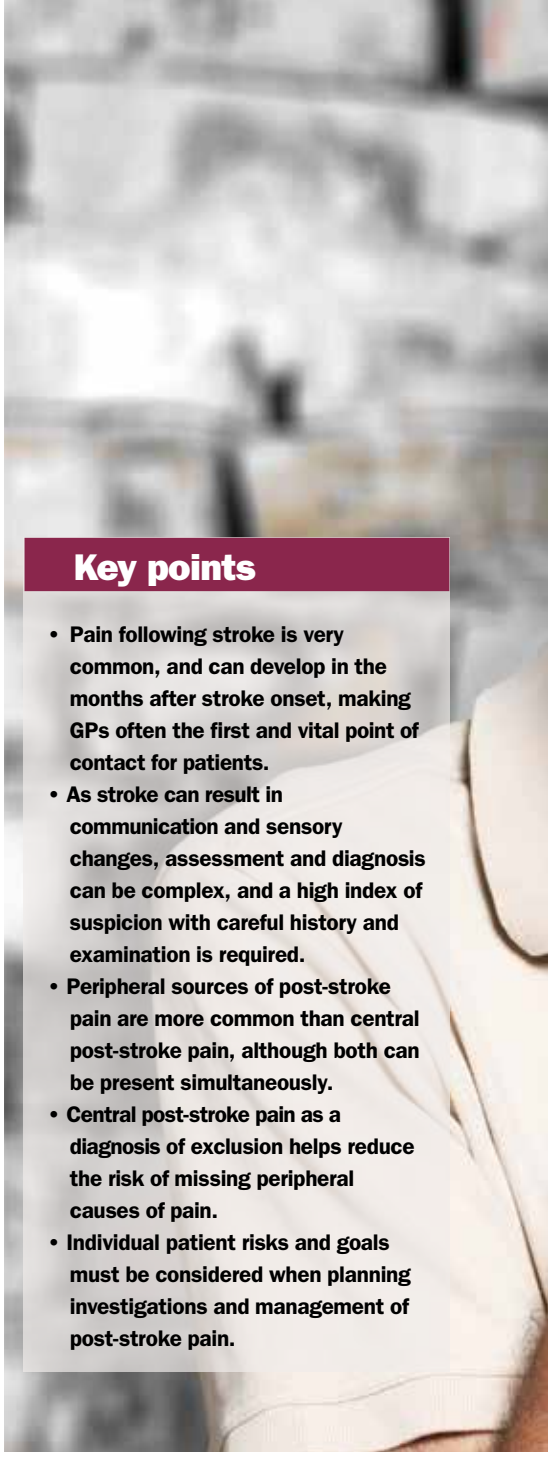
Pain following stroke is common, but accurate assessment of the nature and intensity of pain can be challenging. Awareness of possible pain sources, both peripheral and central, can help clinicians advocate for patients to ensure they receive appropriate management.



Key points

- **Pain following stroke is very common, and can develop in the months after stroke onset, making GPs often the first and vital point of contact for patients.**
- **As stroke can result in communication and sensory changes, assessment and diagnosis can be complex, and a high index of suspicion with careful history and examination is required.**
- **Peripheral sources of post-stroke pain are more common than central post-stroke pain, although both can be present simultaneously.**
- **Central post-stroke pain as a diagnosis of exclusion helps reduce the risk of missing peripheral causes of pain.**
- **Individual patient risks and goals must be considered when planning investigations and management of post-stroke pain.**

Pain after stroke is very common, affecting between 32 and 53% of stroke survivors.[1,2] Studies have shown that pain onset is often in the weeks to months following a stroke, but can also occur several years later. As with many pain conditions, pain after stroke can have a significant impact on a person's mood, sleep and their ability to participate in daily activities as well as social activities. These impacts often compound neurological impairments that result from the stroke. Patients with stroke often have a higher risk of associated conditions, including cardiovascular disease, diabetes, smoking-related disease, immobility, age-related health conditions and cancer, which can also be a source of pain.

Post-stroke pain develops in the months after the initial event, so GPs are often the first point of contact for patients. Many specialists, including neurologists, rehabilitation specialists, geriatricians, physiotherapists, occupational therapists, speech therapists and mental health clinicians, are often involved in the care of a patient after stroke. Any of these may also uncover the presence of pain in the course of treatment.

This article reviews the peripheral and central causes of post-stroke pain, and discusses some of the challenges in assessment, diagnosis and management of affected patients.

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Peripheral post-stroke pain

Post-stroke pain can be broadly divided into two categories: peripheral and central. Peripheral sources of pain are much more common than central sources. Peripheral post-stroke pain can be directly related to the neurological effects of stroke or indirectly related to stroke as a result of treatment, therapy or immobility. Sites of old injuries or pre-existing pain conditions may also be peripheral sources of pain. One report of moderate-severe pain after stroke found 38 to 40% of participants described pain onset before the stroke.[1]

Musculoskeletal causes of post-stroke pain

Several potential musculoskeletal causes of peripheral post-stroke pain exist. The most commonly reported cause is shoulder pain.

Shoulder pain can be present in up to

one-third of patients after stroke, and can have a significant impact on their participation in rehabilitation processes and daily activities.[3] Possible causes of shoulder pain include subluxation, adhesive capsulitis and spasticity. However, it is important to also consider causes not related to stroke, including old rotator cuff injuries and pain referred from the neck or diaphragm. There is also emerging evidence that central mechanisms can be involved in the persistence of post-stroke shoulder pain.[4]

Other sources of musculoskeletal pain after stroke include joint or muscle stiffness, myofascial pain syndrome, postural changes, osteoarthritis and trauma from falls.

Relation between spasticity and pain

Spasticity, or a velocity-dependent increase in tone, is an 'upper motor neuron' sign found in stroke, and is a result of impaired regulation of muscle reflexes. It is particularly important to consider spasticity in patients with post-stroke pain because it can result in a cycle of nociception, where spasticity can produce muscle pain and joint stiffness and increasing muscle and joint pain can worsen spasticity. If spasticity is present and problematic, a comprehensive multidisciplinary approach may include physical therapy and the use of pharmacological agents.

Other peripheral sources of post-stroke pain

Headache can occur acutely in up to one-quarter of patients after stroke.[5] There are several possible causes of headache, including migraine, tension, cerebral oedema and seizure.

Bowel and bladder dysfunction, including constipation and increased incidence of urinary tract infections, can be a source of post-stroke pain. There are also consequences of immobility that can lead to pain, including pressure areas, limb oedema, increased risk of osteoporosis and fracture, and deep venous thrombosis.

Treatment-related sources of post-stroke pain should also be considered. These include myalgia resulting from the use of statins as secondary stroke prevention, higher risk of peptic ulcers (and increased bleeding risk with antithrombotic therapies) and discomfort following exercises used in therapy.

Central post-stroke pain

Central post-stroke pain (CPSP) is defined as a neuropathic pain syndrome associated with sensory abnormalities due to the formation of lesions in the central nervous system following a cerebrovascular insult.[6] The concept was reported as early as the 19th century by Edinger, but only comprehensively described by Déjerine and Roussy in 1906.[7]

From these early case series, central pain following stroke was classically thought to be due to vascular lesions in the thalamus or posterior limb of the internal capsule. It is now understood that CPSP can occur from lesions found anywhere in the somatosensory pathways, including the dorsolateral medulla, thalamic-capsular connections and interconnections relating to the secondary somatosensory cortex in the parietal lobe. There are several proposed mechanisms of CPSP, most of which involve the disinhibition of the medial thalamus, indicating the key importance of this structure to the pain experience.[6]

The overall prevalence of CPSP reported in the literature is between 1 and 8%.[1,8,9]

Case study

A 75-year-old woman has a right infarctive subcortical stroke, on a background history of previous anxiety and depression, and cancer of the left breast 10 years previously without axillary clearance or node biopsy. She presents two months after the stroke with severe pain in her left shoulder and a 'wandering' hand, which she describes as having 'a mind of its own'. She has mild to moderate persisting spasticity in her left arm.

In this patient, an assessment of left shoulder pain would need to consider the potential peripheral causes of shoulder pain, the role of spasticity in contributing to pain (or resulting from pain), the influence of depression and anxiety on the pain experience and the potential involvement of previous breast cancer. Also, lung, diaphragm or bony involvement would need to be considered, and whether central mechanisms predominate if there are neuropathic features with sensory abnormality on examination.

Prevalence is associated with the site of the lesion, with much higher rates in lesions of the lateral medulla or ventral-posterior thalamus. It appears that there is no relation between the development of CPSP and side of the lesion, or age or sex of the patient.[8]

Diagnosis

CPSP can be considered a diagnosis of exclusion, given there are no pathognomonic features. Diagnostic criteria for CPSP have been outlined, with mandatory criteria as follows:[6]

- pain in a region corresponding to the lesion
- confirmation of a lesion on imaging
- sensory signs confined to the region corresponding to the lesion
- onset following stroke.

Supporting diagnostic features are:

- pain that is not primarily or solely brought on by movement
- presence of allodynia or dysaesthesia
- presence of characteristic pain descriptors such as burning, aching or an 'electric shock'.

The presentation of CPSP is consistent with other neuropathic pain syndromes. Although pain is most commonly described by patients as burning, it can also be pricking, freezing, squeezing, annoying or tiring. About 80% of patients with CPSP present to their GP within the first three months after stroke.[8]

CPSP occurs in the region of neurological sensory deficit, which can often be an area of both hypersensitivity and hyposensitivity. The affected area can be small and localised, although it is usually distributed to a larger region of the body. The location of the central lesion can impact on the area of pain sensation: thalamic lesions often result in hemibody pain and medullary lesions often involve the face or periorbital region.[10,11]

In most cases, pain is described as continuous, rather than intermittent. In a series of 15 patients with CPSP, median pain intensity was reported to be six out of 10,[9] although it can be severe, even intolerable. Often the pain is so troubling it will wake patients from sleep. Factors that aggravate CPSP can include contact with hot or cold, movement of the affected limb and mood disturbance. Often, exacerbations are unpredictable.

Assessment of post-stroke pain

Use of usual pain assessment tools and methods can be problematic in patients with post-stroke pain. There may be aphasias, perceptual deficits (including impaired right-left discrimination), sensory deficits, depression and anxiety, all of which can affect the ability of patients to communicate their pain experience. Questions to ask before assessment include: Is the patient aware of pain? Can they express their pain in a meaningful way? Can they accurately localise or describe their pain? Taking collateral histories from relatives or carers is important, because they may have learnt to recognise pain behaviours, which can help with assessment and during examination.

A high index of suspicion is required to detect the presence of pain, the effect of pain on the patient's function and the possible peripheral and central causes. Given the challenges in pain assessment in patients with stroke, the role of the clinician as an advocate for the patient is crucial. An example of a case of post-stroke pain is given in the Box.

History

As for other pain conditions, assessment of post-stroke pain should include a detailed pain history: pain onset, location and radiation, descriptors, aggravating and relieving factors. In particular the patient's mood status should be considered, given the higher prevalence of mood disorders and emotional lability following stroke, the strong emotional and psychological links to the pain experience, and the potential avenues for therapy.

Examination

History taking should be complemented by a thorough clinical examination of the patient, which may be targeted if a particular affected region or joint is identified. Evaluation of both musculoskeletal and neurological systems can help differentiate causes of pain, particularly as sensory abnormalities are an important diagnostic feature of CPSP. It may also be useful to consider physiological signs of pain (such as increased heart rate, increased blood pressure, the presence of spasticity), especially if verbal expression of pain is limited.

Investigations

Depending on the patient's history and examination findings, further investigation may not be necessary. If investigations are to be performed, a trial of therapy based on the most likely diagnosis should be considered while awaiting results. This also provides an opportunity for evaluation of the pain management strategy, as well as discussion of investigation results, in the follow-up visit.

Management of post-stroke pain

Peripheral post-stroke pain

If peripheral causes of post-stroke pain are found, patients should be managed appropriately as per guidelines or usual care. Peripheral post-stroke pain and CPSP can coexist and if they do, it may often be worthwhile targeting treatment to peripheral causes first.

As with any therapeutic intervention, there needs to be an awareness about the potential impacts on quality of life, drug interactions and side effects. Clinicians can work with patients to identify functional goals and then use these to guide management.

Table. Pharmacological therapies for central post-stroke pain

Drug class	Medication (maximum titrated daily dose)	Study	Study size (number of patients)	Effect
Antidepressants	Amitriptyline* 75 mg	Leijon and Boivie, 1989[12]	15	Significant; NNT = 2
	Fluvoxamine* 125 mg	Shimodozono et al, 2002[13]	31	Significant reduction after treatment, but only less than one year post-stroke
Anticonvulsants	Lamotrigine* 200 mg	Vestergaard et al, 2001[14]	30	Significant; NNT = 4
	Pregabalin 600 mg	Kim et al, 2011[15]	219 (pregabalin n = 110; placebo n = 109)	Improved secondary outcomes (sleep, anxiety)
	Gabapentin 600 mg	Hesami et al, 2015[16]	84	Clinically significant reduction in numerical pain scores, but no control group for comparison
	Carbamazepine* 800 mg	Leijon and Boivie, 1989[12]	15	No effect
	Levetiracetam* 3000 mg	Jungehulsing et al, 2013[17]	33	No effect
Opioids	Naloxone* 8 mg	Bainton et al, 1992[18]	20	No effect

Abbreviation: NNT = number needed to treat. * Used off label for post-stroke pain.

Central post-stroke pain

Management of patients with CPSP can be difficult, as with many neuropathic pain syndromes. A multimodal biopsychosocial approach to treatment is needed. A process of trial and error is usually required to identify which combination of pharmacological agents works best for each individual. Unfortunately, studies have been performed largely with single-drug regimens, which may not reflect clinical practice.

Caution needs to be taken when prescribing medications at higher doses, especially in elderly patients, due to the increase in side effects and complications in this age group. Moderate improvements in pain and function should be the aim of treatment. It might also be worthwhile considering clinically useful side effects of the drugs: for example, amitriptyline (off-label use for treatment of pain) can also improve for bladder continence and reduce sleep disturbance.

A summary of the evidence regarding oral pharmacological therapies in CPSP is provided in the Table.[12-18] As with other neuropathic pain conditions, the tricyclic antidepressant amitriptyline is often used as a first-line agent and there is some evidence (with a small sample size) for its effectiveness in reducing pain. There is also evidence in a larger trial for use of the anticonvulsant pregabalin, and reports of positive outcomes using gabapentin,[16,19] while a small trial showed some benefit with lamotrigine. The selective serotonin reuptake inhibitor fluvoxamine (off-label use) and serotonin and noradrenaline reuptake inhibitors (such as duloxetine) are less well studied in patients with CPSP but their use may be considered. Opioid analgesics are considered third-line agents.

Nonpharmacological agents should be considered in conjunction with medications. There is certainly a role for psychological therapies including relaxation, coping strategies and distraction techniques for pain management, as well as traditional cognitive behavioural therapy. There have been promising results from research in neuromodulation interventions (including deep brain stimulation and transcranial magnetic stimulation), but further study is required.

Follow up

It is very important that there is continual review and monitoring of patients with pain after stroke for change in pain location or description, and titration of medications as appropriate. The diagnosis and management should be reconsidered if pain is not reasonably controlled. Worsening pain can also be a presentation of mood dysfunction.

Conclusion

Pain is common in the months and years following stroke, and can be a direct consequence of the stroke, caused indirectly through therapy or immobility, or can be pre-existing. Assessment of these patients can be challenging due to communication, sensory and perceptual dysfunction, and the role of the clinician as a diligent and alert advocate for the patient is crucial. CPSP should be considered a diagnosis of exclusion, although both peripheral and central causes can be present simultaneously. Integrated biopsychosocial approaches, with an awareness of patient goals and potential side effects of therapy, are important concepts in the management of pain in the stroke patient. **PMT**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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