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Challenges in NEUROPATHIC PAIN Newsletter

MISSION STATEMENT

"To improve the awareness and understanding of neuropathic pain among the general public and medical practitioners, and to improve the diagnosis, treatment and patient quality of life in Hong Kong"

OBJECTIVES

- To enhance the understanding and knowledge of neuropathic pain and available treatment options
- To improve the diagnosis and management of neuropathic pain in Hong Kong
- To educate the public and reduce the suffering resulting from neuropathic pain
- To develop and implement scientific programmes that evaluate the quality of care for sufferers of neuropathic pain
- To act as an information source for medical professionals on the treatment and management of neuropathic pain
- To provide medical professionals with an evidence-based resource on neuropathic pain

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Introducing the Multidisciplinary Panel on Neuropathic Pain

神經痛跨學科研究小組

Welcome to the first issue of the Challenges in Neuropathic Pain Newsletter, which aims to provide you with the latest, relevant information in neuropathic pain and its management. With exciting developments afoot in the evolving specialty of pain medicine, the newsletter will prove an invaluable information resource. The newsletter will also be a useful forum for the newly formed Multidisciplinary Panel on Neuropathic Pain. This panel held its inaugural meeting in December 2001 and comprises experts in the fields of neurology, neurosurgery, orthopaedics, anaesthesiology and gerontology in Hong Kong.

Several compelling reasons justified the formation of a group of neuropathic pain experts. Identifying patients with neuropathic pain in the family clinic setting can be challenging because of an absence of objective diagnostic criteria and effective laboratory tests. Furthermore, Hong Kong physicians are currently unaided by local guidelines for managing neuropathic pain, and may be unaware of the most appropriate referral pathways and treatments. With this in mind, the Multidisciplinary Panel on Neuropathic Pain strives to improve the understanding and general awareness of neuropathic pain syndromes, and to contribute to better diagnosis, management and treatment of these conditions in Hong Kong.

Using a multidisciplinary approach, this group of experts is developing several initiatives that will be extremely useful for physicians and specialists who encounter patients with neuropathic pain. Physician education is the primary objective; therefore, training and education programmes, meetings and workshops, and management and treatment guidelines are a few examples of the innovative projects that the panel wishes to develop, some of which will be disseminated via this newsletter.

Pertinent topics will be discussed using regular features, such as case studies and educational articles, and the panel will aim to provide practical advice and recommendations on neuropathic pain syndromes. It is hoped that the Multidisciplinary Panel on Neuropathic Pain and this newsletter will be a valuable reference source for enhancing the management of neuropathic pain in Hong Kong.

Defining Neuropathic Pain and its Underlying Pathophysiology

Neuropathic pain is a complex and sometimes ambiguous field of medicine for many physicians. Several factors contribute to this ambiguity, one of which is the interchangeable use of pain-related terminology. Therefore, to clarify and standardize vocabulary, this article presents some basic pain definitions that have recently been set out by the International Coalition for Neuropathic Pain (ICNeP). The underlying pathology of neuropathic pain will also be briefly reviewed, explaining why doctors should focus more on specific symptoms and their mechanisms, rather than the neuropathic pain condition.

Nociceptive vs neuropathic pain

Nociceptive pain is an appropriate physiological response to a painful stimulus. This type of pain can usually be controlled with standard analgesics.

Conversely, neuropathic pain is an inappropriate response caused by a lesion or dysfunction in the peripheral or central nervous system. Neuropathic pain can manifest itself as either pain without a stimulus (stimulus-independent pain) and/or as pain hypersensitivity elicited after a stimulus (stimulus-evoked pain). Stimulus-independent pain includes symptoms described by the patient:

- Continuous, burning pain
- Intermittent shooting, lancinating pain
- Electric shock-like pain
- Some paraesthesias
- Some dysaesthesias

Acute vs chronic pain

Acute pain typically lasts less than 3-6 months, whereas chronic pain, such as neuropathic pain, is recurring and persists for at least 3-6 months after the initial attack has resolved.

Conversely, stimulus-evoked pain describes signs the physician induces after mechanical, thermal or chemical stimulation, and usually involves hyperalgesia or allodynia.

Paraesthesia vs dysaesthesia

Paraesthesia describes abnormal sensations that are not unpleasant, and dysaesthesia refers to unpleasant, abnormal sensations.

Hyperalgesia vs allodynia

These terms are often used interchangeably, but are actually very different. Hyperalgesia refers to an increased response to a stimulus that is normally painful, whereas allodynia is pain due to a stimulus that is not normally painful.

The Importance of Mechanisms

Traditionally, physicians treating neuropathic pain have used a disease-orientated approach; ie, all patients with diabetic neuropathy received identical treatments. However, patients with the same neuropathic pain syndrome often present with very different symptoms and respond to the same therapy with varying success, thus complicating disease management. It has become clear that physicians should now adopt a more symptom- and disease mechanism-based approach to selecting therapy. As understanding the underlying pathology of the different types of pain is key to choosing the most appropriate therapy for patients, a brief introduction to some of the mechanisms involved in neuropathic pain is appropriate.

The underlying mechanisms of neuropathic pain symptoms are:[1]

- Peripheral sensitization
- Ectopic discharges
- Central sensitization
- Central reorganization of Aß fibres
- Loss of inhibitory controls

Mechanical and thermal hyperalgesia[2]

These hyperalgesias are thought to arise from *peripheral sensitization*. Normally, painful stimuli cause propagation of impulses towards the spinal cord along A and C afferent nociceptive fibres. Following nerve injury, inflammatory cells release peripheral inflammatory mediators, such as substance P and bradykinin, which increase the sensitivity of these fibres. Thus, stimuli are perceived to be painful, although in reality they have a lower pain activation threshold.

Allodynia

Allodynia is more complex and involves several mechanisms, including:

Central sensitization of Aß fibres[3]

A series of biochemical events in the central nervous system causes increased responsiveness of the nociceptive system so that dorsal horn neurons respond in a distorted manner to normally innocuous stimuli. Allodynia caused by this mechanism is usually associated with spontaneous pain symptoms.

Central reorganization of Aß fibres[1,4]

Patients with non-spontaneous allodynia may have an Aß fibre-mediated pain mechanism. Pain fibres in the spinal cord may reorganize so that sections of the spinal cord that normally receive noxious input from peripheral C fibres now receive information regarding non-noxious stimuli from Aß fibre terminals that sprout into the superficial horn following nerve damage.

Loss of inhibitory controls[1-3]

After nerve injury, inhibitory controls may be lost or impaired at the spinal cord level, causing the dorsal horn neuron to fire in an exaggerated manner in response to afferent input.

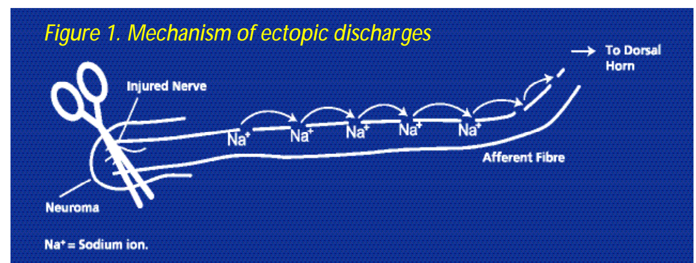
Peripheral sensitization of nociceptors[2]

See under '*mechanical and thermal hyperalgesia*' for a discussion of this mechanism.

Paraesthesia and dysaesthesia[3,5]

These may be caused by spontaneous ectopic discharges along Aß fibres, and are associated with an accumulation of sodium channels (Figure 1).

Figure 1. Mechanism of ectopic discharges



Continuous burning pain[3]

This symptom usually results from peripheral nociceptor sensitization, ectopic discharges in C fibres or loss of inhibitory controls.

Shooting or lancinating pain[3]

Ectopic discharges in nociceptive fibres are thought to be responsible for this type of pain (Figure 1).

Targeting Symptoms, not the Disease

This brief review shows neuropathic pain symptoms can be associated with several nerve pathways and pathological mechanisms, indicating that one drug will probably not be effective for all. In reality, patients present with a combination of symptoms that will necessitate the use of multiple, but targeted, agents for effective pain relief.

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CASE PRESENTATION

In each issue, a case study will be presented on a relevant neuropathic pain syndrome. Reviewing case studies will help to improve your diagnostic approach to neuropathic pain and increase your understanding of basing treatment strategies on presenting symptoms. In this issue, a case of trigeminal neuralgia is discussed.

Trigeminal Neuralgia

Presenting symptoms

A 57-year-old woman was referred to an outpatient pain clinic to evaluate her recurring facial pain. She complained of episodes of throbbing, jabbing pain localized in her right cheek and palate, which lasted for 30-120 seconds. Although she had pain-free days, she also experienced periods of frequent attacks, during which 2-3 pain episodes could occur in 1 hour. During these frequent attacks, she had difficulty speaking, eating, washing her face and brushing her teeth. The patient reported that normal face movements triggered attacks.

Medical history

Generally, the patient had an unremarkable medical history. Four years previously, she developed sudden pain in her right cheek, which was attributed to an apical abscess in her second molar, and was successfully treated. She was pain-free for 1 year, but then experienced sudden, intense attacks of pain in her right upper cheek. The dentist was unable to identify a cause for her pain.

Two years later, the condition had deteriorated; the attacks became more frequent and intense and the pain was radiating towards her right ear. A more thorough dental evaluation and X-ray examinations failed to identify an underlying dental problem. A few months later, the patient found that eating, speaking and brushing her teeth precipitated attacks of pain.

Clinical examination

On investigation, the patient was in good physical health. She had a normal neurological examination, including a normal touch and pinprick sensation in her face and palate. Her average pain intensity on the Visual Analogue Scale (VAS) was 81 mm over the previous week.

She was referred for several investigations, primarily to rule out any dental or CNS involvement, including:

- X-ray examination of the right maxilla
- Magnetic resonance image of the brain (with and without contrast)

In particular, the eighth cranial nerve (vestibulocochlear nerve) was carefully evaluated to exclude the presence of a tumour or other lesion on the cerebellar pontine angle. All these investigations were normal.

Interpretation

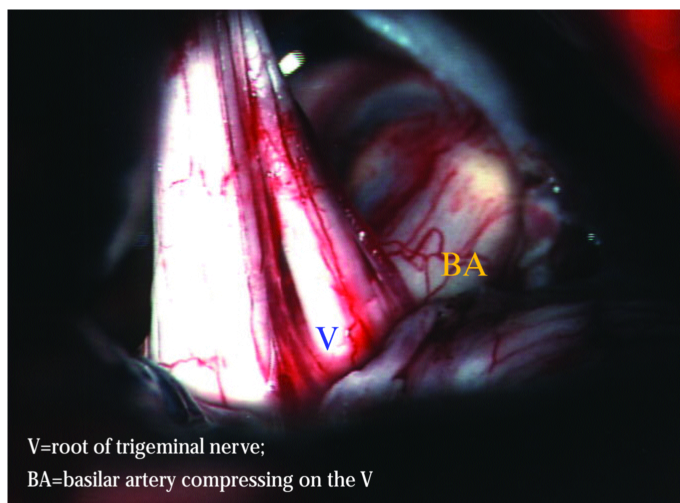
This scenario is fairly typical for trigeminal neuralgia, which was the definitive diagnosis. This neuropathic pain syndrome most commonly occurs in middle-aged women, and it predominantly affects the second and third distribution of the trigeminal nerve. Frequently, patients have a trigger point, such as touching specific parts of the face or chewing; in this case, attacks were triggered by the patient moving her face. The pain of trigeminal neuralgia is typically described as lancinating, shooting or an electric-like sensation, and it can last from a few seconds to a couple of minutes. Another clinical feature of trigeminal neuralgia, which is also demonstrated in this case study, is that the patient generally has a normal neurological examination.

Management

The most rational treatment approach for the sharp, paroxysmal pain associated with trigeminal neuralgia is to use sodium channel blocking agents, since this type of pain appears to arise from ectopic impulses generated from an accumulation of sodium channels along the length of the axon. Carbamazepine is generally considered the first-line sodium channel blocking agent for trigeminal neuralgia.

Therefore, this patient was started on low-dose carbamazepine (100 mg bid), which was gradually increased according to the frequency and severity of attacks (up to 200 mg tid).

After 2 weeks, the patient started to achieve pain relief and experienced fewer attacks. Her average VAS score reduced from 81 mm (at baseline) to 41 mm. Following several months of carbamazepine therapy, the patient was almost pain-free, and her VAS score further reduced to 22 mm. While it appears in this case that drug therapy was successful, it should be remembered that trigeminal neuralgia is a remitting condition, and improvements may occur spontaneously.



V=root of trigeminal nerve;
BA=basilar artery compressing on the V

In cases of trigeminal neuralgia that are resistant to drug therapy, surgery may be an option. This photograph depicts the basilar artery compressing the root of the trigeminal nerve, causing severe left-sided trigeminal neuralgia that was refractory to therapy. The patient's symptoms were relieved by microvascular decompression.

Q&A

Each issue, readers are encouraged to send in questions to be answered by members of the Multidisciplinary Panel on Neuropathic Pain. Please forward your questions concerning any aspect of neuropathic pain and its management to mpnp@medimedia.com.hk or fax to (852) 2559 6910.

When taking a medical history from a patient with possible neuropathic pain, what information should be obtained?

One of the most important diagnostic tools in assessing neuropathic pain is the taking of a full medical history. Firstly, questions should be asked to determine the underlying causes of the patient's pain. Neuropathic pain can have peripheral or central causes. Peripheral causes of nerve injury include trauma or surgery, metabolic disturbances (especially diabetes mellitus), infections, cancer, exposure to toxins, drugs or alcohol, vascular disorders and nutritional deficiencies. Inappropriate central nerve functioning can be associated with stroke, multiple sclerosis, spinal cord lesions and tumours. It is also essential to characterize the nature of the patient's pain, ie, its quality, intensity, location and pattern. There are numerous scales to help you achieve this, such as the McGill Pain Questionnaire, VAS, Neuropathic Pain Scale and patient diaries. The same tool(s) should be used routinely to assess changes in pain over time.

LITERATURE REVIEW

Rice AS, Maton S. Gabapentin in postherpetic neuralgia: a randomized, double-blind, placebo-controlled study. Pain 2001;94(2):215-24.

This was a multicentre, double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of gabapentin in postherpetic neuralgia. Patients (n=334) who had pain for more than 3 months after herpes zoster skin lesions had healed were randomized to receive either placebo or gabapentin 1,800 mg or 2,400 mg in three divided doses with a forced titration schedule. The primary outcome measure was change in average daily pain diary score from baseline to the final week of treatment. Patients treated with gabapentin had a significantly greater pain score reduction than placebo-treated patients at the end of the trial, with the following reductions in pain scores: -34.5% for the 1,800 mg dose; -34.4% for the 2,400 mg dose and -15.7% for the placebo group. A significantly greater improvement in sleep interference in both gabapentin-treated groups occurred within the first week, compared with placebo. Furthermore, gabapentin induced significantly greater improvements in most aspects of the Short-Form McGill Pain Questionnaire, Clinician and Patient Global Impression of Change and the SF-36 Quality of Life Questionnaire. Gabapentin was well tolerated at the study doses, with dizziness and somnolence being the most commonly reported adverse events. Hence, this trial confirmed gabapentin as an efficacious and safe treatment for patients with postherpetic neuralgia.

CONFERENCE CALENDAR

MEETING	1st World Congress on Regional Anaesthesia & Pain Therapy	16th Annual Congress of the Hong Kong Society for Surgery of the Hand	10th World Congress on Pain	Hong Kong College of Anaesthesiologists & Society of Anaesthetists of Hong Kong Annual Scientific Meeting 2002
LOCATION	Barcelona, SPAIN	Hong Kong	San Diego, USA	Hong Kong
DATE	29 May-1 June 2002	1-2 June 2002	17-22 August 2002	1-3 November 2002
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