Chapter 12
Management of Orofacial Neuropathic Pain

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Introduction

The International Association for the Study of Pain (IASP) defined neuropathic pain originally as pain "initiated or caused by a primary lesion or dysfunction in the nervous system" [1]. A revised definition of neuropathic pain as "pain arising as a direct consequence of a lesion or a disease affecting the somatosensory system" was proposed later by the IASP Special Interest Group on neuropathic pain [2]. Neuropathic pain poses a significant challenge to clinicians due to the complexity involved in diagnosing as well as in managing the condition appropriately. For example, a patient with trigeminal neuralgia could undergo multiple dental interventions in an attempt to address the pain, only to have the pain recur elsewhere along the distribution of the trigeminal nerve, thus contributing to frustrations for both the clinician and the patient. Also, in most clinical scenarios, neuropathic pain presents as a chronic pain condition often impacting the quality of life of the patients suffering from it.

A population-based study from Europe estimated the prevalence of chronic pain of neuropathic origin to be at 8 % [3]. In the United States, it is estimated that approximately 3.8 million people have neuropathic pain, including neuropathic back pain [4].

Neuropathic pain is classified based on the location within the nervous system that appears to mediate the pain (peripheral or central), based on the etiology of injury to the nerves (such as trauma, infection, inflammation, neurotoxicity, vitamin deficiency, neuro-degeneration, metabolic disorder) and based on the duration of signs and symptoms of pain presentation, and it is classified as either episodic or continuous pain (Fig. 12.1).

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N. Vadivelu et al. (eds.), *Orofacial Pain: A Clinician's Guide*,
DOI 10.1007/978-3-319-01875-1_12,

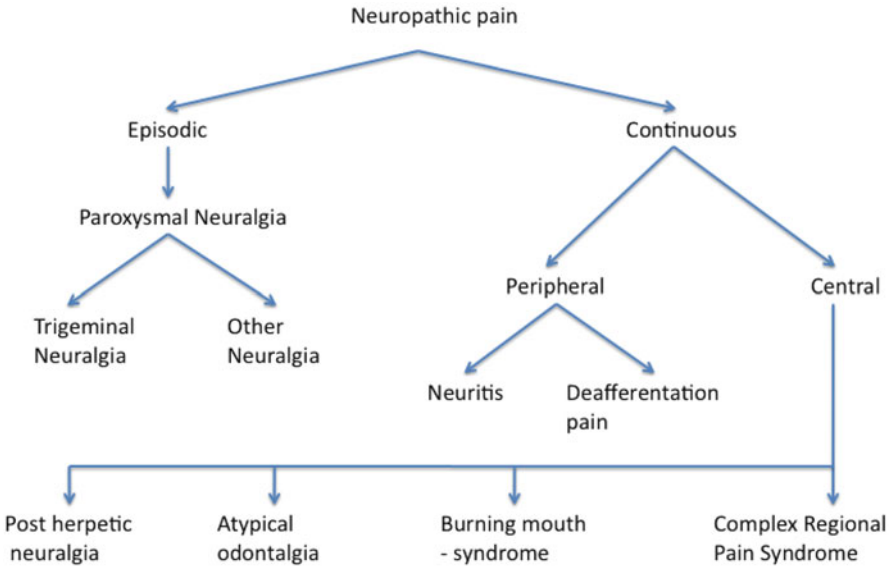

Fig. 12.1 Classification

In this chapter, orofacial neuropathic pain is discussed under the categories of episodic and continuous pain.

Episodic Neuropathic Pain

Episodic neuropathic pain can be further categorized into neurovascular pain and paroxysmal neuralgias. Some examples of episodic neuropathic pain that is neurovascular in presentation include certain primary headache conditions such as migraine, cluster headache, and other autonomic cephalalgia. The discussion on episodic neuropathic pain is limited to paroxysmal neuralgias in this chapter.

Paroxysmal Neuralgia

Clinical Features

Paroxysmal neuralgia is characterized by sudden electric pain that has a bright stimulating quality to it. Other terms used to describe the quality of the pain includes burning, shooting, stabbing, hot, or shocking. Paroxysmal neuralgia occurs predominantly during middle and old age with increase in incidence with age. It is also

more prevalent in women than men. The pain presents unilaterally and is felt in the precise anatomic distribution of the involved nerve [5].

The paroxysmal pain is also characterized by the presence of a site in the periphery, in the orofacial region that acts a "trigger zone," which when lightly touched triggers the paroxysmal pain. The location of this "trigger zone" is anatomically related to the location of the pain. Patients are known to report daily activities that trigger the pain including talking, eating, combing hair, or shaving. The paroxysms of pain are frequently followed by a refractory period during which pain cannot be induced by stimulating the "trigger zone." Each paroxysmal episode of pain lasts only for a few seconds at a time. Occasionally patients also report a background dull continuous pain.

Paroxysmal neuralgias are further divided into categories based on location and specific cranial nerve involved in the pain. These include trigeminal neuralgia ("tic douloureux"), glossopharyngeal neuralgia, geniculate neuralgia, superior laryngeal neuralgia, and occipital neuralgia.

Trigeminal neuralgia is the most common clinical diagnosis of all the cranial paroxysmal neuralgia. Due to the anatomic distribution of the trigeminal nerve, trigeminal neuralgia needs to be carefully distinguished from masticatory pain and dental pain. For example, jaw movements such as chewing or swallowing can trigger a paroxysmal episode by stimulating the trigger zone, thus mimicking presentation of masticatory pain. Similarly, triggered pain from occlusal contact on a particular tooth and arresting of the pain from an anesthetic block can indeed pose as a true conflict in accurately diagnosing this pain presentation as trigeminal neuralgia versus odontogenic pain.

Pathophysiology

A complete understanding of the mechanism behind paroxysmal neuralgia is yet to emerge. However, evidence from research has identified demyelination of nerve fibers in the ganglion and/or dorsal horn in neuralgia [6].

Specifically, with respect to trigeminal neuralgia, this can occur by the compression of the trigeminal nerve root as it exited the pons in the posterior cranial fossa, by an aberrant vascular loop of the superior cerebellar artery [7]. Other sources of compression of nerve trunk can be a space-occupying lesion such as a tumor of the cerebropontine angle, arterial aneurysms, or, rarely, malignant tumors that are extramedullary in location. Demyelination of the trigeminal nerve can also be associated with systemic conditions such as multiple sclerosis.

Management

Treatment of paroxysmal neuralgia has to begin with a thorough clinical evaluation of the symptoms and signs followed by appropriate diagnostic testing to exclude systemic conditions as well as space-occupying lesions that may be contributing to the clinical presentation.

(a) Pharmacological treatment strategies

The most effective medication in the management of paroxysmal neuralgia has been carbamazepine. The medication's effectiveness is significant enough that it is prescribed as a diagnostic strategy early in the course of pain management. Carbamazepine, an anticonvulsant, enhances the inactivation of voltage-gated sodium channels, thus delaying the recovery of a nerve that is stimulated by repeat firing of action potentials [8]. This in turn is considered to be its mechanism in reducing spontaneous activity of the involved nerve in neuralgia.

Long-term use of this medication is strongly influenced by its side effect profile including ataxia, drowsiness, fatigue, and, most critically, blood dyscrasias.

Recently, oxcarbazepine has been identified as a comparable medication with respect to its clinical effectiveness against neuralgia, however with less critical side effects. Oxcarbazepine shares the effects of carbamazepine on the voltage-gated sodium channels, thus providing for the same mechanism of action with reduced side effects.

Gabapentin, a calcium channel blocker, has shown clinical effectiveness in the management of neuralgia. Due to its side effects of drowsiness and fatigue, it must be gradually titrated it to an optimal clinical dose. Many of the patients do not reach the target dose of gabapentin related to side effects. A once-daily, gastroretentive formulation of gabapentin, Gralise, was introduced in the marketplace in 2011 with similar efficacy and significantly increased tolerability. Pregabalin is emerging as a noteworthy medication in the management of neuralgic pain although further research in the specific mechanism is warranted [9]. Other medications used independently or concurrent with the medication options listed above include topiramate, baclofen, lamotrigine, amitriptyline, and clonazepam.

Other pharmacological treatment strategies include the use of topical medications on the "trigger zone." Topical application of a long-acting anesthetic agent along with the use of capsaicin has been shown to be clinically effective in providing temporary relief.

(b) Neurosurgical treatment strategies

Patients with paroxysmal neuralgia gain only partial improvement with pharmacological strategies. Approximately 25 % to as high as 50 % of the patients report unsatisfactory results with respect to pain control when medications were used to address their pain. Neurosurgical procedure, albeit being invasive, provides an option for patients suffering from this debilitating condition.

As a better understanding of the demyelination mechanism underlying neuralgia has emerged, peripheral neurosurgical procedures are rarely being attempted to address the pain. Procedures such as peripheral neurectomy and use of neurolytic blocks are now attempted much more cautiously and are usually not one of the primary surgical management options.

Peripheral radiofrequency thermolysis is considered a temporary alternative to the more invasive procedures as it temporarily raises the threshold for pain.

The most common procedures used to treat trigeminal neuralgia are microvascular decompression and rhizotomy. The microvascular decompression is an intracranial

procedure in which a physical barrier in the form of a stent or an inflated balloon is placed between the compressed nerve trunk and the offending structure, usually a blood vessel, to prevent compression from contributing to the pain. However, this procedure is a major surgery with all the associated risks, and hence patient selection is a crucial factor in the effectiveness of this procedure [5].

Rhizotomy is a procedure wherein the selected nerve fibers within the ganglion are destroyed by radiofrequency thermocoagulation or with the use of a toxic agent such as glycerol. Rhizotomy is associated with significant risks including but not limited to facial muscle weakness, corneal anesthesia, and loss of facial sensation.

Thus rhizotomy, while offering a neurosurgical option in the management of neuralgia, is also associated with significant risks and like the other procedures outline here needs to be considered carefully.

Continuous Neuropathic Pain

Continuous neuropathic pain conditions are conditions that present as constant, unremitting pain of varying quality and intensity with no period of total remission. These can be further categorized into peripheral, central, and metabolic polyneuropathy. Even though these categories can be recognized with reasonable clarity in the clinical environment, how they vary in their underlying mechanism is yet to be understood.

Pathophysiology

Mechanisms underlying the pathophysiology of continuous neuropathic are both complex and not completely understood. Available evidence indicates the existence of both peripheral and central mechanisms that appear to interact and contribute at different levels to the overall presentation of pain which somewhat explains the varied presentation of continuous neuropathic pain conditions. Peripheral sensitization is a known mechanism wherein the threshold for neural depolarization is lowered by the expression of additional sodium channels and other ion channels in the peripheral nerve following the release of inflammatory mediators associated with nerve injury [10]. Central sensitization is the phenomenon where the depolarization threshold of the spinal tract neurons is lowered following the cascade of events after peripheral sensitization including the release of neurochemicals such as substance P and CGRP [11]. When the processes of peripheral and central sensitization contribute to a prolonged condition, altered gene expression can occur which in turn influences the types and the number of receptors expressed by a nerve. This phenomenon is called neuroplasticity, and once this has occurred, even after the healing of the original source of pain, sustained pain can be present and come to define a continuous neuropathic pain disorder.

Peripheral Continuous Neuropathic Pain

Neuritis Pain

Clinical Features

Neuritis pain occurs after an injury or infection affects the peripheral nerve trunk. This results in a lowered threshold for depolarization in the peripheral nerve and presents as a continuous burning pain along with the other qualities of stimulating sharp or bright pain localized to the site of known inflammation or infection. Neuritis may present with other sensory symptoms of hyperesthesia, hypoesthesia, paresthesia, dysesthesia, or anesthesia. If neuritis is associated with a motor nerve trunk then muscular symptoms of ticks, weakness, or paralysis may co-occur with pain [5]. Some examples of neuritis pain include pain with trigeminal neuritis involving a tooth following surgical procedure, facial nerve neuritis ("Bell's palsy"), glossopharyngeal neuritis, and Tolosa–Hunt syndrome.

Management

Once the etiology of the inflammation or the infection is identified, management of the source of infection is warranted as priority. In the case of a suspected bacterial infection, antibiotics are used. When no identifiable infective source is determined, then administration of steroids should be considered. Early steroid therapy during the course of neuritis appears to reduce the risk of long-term symptoms for the patients.

One of the most significant long-term risks with neuritis pain is associated specifically with herpes zoster infection of the peripheral nerve contributing to post-herpetic neuralgia. Post-herpetic neuralgia is managed with the long-term use of medications such as amitriptyline and gabapentin and occasionally supplemented with the use of topical medications such as capsaicin cream (0.025 or 0.075 %) with long-acting topical anesthetic agents. Neurosurgical procedures outlined earlier have been attempted to treat post-herpetic neuralgia with varying degrees of success.

Deafferentation Pain

Clinical Features

Injury to the peripheral nerve trunk, that is surgical or nonsurgical in nature, can result in the deafferentation of nerve fibers. The resulting pain persists even after considerable regeneration of nerve fibers. Deafferentation pain is characterized by symptoms of paresthesia and dysesthesia, alongside continuous burning pain with a distinct area of numbness or even severe pain.

Management

If the injury to the peripheral nerve trunk is minor, the tissue may gradually heal. But if the injury is significant, microsurgical repair of the injured peripheral nerve trunk has been accomplished successfully. Topical medication, such as capsaicin, can be applied to the painful area along the nerve trunk and has been shown to be effective [12]. A low dose of tricyclic antidepressant such as amitriptyline or the use of gabapentin also shows some clinical effectiveness.

Central Continuous Neuropathic Pain

Atypical Odontalgia

Clinical Features

By definition, known as "toothache of unknown cause," atypical odontalgia, presents as one of the most frustrating conditions for clinicians. Most if not all of the patients presenting this condition have had multiple dental treatments including endodontic procedures, and even extractions, in an attempt to alleviate this pain. Atypical odontalgia has been described as "phantom tooth pain" when it occurs in the site of tooth extraction. This occurs as a continuous dull aching pain that can vary considerably in quality and intensity but is unremitting in nature and can remain unaltered for years with or without intervention.

Management

Owing to the lack of identifiable peripheral etiological factors for this type of continuous neuropathic pain, all treatment strategies attempt to address the probable underlying central mechanism. Tricyclic antidepressants, once again, are proving to be effective in the management of atypical odontalgia.

As adjunctive therapy, gabapentin and pregabalin have also shown improved clinical outcomes.

Summary

Orofacial neuropathic pain conditions, both episodic and continuous, are some of the most frustrating conditions for both the clinicians attempting to manage them and for the patients suffering from them. Management strategies for these pain conditions are primarily medication based. Cognitive Behavioral therapy and, palliative therapy for secondary masticatory pain should be considered concurrently to maximize pain relief for the patients.

Acknowledgement None declared.

Conflict of Interest None declared.

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