Oral surgery II: Part 5. Chronic orofacial pain

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In brief

Discusses how the diagnosis of orofacial pain can be complex.

Provides some ideas are provided for differentiating neuropathic from inflammatory pain.

Outlines principles for the management of orofacial pain.

Chronic orofacial pain syndromes represent a diagnostic challenge for any practitioner. Patients are frequently misdiagnosed or attribute their pain to a prior event such as a dental procedure, ENT problem or facial trauma. Psychiatric symptoms of depression and anxiety are prevalent in this population and compound the diagnostic conundrum. Treatment is less effective than in other pain syndromes and thus often requires a multidisciplinary approach to address the many facets of these conditions.

Introduction

Orofacial pain is pain (emanating from or perceived) within the trigeminal system. The trigeminal nerve supplies general sensory innervation to most of the face, scalp and mouth (Fig. 1a). A large proportion (>40%) of the sensory cortex represents the trigeminal input (Fig. 1b), and hence persistent pain in the orofacial region has significant impact on the sufferer, resulting in both functional and psychological consequences. Treatment

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ORAL SURGERY II*

Part 1. Acute management of dentoalveolar trauma

Part 2. The maxillary sinus (antrum) and oral surgery

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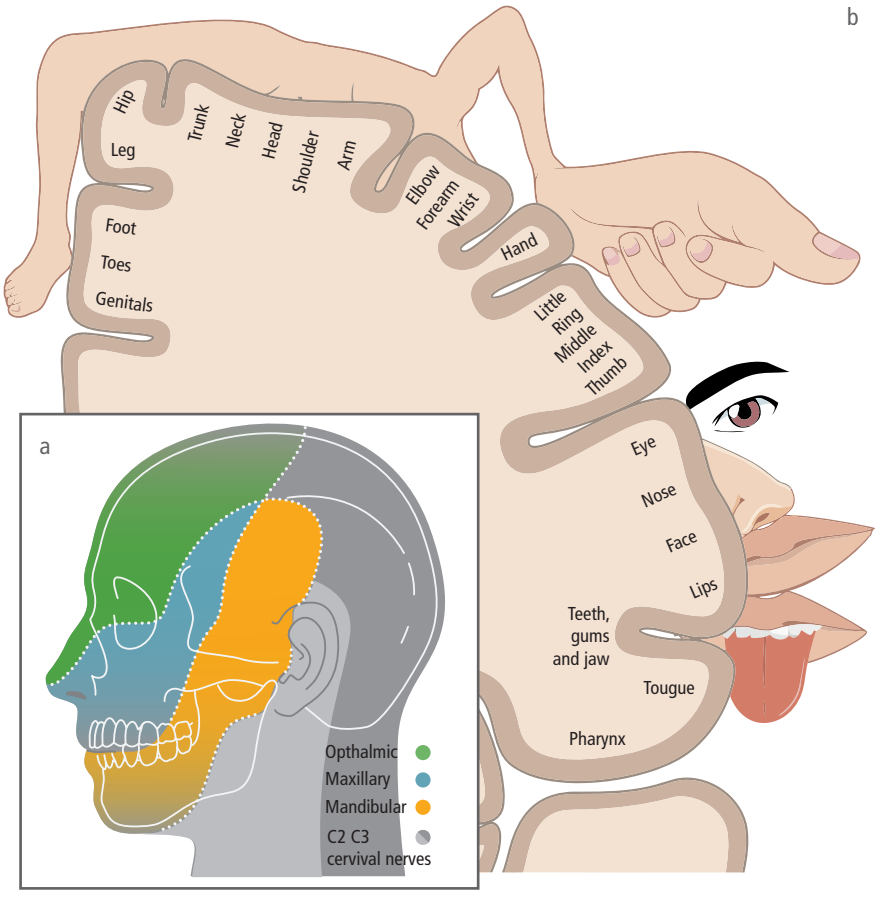

Fig. 1 The trigeminal nerve. a) Sensory distribution and b) its representation in the sensory cortex

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is less effective than in other pain syndromes and thus often requires a multidisciplinary approach to address the many facets of these conditions.[1]

Chronic pain is defined as pain that persists after the inflammatory response to the acute cause of pain has ceased (International Association for the Study of Pain, IASP). Increasingly, it is perceived as a disease entity in itself, having evidence of structural (grey matter loss), neurophysiological and genetic changes within the neuromatrix. Chronic pain encompasses two broad categories:

- Nerve-derived 'neuropathic' pain (eg headaches and neuralgias)
- Refractory persistent inflammatory pain (eg arthritis).

Although effective pain management interventions and programmes exist, provision of these services is inconsistent, and chronic pain is not given the priority it requires in view of the extent of its burden on individuals and society. The costs of back pain alone account for 20% of the UK's total health expenditure.[2]

The prevalence of chronic pain is estimated at 8–60% of the population, depending on the definition.[3] Severe pain is estimated at 11% for adults and 8% for children. Older age, female sex, poor housing and type of employment (for example heavy manual work) are significant predictors of chronic pain in the community.

It is also common in the US, estimated to affect 30% of the adult population (100 million in US alone), impacting both the individual and society with estimated costs of $635 billion each year in medical treatment and lost productivity.[4]

Aetiology

Pain can be divided into two healthy pain scenarios (Figs 2a & b) and two unhealthy, chronic pain scenarios (Fig. 2c).[5]

Facial pain can be associated with pathological conditions or disorders related to both somatic and neurological structures. There is a wide range of causes of chronic orofacial pain and these have been divided into three broad categories by Hapak *et al.*[1] and Woda *et al.*[6] (see the Classification section in this article and Table 5 for more detail).

1. Neurovascular
2. Neurological
3. Idiopathic or dysfunctional (fibromyalgia, irritable bowel syndrome and temporomandibular disorder, arthromyalgic pain conditions, non-clustering).[3]

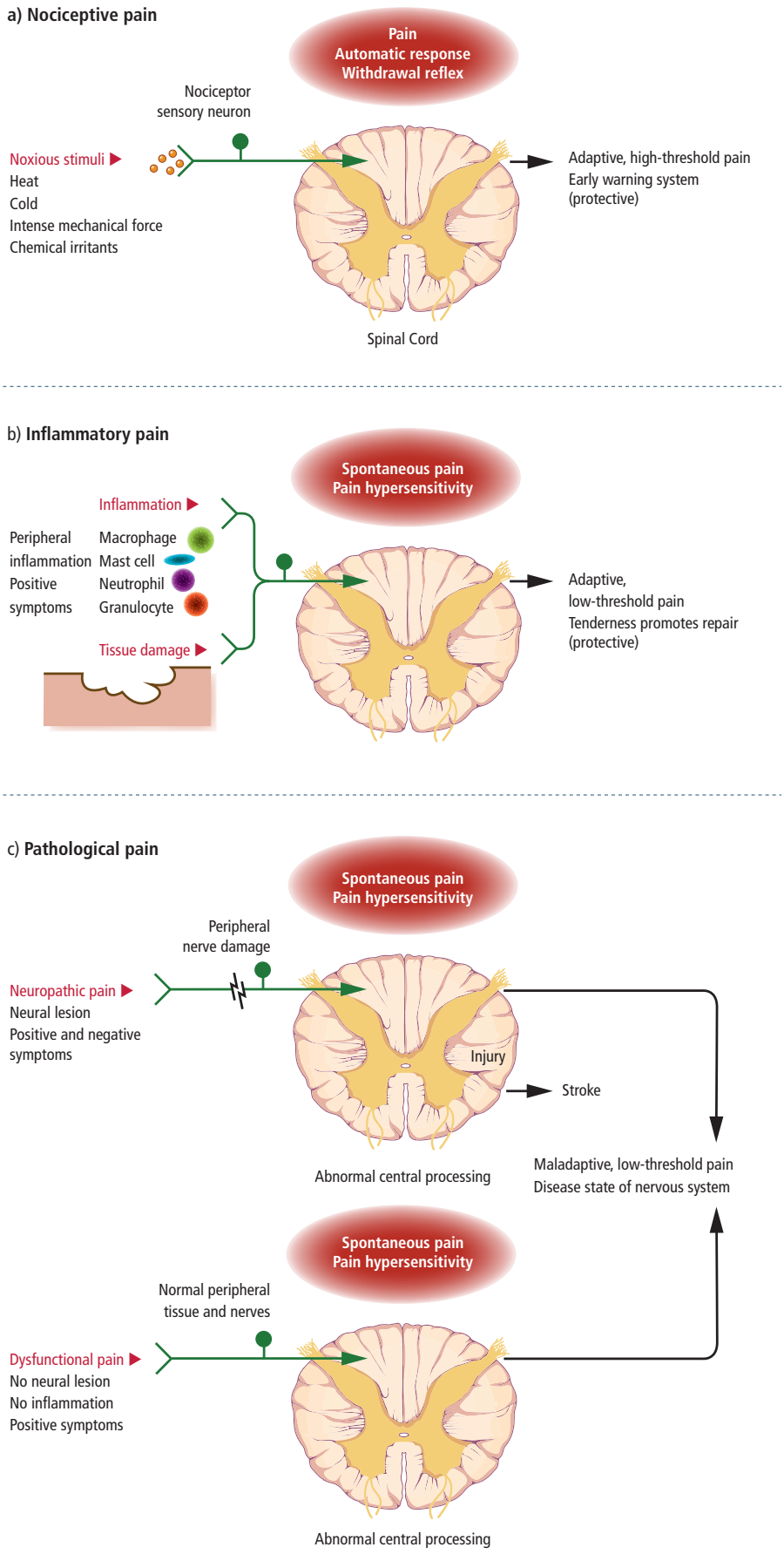

Fig. 2 Pain scenarios

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Table 1 Systemic conditions associated with headache and orofacial pain
• Paget's disease
• Metastatic disease
• Hyperthyroidism
• Multiple myeloma
• Hyperparathyroidism
• Vitamin B deficiencies
• Systemic lupus erythematosus
• Vincristine and other chemotherapy for cancer
• Folic acid and iron deficiency anaemias

Table 2 Red flags – orofacial pain symptoms that may indicate serious or malignant disease[14]
• Spontaneously occurring focal neuropathy with pain and/or altered sensation, confirmed by physical examination, may indicate tumour invasion of nerve
• Pain at the angle of the mandible, brought on by exertion and relieved by rest, may indicate cardiac ischaemia
• Patient aged over 50 years with a known history of carcinoma and localised progressive headache, superficial temporal artery swelling, tenderness and lack of pulse
• Jaw claudication, visual symptoms and palpably tender superficial temporal arteries suggest temporal arteritis
• Systemic symptoms of fever, weight loss, anorexia, malaise, myalgia, chills and sweating are unlikely to be associated with concurrent orofacial pain
• New-onset headache in adult life of increasing severity, with nausea and vomiting but without evidence of migraine or systemic illness; nocturnal occurrence; precipitation or exacerbation through changes in posture; confusion, seizures or weakness; any abnormal neurological sign suggests a mass effect in the cranial cavity (intracranial tumour)
• Earache, trismus and altered sensation in the mandibular branch distribution suggests infratemporal fossa or acoustic nerve impingement, for example by a tumour
• Trigeminal neuralgia in a person <50 years of age may be suggestive of multiple sclerosis

The commonest causes of chronic orofacial pain are the temporomandibular disorders (TMDs), which are principally myofascial in nature.[7]

As the mechanisms underlying these types of pain begin to be identified, more accurate mechanism-based classifications may come to be used. A significant example of this is that burning mouth syndrome almost certainly has a neuropathic cause using the new definitions, rather than being a pain owing to psychological causes.

Impact

The impact of trigeminal pain must not be underestimated. Consequences include the interruption of daily social function such as eating, drinking, speaking, kissing, applying make-up, shaving and sleeping.[8] Burning mouth syndrome has been reported to cause significant psychological impact in 70% of patients,[9] and 29% of patients experiencing temporomandibular joint pain report a high level of disability resulting in unemployment.[10]

Incidence

Chronic orofacial pain is comparable with other pain conditions in the body, and accounts for 20–25% of chronic pain conditions.[9,10] A 6-month prevalence of facial pain has been reported by between 1%[10] and 3%[10] of the population. In a study by Locker and Grushka,[9] some pain or discomfort in the jaws, oral mucosa or face had been experienced by less than 10% of the population in the past 4 weeks.

A US report estimated that 20% of American adults (42 million people) report that pain or physical discomfort disrupts their sleep a few nights a week or more.[11] When asked about four common types of pain, respondents to a National Institutes of Health statistics survey indicated that low-back pain was the most common (27%), followed by severe headache or migraine pain (15%), neck pain (15%) and facial ache or pain (4%).[11] Most population-based studies have shown that women report more facial pain than men,[9,10] with rates approximately twice as high among women compared with men. In clinical populations the rates for women are even higher.[1] By contrast, other studies have found no sex difference in the prevalence of orofacial pain. Several studies have also shown variability in the prevalence across age groups. The age distribution of the facial pain population differs from that of the most usual pain conditions. In contrast to chest and back pain, for example, facial pain has been suggested to be less prevalent in older age.[10]

Diagnosis

The International Headache Society has published diagnostic criteria for primary and secondary headaches as well as facial pain.[12] Criteria have also been published by the IASP.[13]

Systemic disorders that may contribute to or cause chronic orofacial pain must be excluded (Table 1). In addition, signs of serious or neoplastic disease must be recognised and urgently referred as appropriate (Table 2).

Many orofacial pain conditions may mimic toothache (Table 3) and the general dental practitioner must always consider neuropathic pain as a possible cause of 'refractory toothache', so that irreversible and damaging treatment, done with the best intentions, is avoided.

Necessary investigations include haematological and radiographic examinations (Table 4). Routine dental panoramic tomographs are the view of choice to exclude local disease. If the patient presents with neuropathy and/or neuralgia-like symptoms an MRI may be required to exclude space-occupying lesions, demyelination (for multiple sclerosis) and vascular compromise (for trigeminal neuralgia).

The differential diagnosis for chronic trigeminal pain is summarised in Table 5.

Classification

The most common causes of acute dental pain are trauma or infection of the dental pulp that contains the nerves and vessels supplying the tooth. The aim of this article is to outline the causes of chronic orofacial pain: that lasting >3 months. Unfortunately, several conflicting classifications of chronic orofacial pain have been presented. This article uses the mechanistically based classification of Woda *et al.*[6] as it presents a pragmatic and clinically useful

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tool. Essentially, it consists of three groups, the second being subdivided: Groups 1, 2a, 2b and 3 represent neurovascular pain, neuralgias (subdivided into primary neuropathies and secondary neuropathies) and idiopathic facial pain, respectively (Table 5).

Group 1: Neurovascular (predominantly ophthalmic division [V1]) pain

Headaches comprise most of this group of conditions. A National Guideline (SIGN) provides guidance and pathways for diagnosis and management.[14]

Migraine

Migraines are perhaps the most studied of the headache syndromes. This is due in part to the high incidence and significant loss of productivity and limitation of quality of life suffered by those with the syndrome.[8] It is estimated that 17% of women and 6% of men have migraine headaches. Onset is usually in the second or third decade.[8]

The characteristics of migraine include[16]:

- Female-to-male ratio of 3:1
- Five or more lifetime headache attacks lasting 4–72 hours each and symptom-free between attacks
- Moderate to severe pain
- Pain usually unilateral but can be bilateral
- Pain has a throbbing quality and feels as if it is associated with a pulse
- Pain worsens with exertion and improves with sleep
- Photophobia, phonophobia and osmophobia, plus nausea
- Patient may or may not experience aura (a perceptual disturbance prior to any headache starting).

Pharmacological therapy includes abortive and preventative medications, depending on the frequency and severity of the headaches. Abortive agents include serotonin agonists, ergotamine, isometheptene and anti-inflammatories. Preventative agents include antiepileptic drugs, β-blockers, calcium-channel blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors and angiotensin-receptor blocking agents.

Tension-type headaches

Tension-type headache (TTH) is the most common type of headache.[16] It occurs in 69% of men and 88% of women over a lifetime and the annual prevalence is 63% in men and 88% in women. TTH can be further be distinguished as 'episodic' TTH (ETTH) or 'chronic' TTH (CTTH). The distinction is made largely on the frequency of occurrence (<15 days per month for migraine and >15 days per month for TTH).

The characteristics of TTH include:

- Highest socioeconomic impact, affecting 30–78% of the population
- At least 15 days per month on average
- Infrequent episodes lasting from 30 minutes to 7 days
- Typically bilateral.

Table 3 Orofacial disorders that may be confused with toothache

• Trigeminal neuralgia
• Trigeminal neuropathy (due to trauma or tumour invasion of nerves)
• Atypical facial pain and atypical odontalgia (persistent dentoalveolar pain)
• Cluster headache
• Acute and chronic maxillary sinusitis
• Temporomandibular disorders

Table 4 Diagnostic investigations for chronic orofacial pain

• The most frequently employed haematological investigations include:
• Full blood count – predominately looking for anaemias
• Haematinics (ferritin, vitamin B12, folate) – looking for deficiency states causing secondary burning mouth syndrome
• Zinc levels
• Hypothyroidism – can cause headache
• Diabetes (HbA1c)
• Antibody screen – extractable nuclear antigens and anti-nuclear antibodies
• Erythrocyte sedimentation rate or C-reactive protein – if an inflammatory condition is suspected
• Plain dental radiography (dental panoramic tomogram) to identify caries, infection, bone loss etc.
• MRI to exclude space-occupying lesions, demyelination and vascular compromise of the trigeminal nerve

Medication overuse headaches

This is a newly recognised phenomenon that may characterise most patients with headache in the West (30–78%).[13] It is recognised that long-term ingestion of over-the-counter analgesics can result in compromised pain resistance.

Chronic daily headache

Chronic daily headache is described as headache occurring at least 6 days per week for a period of at least 6 months.[16] The pain is usually present throughout the day, with little time spent pain free. It is typically bilateral, frontal or occipital, non-throbbing and moderately severe. The syndrome is associated with the overuse and abuse of many common over-the-counter pain medications (aspirin, paracetamol [acetaminophen], ibuprofen etc.), barbiturates and opioid analgesics. A careful history will reveal an increasing need for medications and the emergence of a chronic headache that is qualitatively distinct from the headache for which it was originally taken. This has led to the idea of chronic daily headache being considered to be a 'transformed migraine'.

Trigeminal autonomic cephalgias

This group of conditions is characterised by autonomic signs (facial redness, facial swelling, nasal congestion, conjunctival irritation, tearing and ptosis all associated with concomitant deep high level pain.

Cluster headache: This is characterised by intensely severe pain (sometimes termed 'suicide headache') with boring or burning qualities, located unilaterally in the orbital, supraorbital or temporal area.[16,17]

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Table 5 Chronic orofacial pain differential diagnosis (cont. on page 831)

	Prevalence/ Male:female ratio/Age group affected	Major location and radiation	Timing	Character/severity	Provoking factors	Associated factors
Neurological conditions						
• Primary neuropathy caused by: - Neoplasia (benign or malignant) - Central or peripheral lesions	• Very rare • 1:1 • >50 years	• Demonstrable neuropathy	• Spontaneous • Constant • Worsening	• Sudden onset may be pain, dysaesthesia, paraesthesia, anaesthesia or a combination	• Mechanical/ thermal allodynia and/or hyperalgesia	• Previous cancer • Older age • Smoking history • Alcoholism • Weight loss • Night sweats
• Secondary neuropathy - Many conditions can cause peripheral sensory neuropathies that may present with pain (see Major location and radiation column)	• 1:1 • >50 years	• Diabetes • Viruses (HIV, herpes) • Chemotherapy • Multiple sclerosis • Parkinson's disease • Malignancy • Drugs, eg growth hormone injections • Nutritional	• After onset of disease or after trauma/infection	• Can be of two types: • Constant, dull, moderate pain • Intermittently elicited neuralgic pain	• Stress, tiredness • If elicited pain with mechanical and/ or cold stimulation allodynia	• Functional difficulties • Psychological impact
• Post-traumatic neuropathy (usually iatrogenic) – 70% have neuropathic pain - Mostly caused by third molar surgery, local anaesthetics, implants and root canal therapy	• Fairly common • 1:1 • >50 years	• Any area related to previous surgery • Demonstrable neuropathy	• Post-surgical intervention or local anaesthetic injection	• Burning and/ or neuralgic (mechanical/ thermal allodynia and hyperalgesia) • Continuous variable intensity paraesthesia, dysaesthesia	• Stimuli by a wide variety of functional related pain (touch, cold air, certain foods, kissing, eating, application of make-up, shaving, toothbrushing)	• History of extraction of impacted teeth, local anaesthetic, implants, endodontics, facial fractures, orthognathic surgery
• Post-herpetic neuralgia	• Rare • >50 years increased prevalence	• Commonly first division of trigeminal (ophthalmic) nerve • Unilateral	• Continuous	• Burning, tearing, itching dysaesthesias • Moderate severity	• Tactile allodynia pain on touch or movement	• More than 6 months after acute herpes zoster • Cutaneous scarring • Exclude immune suppression
• Trigeminal neuralgia - Primary: no known cause - Secondary: associated with vascular compromise, multiple sclerosis (classic refers to clinical features)	• Rare • 2:1 • >50 years	• Intra- or extraoral in trigeminal region • Usually unilateral and V1 or V2	• Each episode of pain lasts for seconds to minutes • Refractory periods and long periods of no pain	• Sharp, shooting, stabbing, electric shock-like pain • Moderate to very severe	• Provoked by light touch (eg eating, washing, talking)	• Discrete trigger zones • Relief of pain at night • Mild flushing may be noted during paroxysms • If patient <50 years, exclude multiple sclerosis • MRI scan to exclude central lesions, demyelination and vascular compromise of fifth cranial nerve
• Symptomatic trigeminal neuralgia	• Rare • >50 years	• Intraoral or extraoral in trigeminal region	• Sharp attacks for seconds to minutes • May have persistent or constant background pain with little remission	• Sharp, shooting, moderate to severe but also dull, burning, continuous mild background pain	• Provoked by light touch but continuous type pain not so clearly provoked	• May have small or no trigger areas; variable pattern • MRI, see above
• Glossopharyngeal neuralgia	• Very rare	• Intraoral, in distribution of glossopharyngeal nerve • May radiate to ear	• Each episode lasts for seconds to 2 minutes	• Sharp, stabbing, severe	• Swallowing or ingestion of cold or acid fluids	• Cardiac arrhythmias or syncope may occur in some cases
• Burning mouth syndrome	• Females • 5–11% >60 years	• Tip and lateral borders of tongue • Other mucosa may also be involved	• Continuous • May fluctuate	• Burning, tender, annoying, tiring, nagging • Varies in intensity	• Dry mouth • Spicy or hot foods	• Altered taste, denture intolerance

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Table 5 Chronic orofacial pain differential diagnosis (cont. from page 830)

	Prevalence/ Male:female ratio/Age group affected	Major location and radiation	Timing	Character/severity	Provoking factors	Associated factors
Neurovascular conditions						
• Giant cell arteritis	• Rare • 4:1 • >50 years	• May be bilateral – mostly over temporal areas • Scalp tenderness	• Continuous, new, sudden onset	• Aching, throbbing, boring, sharp • Moderate/severe	• Chewing	• Jaw claudication, neck pain, anorexia, visual symptoms, age • Systemic symptoms, decreased pulse in temporal artery
• Chronic tension headache	• Common • 1:2 • >30 years	• Usually bilateral over frontal, orbital, fronto-occipital, occipital or whole scalp area	• Continuous • Daily for at least 15 days a month	• Dull, aching head pain, symmetrical and frequently global • Mild ache that becomes more intense and chronic • Fluctuates during the day • Little nausea or vomiting • Pain like tight band, pressing, mild/moderate	• Muscle tension and stress, anxiety, depression	• Present daily
• Migraine with and without aura	• Common • 1:3 • 10-50 years	• Unilateral, with pain beginning in frontotemporal area within 60 minutes of aura	• Continuous, from 2 hours to 1 or 2 days	• Throbbing, pulsating pain in attacks • Moderate/severe	• Stress, anxiety, dietary (cheese, chocolate), flashing lights, weather changes, physical activity	• Aura – visual disturbance • Nausea, vomiting, photophobia are better on lying down • Numbness or weakness in mouth and hands
Trigeminal autonomic cephalgias						
• Cluster headache - Episodic pain-free periods	• Rare • 5:1 • 20–40 years	• Ocular, frontal and temporal areas	• Pain lasts 15–180 minutes to several hours • From one episode every other day to eight times per day	• Hot, searing, punctate, very severe	• Vasodilators, eg alcohol, during the bout, stress, glyceryl trinitrate, exercise • Relieved by drinking water and oxygen inhalation	• Conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, sweating, miosis, ptosis, eyelid oedema • No nausea • Seasonal: spring/ autumn (weeks to months) • Remissions last 6–18 months
• Chronic paroxysmal hemicrania	• Very rare • 1:2 • 30 years	• Ocular, frontal and temporal areas • Unilateral	• Pain lasts 2–30 minutes • 5–10 episodes daily	• Stabbing, throbbing, boring	• Head movements • Responds to indometecin • Neck movements	• Autonomic symptoms as for SUNCT
• Short-lasting, unilateral neuralgiform, conjuntival injection and tearing (SUNCT)	• Very rare • 2:1 40–70 years	• Ocular/periocular but may radiate to frontotemporal area, upper jaw and palate • V1 and V2	• Each episode lasts up to 2 minutes • Intermittent: several attacks a day and then may remit	• Burning, electrical, stabbing, severe	• Cutaneous stimulation causes pain – mechanical allodynia	• Conjunctival injection, lacrimation, nasal stuffiness, rhinorrhoea and facial flushing
• Short-lasting, unilateral neuralgiform headache attacks with autonomic symptoms (SUNA)	• Very rare • 2:1 • 40–70 years	• See above V1 and V2	• See above	• See above	• See above	• Conjunctival injection, lacrimation, nasal stuffiness, rhinorrhoea and facial flushing with scalp sensitivity

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Table 5: Chronic orofacial pain differential diagnosis (cont. from page 831)

	Prevalence/ Male:female ratio/Age group affected	Major location and radiation	Timing	Character/severity	Provoking factors	Associated factors
Idiopathic						
• Chronic idiopathic orofacial pain • There may or may not be a precipitative event	• Fairly common • 1:8 Female • >40 years	• Poorly localised • Presents both intra- and extra-orally • Variants such as atypical odontalgia may be localised to a specific tooth/teeth	• Continuous >2 years • No fluctuation • No response to multiple medications or multiple interventions	• Nagging, aching • Generally non-compliant with specific dermatomes	• Stress, fatigue • Associated pan-chronic pain conditions such as fibromyalgia	• Multiple unilateral and/or bilateral areas affected • Often associated with other idiopathic pain disorders and somatic symptoms, eg chronic widespread pain, irritable bowel syndrome, chronic fatigue • Psychosocial factors: anxiety, depression, adverse life events
• Atypical odontalgia - Persistent dentoalveolar pain	• Rare • 1:2 • >40 years	• Precisely localised in tooth socket	• Continuous >2 years • No fluctuation • No response to multiple medications	• Nagging, aching • No neuropathic zone • Neuralgic or burning	• Stress and tiredness	• Previous surgical or dental event • Multiple interventions may have provided temporary relief for weeks or months, then the pain returns • Increasing belief that this is post-traumatic neuropathic pain

The characteristics of cluster headaches include:

- Male:female ratio of 6:1
- Sudden onset of pain
- Unilateral orbital, supraorbital or temporal
- Severe episodic pain lasting 15 minutes to 3 hours
- Varying frequencies, from eight times daily to every other day for a period of 2–12 weeks.
- Pain characterised as severe, penetrating and burning
- Pain wakens the patient from sleep and does not improve with rest. Many individuals pace around and may injure themselves because of the severity of the pain
- Associated symptoms include ipsilateral conjunctival injection, tearing and nasal congestion.

Treatment to relieve the pain includes oxygen, sumatriptan injections and/or dihydroergotamine. Preventative treatment includes verapamil, lithium, valproate semisodium and topiramate.

Short-lasting unilateral neuralgiform conjunctival irritation and tearing (SUNCT): Is characterised by brief (15–120 seconds) bursts of pain in the eyes, temple or face. The pain is usually unilateral and is described as burning, stabbing or electric. It occurs frequently over a 24-hour period (>100 episodes). Importantly this condition can be confused with trigeminal neuralgia leading to a misdiagnosis and inappropriate treatment of the patient. Alcohol, exercise and neck movements may trigger the pain. SUNCT syndrome is refractory to medical therapy but there is increasing evidence for treatment with lamotrigine.[17]

Temporal arteritis

Temporal arteritis is characterised by daily headaches of moderate to severe intensity, scalp sensitivity, fatigue and various non-specific complaints with a general sense of illness. Ninety-five per cent of patients are over 60 years old.[18] The pain is usually unilateral, although some cases of bilateral or occipital pain do occur. Pain may also be felt in the tongue and is a continuous ache with superimposed sharp, shooting head pains. The pain is similar to and may be confused with that of cluster headache but cluster headache tends to occur in younger patients. The two may also be distinguished on physical examination, when dilated and tortuous scalp arteries are noted. The erythrocyte sedimentation rate (ESR) is markedly elevated in temporal arteritis. A definitive diagnosis is made by artery biopsy from the region of the pain, although a negative biopsy may be caused by the spotty nature of the disease and does rule out the diagnosis.

High-dose steroid therapy usually precipitates a dramatic decrease in head pain. Failure to respond to steroid therapy together with a negative biopsy should call the diagnosis into question. If the diagnosis seems likely based on the history and physical examination, steroids should be started immediately to avoid vision loss, the most common complication of the disorder, occurring in 30% of untreated cases. The biopsy remains positive for 7–10 days from starting steroid therapy. Steroids may be tapered to an every other day maintenance schedule when the pain resolves and the ESR normalises. The disease is usually active for 1–2 years, during which time steroids should be continued to prevent vision loss.[17]

Group 2: Neuralgia (primary and secondary neuropathies)

Group 2 includes primary neuro-pathies (trigeminal neuralgia [classic or symptomatic], glossopharyngeal neuralgia) and secondary neuro-pathies (including post-herpetic neuralgia and post-traumatic trigeminal

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neuralgia). Other peripheral neuro-pathies affecting the trigeminal system, eg nutritional neuropathy, diabetes mellitus, human immunodeficiency virus (HIV), chemotherapy and multiple sclerosis (MS) are not covered in this review but can present as orofacial pain.

Group 2a: Primary neuropathies

Trigeminal neuralgia (classic or symptomatic)

Classic trigeminal neuralgia is characterised by severe bursts of pain in one or more branches of the trigeminal nerve of unknown aetiology. Bursts are quick, repetitive, electric shock-like sensations with paroxysmal pain attacks lasting from a few seconds to less than 2 minutes. The pain is severe and distributed along one or more of the branches of the trigeminal nerve with a sudden, sharp, intense stabbing or burning quality. Between attacks the patient is completely asymptomatic and without gross neurological defects. The pain may be precipitated from trigger areas or with certain daily activities such as eating, talking, washing the face or brushing the teeth. Attacks are the same in an individual patient. If there is no specific trigger zone or the pain lasts longer than 15–20 seconds, then symptomatic trigeminal neuralgia may be diagnosed. Structural causes of facial pain should also be excluded. The syndrome is most common in patients over 50 years. The course may fluctuate over many years, and remissions of months or years are not uncommon.

Aetiology

Although the cause of classic trigeminal neuralgia is unknown, in 60–88% of cases MRI identified vascular compression of the trigeminal ganglion, leading to demyelination and hence 'short-circuiting' of Aβ fibres with Aδ and C fibres, so is considered as a possible cause. In a smaller group of patients, trigeminal neuralgia is 'symptomatic' owing to tumours, arteriovenous malformations or MS. International guidelines on trigeminal neuralgia have been published.[19]

Features

The presence of trigeminal sensory deficits, bilateral involvement and abnormal trigeminal reflexes may indicate the presence of symptomatic trigeminal neuralgia due to tumours, arteriovenous malformations and MS. A younger age of onset, involvement of the first division and unresponsiveness to treatment do not correlate consistently with symptomatic trigeminal neuralgia. Abnormal trigeminal reflexes are associated with an increased risk of symptomatic trigeminal neuralgia and should be considered useful in distinguishing symptomatic trigeminal neuralgia from classic trigeminal neuralgia. Routine head imaging identifies structural causes in up to 15% of patients.[19]

Treatment

The first-line treatments of choice are anticonvulsant medications. Carbamazepine remains the gold-standard drug but there is now evidence that oxcarbazepine is equally effective and has improved tolerability, although full randomised controlled trials (RCT) have not been published. Baclofen and lamotrigine may also be considered useful.[18] More recently, an RCT using Consolidated Standards of Reporting Trials (CONSORT) guidelines reported that gabapentin, together with weekly injections of ropivacaine into the trigger area, yielded a number needed to treat of 2.4 (50% reduction of pain) at 4 weeks.[18]

There are only limited data to help patients decide when and whether to have surgery, but the factors often used are refractoriness to medical therapy and loss of tolerability. Surgery such as microvascular decompression or radiofrequency ganglio-lysis offers good results, although there is associated long-term morbidity of facial paraesthesia, which can be a major complaint among patients. A wide variety of surgical techniques is available. Gasserian ganglion percutaneous surgery, gamma knife (high-dose gamma radiation) and microvascular decompression are all options. Microvascular decompression may be considered over other surgical techniques to provide the longest duration of pain freedom, but it is the most invasive procedure. Although it is less invasive, results from gamma knife therapy show nerve damage, and sensory loss can sometimes develop 6 months after the procedure has been performed. It can be disturbing in 5% of patients and some patients have developed anaesthesia dolorosa.

The role of surgery versus pharmacotherapy in the management of trigeminal neuralgia in patients with MS presenting with symptomatic trigeminal neuralgia remains uncertain. A decision analysis study done with 156 patients with trigeminal neuralgia showed that surgical techniques narrowly offer the highest chance of maximising quality of life. However, surgery is not right for everyone, and patients should be informed about their full range of options. Patients are keen to remain informed about trigeminal neuralgia, as shown by their attendance at conferences and the demand for specific printed patient-orientated information.

Glossopharyngeal neuralgia

Glossopharyngeal neuralgia is characterised by pain attacks similar to those in trigeminal neuralgia, but is located unilaterally in the distribution of the glossopharyngeal nerve. Pain is most common in the posterior pharynx, soft palate, base of the tongue, ear, mastoid or side of the head. Swallowing, yawning, coughing or phonation may trigger the pain. Management is similar to that for trigeminal neuralgia.[4,6,10]

Group 2b: Secondary neuropathies

Many conditions can cause peripheral sensory neuropathies that may present with pain, including[20]:

- Diabetes
- Post-herpetic neuralgia
- HIV
- Chemotherapy
- MS
- Post-surgical traumatic neuropathy
- Parkinson's disease
- Malignancy
- Drugs (eg growth hormone injections)
- Nutritional neuropathy.

The most common causes of trigeminal neuropathy include post-traumatic neuropathy, post-herpetic neuralgia and idiopathic persistent post-surgical pain.

Post-herpetic neuralgia

In patients over 50 years of age there is a 60% incidence of developing post-herpetic pain.[21] Herpetic skin eruption is caused by the reactivation of latent varicella zoster virus from the sensory nerve ganglia. The reactivated virus is carried via the axons distally to the skin, where it produces a painful rash with crusting vesicles in a dermatomal distribution. The trigeminal nerve is the second most commonly affected after nerves in the thoracic region. Ramsay Hunt syndrome occurs when herpes zoster infection of the geniculate ganglion causes earache and facial palsy.

Pain that persists for more than 2 months after the acute eruption is known as post-herpetic neuralgia. The pain is neuropathic in nature, severe and it is associated with allodynia and hyperalgesia, most commonly affecting the ophthalmic (VI) distribution of the trigeminal nerve. High doses of antivirals, steroids and amitriptyline are often used for the acute eruption in otherwise healthy individuals. Antivirals, NSAIDs and opiates are often used in immunocompromised patients. There is evidence that topical 5% lidocaine

patches worn 12 hours on and 12 hours off is effective.[22]

Post-traumatic trigeminal neuropathy

The most problematic outcome of dental surgical procedures, with major medico-legal implications, is injury to the trigeminal nerve.[23] The prevalence of temporarily impaired lingual and inferior alveolar nerve function is thought to range between 0.15 and 0.54%, per wisdom tooth extraction whereas permanent injury caused by injection of local analgesics is much less frequent at 0.0001–0.01%per injection.[23] Traumatic injuries to the lingual and inferior alveolar nerves may induce a pain syndrome due to the development of a neuroma. The most commonly injured trigeminal nerve branches, the inferior alveolar and lingual nerves, are different entities: the lingual nerve sits loosely in soft tissue and has a different intracranial origin/route, whereas the inferior alveolar nerve resides in a bony canal. Injury to the third division of the trigeminal nerve may occur due to a variety of different treatment modalities, such as major maxillofacial and minor oral surgery.[23] Peripheral sensory nerve injuries are more likely to be persistent when the injury is severe; the patient is older; the time elapsed between the cause of the injury and the review of the patient is of longer duration; and when the injury is more proximal to the cell body.

Subsequent to iatrogenic trigeminal nerve injury, patients often complain about a reduced quality of life, psychological discomfort, social disabilities and handicap.[24] Patients often find it hard to cope with such negative outcomes of dental surgery since they usually expect significant improvements, not only regarding jaw function but also in relation to dental, facial and even overall body image after oral rehabilitation. Altered sensation and pain in the orofacial region may interfere with speaking, eating, kissing, shaving, applying make-up, toothbrushing and drinking; in fact just about every social interaction we take for granted as discussed in Chapter 8 in Book 1. In a prospective assessment of 252 patients with iatrogenic trigeminal nerve injuries,[24] most were caused by third molar surgery but implants and administration of local anaesthesia were also significant contributors.

The diagnosis of post-traumatic neuralgia/neuropathy is based upon a history of surgery or trauma temporally correlated with the development of the characteristic neuropathic pain. Age, poor wound closure, infections, foreign material in the wound, haematoma, skull fracture, diabetes mellitus or peripheral neuropathy elsewhere in the body can all predispose to neuroma development. The pain commonly persists for months after the injury and can be permanent. Medical therapy is similar to that used in neuropathic pain conditions, depending on the patients' symptoms. Pain was the presenting factor in 70% of patients.[24] This highlights the problems related to post-surgical neuropathy, aggravated by the fact that many patients may not have been warned at all about nerve injury or told that they would risk only numbness.

Traumatic injuries to peripheral nerves pose complex challenges, and treatment of nerve injuries must consider all aspects of the inherent disability. Pain control is of paramount importance and rehabilitation needs to be instituted as first-line treatment. Early intervention is important for optimal physiological and functional recovery.[24] Reparative surgery may be indicated when the patient complains of persistent problems related to the nerve injury; however, there remains a significant deficiency in the evidence base to support this practice. The patient's presenting complaints may include functional problems due to the reduced sensation, intolerable changed sensation or pain, the latter being predominantly intransigent to surgery.[24] Less-often highlighted are the psychological problems relating to the iatrogenesis of the injury and chronic pain. Generally, for lesions of the peripheral sensory nerves, the gold standard is to repair the nerve as soon as possible after injury. However, the relatively few series on trigeminal nerve repair in human subjects relate mainly to repairs undertaken more than 6 months after injury.[24]

It is evident from the literature review that there needs to be a cultural change in the choice of intervention, timing and outcome criteria that should be evaluated for interventions for trigeminal nerve injuries. To date, there have been a very limited number of prospective randomised studies to evaluate the effect of treatment delay and the surgical, medical or counselling outcomes for trigeminal nerve injuries.

Persistent post-surgical neuropathic pain related to surgical trauma but without demonstrable neuropathy

This is defined as present at 1 year or more post-operatively when the pain is unexplained by local factors, and is best described as neuropathic in nature.

Non-odontogenic dentoalveolar pain is often difficult to diagnose because it is poorly understood.[25] Even defining and categorising such persistent pain is challenging. Non-odontogenic pain is not an uncommon outcome after root canal therapy and may represent half of all cases of persistent tooth pain. A systematic review of prospective studies reported the frequency of non-odontogenic pain in patients who had undergone endodontic procedures.[25] Non-odontogenic pain was defined as dentoalveolar pain present for 6 months or more after endodontic treatment without evidence of dental pathology. The endodontic procedures reviewed were non-surgical root canal treatment, retreatment and surgical root canal treatment. A total of 770 articles were retrieved and reviewed; only 10 met the inclusion criteria and a total of 3,343 teeth were enrolled within the included studies, of which 1,125 had follow-up information regarding pain status. Non-odontogenic pain was identified at a frequency of 3.4% in these, with a 95% confidence interval of 1.4–5.5%.[25]

The prevalence of persistent post-surgical pain in the trigeminal system may appear to be low compared with other surgical sites. However, when one considers the significant frequency of dental surgical procedures undertaken, significant numbers of individuals may be affected by both post-traumatic neuropathy and persistent post-surgical pain.

Risk factors for developing persistent post-surgical pain include[24]:

- Genetics
- Preceding pain (intensity and chronicity)
- Psychosocial factors (eg fear, memories, work, social and environmental factors, levels of physical activity, somatisation)
- Age (older = increased risk)
- Gender (female = increased risk)
- Surgical procedure and technique (tension due to retraction).[24]

Persistent post-surgical pain conditions may be attributable to the patient's preoperative susceptibility to neuropathic pain or to a pre-existing neuropathic pain condition which was inappropriately surgically treated (surgery does not treat neuropathic pain). The significantly decreased incidence of this condition in the trigeminal region may reflect the lack of central sensitisation owing to most procedures being undertaken under local anaesthetic.

Group 3: Idiopathic chronic orofacial pain

This group includes pre-auricular pain related to temporomandibular joint disorders, burning mouth syndrome and persistent idiopathic facial pain.

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Stomatodynia (burning mouth syndrome)

Burning mouth syndrome is defined as an intraoral burning sensation or other dysaesthesia for which no medical or dental cause can be found and in which the oral mucosa is of grossly normal appearance.[25] Many patients will also have subjective dryness, paraesthesia and altered taste, which initiates spontaneously and is not related to any prior intervention. The psychological morbidity is high and patients often display high HADS (hospital anxiety and depression scale) scores.[9] This is understandable when considering that these patients experience high levels of constant discomfort of unknown aetiology, severely affecting their quality of life.[26]

The aetiology of burning mouth syndrome remains controversial. Suggested causes include psychogenic factors, hormone disorders, neuropathic alterations, oral phantom pain, neuroplasticity and neuroinflammation. However, there is increasing evidence to show that it is primarily a neuropathic pain with secondary psychological features.

Diagnosis of burning mouth syndrome is by exclusion,[26] and suggested screening includes saliva tests, psychometric testing, histological tests, candidal counts and, most importantly, blood tests. These may be used to establish the possible systemic and local causes for the patient's symptoms. Routine blood tests may include or exclude:

- Nutritional neuropathy: deficiencies may occur due to dietary deficiency, malabsorption or haemorrhage (possible factors include iron, ferritin, vitamins B1, B2, B3, B6, B12 and E, folate, zinc, calcium and phosphate)
- Blood dyscrasias (full blood cell count, haematinics (Fe, B12 and folate levels), erthrocyte sedimentation rate or C-reactive protein level)
- Chronic liver disease/alcoholic liver disease (liver function tests – total protein, albumin, bilirubin, alkaline phosphatase, cholesterol)
- Kidney disease (kidney function tests – urea, creatinine)
- Endocrine disease (diabetes [random blood glucose], cortisol, oestrogen, thyroid function)
- Connective tissue disease (anti-nuclear antibodies, extra-nuclear antibodies)
- Gastrointestinal disease, gastric reflux (*Helicobacter*)
- Others including inflammatory factors (IL-6, IL-2, substance P, NKA, CGRP), allergy immunoglobulin E, Parkinson's disease and gluten-sensitivity neuropathy (coeliac disease).

Management remains difficult owing to the lack of understanding about the basic underlying biological mechanisms, as well as the absence of high-quality randomised controlled clinical trials. To date the only evidence-based intervention is cognitive behavioural therapy, but empirical evidence suggests that topical clonazepam, tricyclic antidepressants, pregabalin or gabapentin may be moderately effective for these patients.[26]

Persistent idiopathic facial pain

The term atypical facial pain was first introduced in 1924 and is now known as persistent idiopathic facial pain (PIFP).[27] PIFP refers to pain along the territory of the trigeminal nerve that does not fit the classic presentation of other cranial neuralgias.[13] The duration of pain is usually long, lasting most of the day (if not continuously). The pain is unilateral and without autonomic signs or symptoms. It is described as a severe ache, crushing or burning sensation. Upon examination and investigation, no relevant abnormality is noted.

Definition

According to the IASP,[13] chronic PIFP refers to symptoms that have been present for at least 6 months. 'Atypical' pain is a diagnosis of exclusion after other conditions have been considered and eliminated (i.e. it is idiopathic), and is characterised by chronic, constant pain in the absence of any apparent cause in the face or brain. Many information sources suggest that all 'unexplained' facial pains are termed atypical facial pain but this is not the case. Categories of idiopathic facial pain conditions include neuropathic pain due to sensory nerve damage, chronic regional pain syndrome from sympathetic nerve damage and atypical facial pain.

Epidemiology

Atypical facial pain is more common in women than in men; most patients attending a facial pain clinic are women aged between 30 and 50 years. Although any area of the face can be involved, the most commonly affected area is the maxillary region. In the majority of patients there is no disease or other cause found. In a few patients the symptoms represent serious disease. In a small number of patients the pain may be one consequence of significant psychological or psychiatric disease.

Clinical presentation

Atypical facial pain has a very variable presentation. Often it is characterised by continuous daily pain of variable intensity. Typically, the pain is deep and poorly localised, is described as dull and aching, and does not awaken the patient from sleep. At onset the pain may be confined to a limited area on one side of the face, while later it may spread to involve a larger area. The pain is not triggered and is not electrical in quality. Intensity fluctuates but the patient is rarely pain free. Pain is typically located in the face and seldom spreads to the cranium in contradistinction to tension headache. It is more common in women aged 30–50 years. Between 60 and 70% of these patients have significant psychiatric findings, usually depression, somatisation or adjustment disorders, and psychiatric evaluation is therefore indicated.

Accurate figures are difficult to obtain because of the lack of agreement on classification criteria. The estimated incidence is 1 case per 100,000 population, although this number may be underestimated. The disorder mainly affects adults and is rare in children. PIFP is essentially a diagnosis of exclusion. Daily or near-daily headaches are a widespread problem in clinical practice. According to population-based data from the United States, Europe, and Asia, chronic daily headache affects a large number (approximately 4–5% of the population) of patients. Importantly, PIFP must be distinguished from various other chronic daily headache and orofacial pain syndromes.

A careful history and physical examination, including a dental consultation, laboratory studies and imaging studies, may be necessary to rule out occult pathology. Underlying pathology such as malignancy, vasculitis, infection and central or peripheral demyelination may manifest early as neuralgia, and not until focal neurological deficits, imaging abnormalities or laboratory abnormalities are discovered does the diagnosis become evident. Rarely, cases of referred pain must also be considered. Treatment usually involves psychological and or medical interventions including antidepressants, beginning with low-dose amitriptyline (or nortriptyline) at bedtime and increasing the dose until pain and sleep are improved.

Medical care

Medical treatment of PIFP is usually less satisfactory than medical treatment for other facial pain syndromes. Medications used to treat PIFP include antidepressants, anticonvulsants, substance P depletion agents, topical anaesthetics, *N*-methyl-D-aspartate (NMDA) antagonists and opiate medications. Of these, anticonvulsants

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and antidepressants appear to be the most effective, with the neuropathic component of pain responding well. Pharmacotherapeutic knowledge is paramount in the treatment of this refractory pain syndrome. A multi-mechanistic approach, using modulation of both ascending and descending pain pathways, is frequently necessary. The goal of therapy is to manage the pain effectively with the fewest adverse medication effects. Alternative therapies such as acupuncture and neuromuscular re-education have been tried and should be considered as part of a comprehensive treatment plan. Psychiatric treatment is important in the overall management of a patient with chronic pain. Available data on alternative treatments are limited.

Surgical care

Details of neurosurgical interventions are beyond the scope of this book. Analgesic surgery including implanted neurostimulators or deep brain stimulation should be considered at a centre well versed in these procedures.

Consultations

Psychometric testing may be of benefit in the evaluation and treatment of patients with headache and facial pain. Many tests have been applied, but probably the most widely used is the Minnesota Multiple Personality Inventory. While especially useful in the evaluation of patients with chronic headache and facial pain, a thorough discussion of psychometric testing is beyond the scope of this book and is mentioned here only for completeness. Consultation with a dentist may be of benefit. All treatments should be provided in cooperation with the patient's primary care physician.

Atypical odontalgia

Atypical odontalgia (AO) is characterised by continuous dull, aching or burning pain of moderate intensity in apparently normal teeth or endodontically treated teeth, and occasionally in extraction sites. AO is not usually affected by testing the tooth and surrounding tissues with cold, heat or electrical stimuli. The pain remains constant despite repeated dental treatment, even extractions in the region, often rendering patients with whole quadrants stripped of dentition. Moreover, the toothache characteristics frequently remain unchanged for months or years, contributing to the differentiation of AO from pulpal dental pain. Occasionally, the pain may spread to adjacent teeth, especially after extraction of the painful tooth.

These patients are defined as having pain in a tooth or tooth region in which no clinical or radiological findings can be detected. Several studies have been conducted to define this group more clearly. Patients with AO have more comorbid pain conditions, higher scores for depression and somatisation, significant limitation in jaw function, and lower scores on quality of life measures when compared with controls. When compared with patients who have TMD, patients with AO are more likely to describe their pain as aching, find rest relieving but cold and heat aggravating. Over 80% relate the onset of their pain to dental treatment. The author believes that the relationship with previous surgical intervention implies that this condition may, in some cases, be partial post-surgical neuropathy.

The lack of RCTs makes evidenced-based care in AO difficult. One of the major problems with this condition is convincing the patient, and informing their dentist, that there are no dental causes for their pain, so avoiding unnecessary irreversible invasive dental treatment. Patients with AO are often diagnosed late and therefore need a multidisciplinary approach. In her review,[28] Baad-Hansen presents a sensible progressive approach to managing AO, beginning with topical lidocaine or capsaicin, then tricyclic antidepressants. Ultimately, the drugs used in neuropathic pain are often gabapentin and pregabalin, and finally tramadol or oxycodone.

Conclusion

Chronic orofacial pain continues to present a diagnostic challenge for many practitioners. Patients are frequently misdiagnosed and can suffer from psychiatric symptoms of depression and anxiety. Treatment is less effective than in other pain syndromes and a multidisciplinary approach treatment is desirable.

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