

Facial pain: clinical differential diagnosis

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Differential diagnosis of pain in the face as the presenting complaint can be difficult. We propose an approach based on history and neurological examination, which allows a working diagnosis to be made at the bedside, including aetiological hypotheses, leading to a choice of investigations. Neuralgias are characterised by stabs of short lasting, lancinating pain, and, although neuralgias are often primary, imaging may be needed to exclude symptomatic forms. Facial pain with cranial nerve symptoms and signs is almost exclusively of secondary origin and requires urgent examination. Facial pain with focal autonomic signs is mostly primary and belongs to the group of the idiopathic trigeminal autonomic cephalalgias, but can occasionally be secondary. Pure facial pain is most often due to sinusitis and the chewing apparatus, but also a multitude of other causes. The pain can also be idiopathic. Imaging as well as non-neurological specialist assessment is often necessary in these cases.

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Introduction

Facial pain can be the presenting, and sometimes the only, complaint of many disorders that originate from cranial structures. In the clinical setting, the identification of the underlying cause, and therefore the decision about the investigations needed, occasionally represents a challenge, even for experienced physicians. The classic approach is a topographical one, focusing on the structures from which pain arises.^{1,2} However, in practice, the physician is expected to recognise clinical syndromes. Here we review the different disorders that lead to facial pain and suggest a clinical approach for the differential diagnosis at the bedside. Localisation, time pattern, quality, intensity, precipitating and alleviating factors, and associated symptoms and signs are helpful features in the diagnostic process (panel 1). Our proposed classification is summarised in panel 2.

Neuralgias

The presence of sudden, intense, sharp, aching, lancinating, burning, and stabbing pain lasting from only a few seconds to less than 2 min and recurring repeatedly within short periods of time, which is often triggered by sensory or mechanical stimuli, strongly

suggests a neuralgia. This pattern is characteristic for most neuralgias occurring in the face.

Trigeminal neuralgia

Trigeminal neuralgia is by far the most frequent facial neuralgia, with a reported prevalence of 3–6 per 100 000.^{3,4} Importantly, incidence increases with age. About 70% of patients are older than 60 years at onset.^{4,5} The clinical hallmark of trigeminal neuralgia is a paroxysm of pain, which is very intensive and occurs almost exclusively unilaterally in a trigeminal distribution. The pain is typically located in the second or third and, in only about 5% of patients,^{5,6} in the first division. A localisation in both the second and third division occurs in about a third of patients. In about 3% of cases, pain is bilateral,^{4,5} which suggests a secondary origin.

Trigeminal neuralgia can occur spontaneously or can be precipitated by sensory stimulation of certain areas in the face (cheek, chin, lip, tongue), usually coinciding with pain localisation. Touching or washing the face, shaving, brushing the teeth, and chewing are considered typical triggers, and patients tend to avoid them. Stereotypic pain attacks usually occur many times per day for weeks or months and then suddenly stop, with subsequent pain-free periods lasting months or years. During the course of disease, pain attacks tend to become more frequent over the years, and the remission periods shorter. Rarely, attacks become longer lasting and sometimes a dull background pain becomes permanent, leading to diagnostic difficulties. A disorder called pretrigeminal neuralgia with atypical, longer lasting (several hours) facial pain triggered by jaw

Panel 1: Helpful clinical features in patients with facial pain

Localisation

Time pattern

Onset (sudden, gradual)
Circadian distribution (day, night, random)
Course and progression (constant, paroxysmal-recurrent, slowly/rapidly progressive)

Duration

Quality

Intensity

Precipitating and alleviating factors

Associated symptoms and signs

Panel 2: Proposed clinical classification of facial pain syndromes

Neuralgias

Facial pain syndromes with cranial nerve symptoms and signs
Trigeminal autonomic cephalalgias (episodic facial pain syndromes with focal autonomic signs)
Pure facial pain

movements or by drinking has been reported.^{7,8} The disorder was followed, after a latency of days to years, by a typical neuralgia. Neurological examination is usually normal; however, a slight sensory impairment in the pain region can be identified in 15–25% of patients.^{9–11} In idiopathic forms, the typical clinical pattern is associated with a normal neurological and MRI examination and no cause is detectable. The most common identifiable cause is a compression of the trigeminal nerve root by an aberrant loop of a blood vessel, usually within a few millimetres of the entry into the pons, which accounts for about 60–90% of cases described in neurosurgical and neuroradiological series.^{12–15}

MRI is a valid method to investigate such a cause, although its sensitivity (50–95%) and specificity (65–100%) seems variable,^{16–23} and both false positive (7–15%)^{24,25} and false negative (10%)²³ results are possible. Therefore, the relation between neuro-radiological findings and the clinical picture cannot be established in each patient.

In up to 15% of patients with trigeminal neuralgia an underlying cause can be identified. Multiple sclerosis should be considered as a possible cause of the disorder, especially in young patients and when pain is bilateral, with a prevalence of about 2%.²⁶ Rarely, other structural lesions, mainly localised in the pontine region, can lead to trigeminal neuralgia. These include vestibular or, rarely, trigeminal schwannoma,²⁷ meningiomas,²⁸ epidermoid or other cysts,²⁹ and other compressive disorders.^{30,31} Vascular brainstem lesions, especially pontine infarctions,³² angiomas, or arteriovenous malformations,³³ are further causes of symptomatic trigeminal neuralgia. In these patients, the disorder is often associated with other motor or sensory deficits (already at the beginning or in the course of the disease). Therefore, classic trigeminal neuralgia is quite rare in this group.³⁴

Glossopharyngeal neuralgia

This rare disorder is characterised by paroxysmal neuralgiform pain attacks localised in the throat near the base of the tongue, soft palate, and tonsillar fossa, and can radiate to the angle of the lower jaw and rarely even into the external auditory canal or the neck.³⁵ The pain is often triggered by swallowing, chewing, talking, yawning, laughing, or coughing. Bradycardia, rarely leading to hypotension and even syncope or asystole, can accompany pain attacks.^{36,37} Most cases are regarded as idiopathic.^{35,38} Symptomatic forms³⁹ are often associated with persisting aching pain between the paroxysms and with sensory impairment of the distribution of the glossopharyngeal nerve.

Nervus intermedius (geniculate) neuralgia

This very rare disorder is characterised by paroxysmal pain attacks localised in the auditory canal, external ear, and soft palate, which can radiate to the temporal region

or the jaw angle. Pain attacks can be accompanied by lacrimation, gustatory sensations, and salivation.^{40–42} Herpes zoster infection might be an underlying cause and can also lead to facial palsy, hearing symptoms, or vertigo.

Charlin's neuralgia and Sluder's neuralgia

The pain of these very rare disorders can manifest in association with similar symptoms and signs, and is typically localised in the medial angle of the eye. The pain mainly radiates to the eyebrow and into the orbit or into the nose or jaw. Lacrimation, conjunctival injection, nasal congestion, sneezing, and redness of the skin in the forehead are typical accompanying symptoms.^{43,44} The differential diagnosis to cluster headache, which is a distinct entity, may therefore be difficult.

Supraorbital neuralgia

This very rare disorder is characterised by paroxysmal pain in the supraorbital notch and on the forehead near the midline. Tenderness of the nerve in the supraorbital notch is a common finding.^{45,46}

Facial pain syndromes with cranial nerve symptoms and signs

In this group of syndromes, pain in the face is often the presenting complaint and is accompanied by symptoms and signs caused by a lesion of one or several cranial nerves. They will be discussed systematically according to the cranial nerves affected. The largest group of disorders consists of pain syndromes located in and around the eye that affect the optic nerve or the ocular motor system. The remaining syndromes will be divided into facial pain presenting together with disturbed facial sensation, facial palsy, hypoacusis, and disturbed balance, and with dysphagia, dysphonia, or dysarthria.

Disturbed vision, eye movements, or pupillomotor function

Pain in and around the eye associated with disturbed vision can be a presenting complaint for several ocular disorders. Refractive anomalies and phorias can present as subacute or chronic, featureless, and usually mild to moderate pain, and can be confused with tension headache. Acute glaucoma⁴⁷ or inflammation in the eye, such as keratitis, iridocyclitis, scleritis,⁴⁸ or uveitis are often accompanied by severe, unilateral pain in or around the eye, and are associated with redness of the eye and pupillary abnormalities.^{49,50} The differential diagnosis to trigeminal autonomic cephalalgias or to migraine can sometimes be difficult.

A common neurological disorder, usually presenting with diminished visual acuity and pain, is optic neuritis. It is most often caused by multiple sclerosis, or by other inflammatory or infectious diseases—eg, sarcoidosis or HIV.^{51–53} Colour desaturation of a red pin in the centre of the visual fields is a typical and useful clinical sign. MRI is usually diagnostic, showing T2-signal hyperintensity

Case 1: Temporal arteritis with double vision

An 84-year-old patient lost about 8 kg over 6 months while feeling unwell and complaining about tender neck and shoulders. He had a moderately raised ESR, but a tumour screen was negative and he was subsequently treated with non-steroidal anti-inflammatory drugs. He developed bitemporal swelling and tenderness as well as jaw pain during chewing, and, intermittently, double vision. His ESR was now 80 mm/h and CRP more than 100 mg/dL. A Duplex examination of his temporal arteries showed a characteristic halo on both sides, and treatment was initiated immediately, 2 days before the biopsy. The diagnosis of temporal arteritis was confirmed histologically (figure 1). On methylprednisolone treatment 100 mg per day he became asymptomatic within 2 weeks, apart from minor residual jaw claudication, and ESR and CRP had become normal. Ophthalmological complications, mostly optic neuropathy, occur in about 20% of patients; ocular motor involvement, mostly presenting as double vision, is rare (about 4%).

in the affected, often oedematous, nerve with increased gadolinium uptake in the acute phase.

Temporal arteritis (case 1) typically presents with new onset frontotemporal, and less frequently orbitofrontal (facial), pain in elderly patients. Furthermore, sensations of pain and weakness localised in the jaw and triggered by prolonged chewing (jaw claudication) are typical symptoms of this vasculitis.⁵⁴ Raised erythrocyte sedimentation rate (ESR) and C-reactive protein concentrations (CRP) are almost mandatory laboratory findings. Panel 3 summarises diagnostic criteria.⁵⁵ Rapid diagnosis is crucial to prevent ischaemic sequelae. Ophthalmological complications due to anterior ischaemic optic neuropathy or ocular motor nerve involvement occur in about a fifth of patients (amaurosis fugax 10%, permanent visual impairment 8%, diplopia 4%). A rare, but severe consequence is stroke secondary to arteritis, which happens in 3–7% of patients.^{56,57} Treatment consists of high-dose steroids and is quickly effective. Its initiation must not be delayed for diagnostic reasons because the results of a biopsy are not significantly affected within the first weeks.⁵⁸

Pain localised in the eye, orbit, or forehead associated with ipsilateral ocular motor nerve palsies is the clinical hallmark of the syndrome painful ophthalmoplegia, a group of disorders with various causes. In this situation imaging is mandatory. Various pathologies localised in the orbit, the tip of the orbit or cavernous sinus, or the subarachnoid space (panel 4) can lead to this syndrome. Most commonly, painful disorders of the orbit are inflammatory in origin (45%), followed by vascular (24%) and neoplastic (20%). Infection (2%) and myopathy (1%) are rare.⁵⁹

Ocular myositis (case 2) is a rare unspecific inflammation, which commonly affects eye muscles of

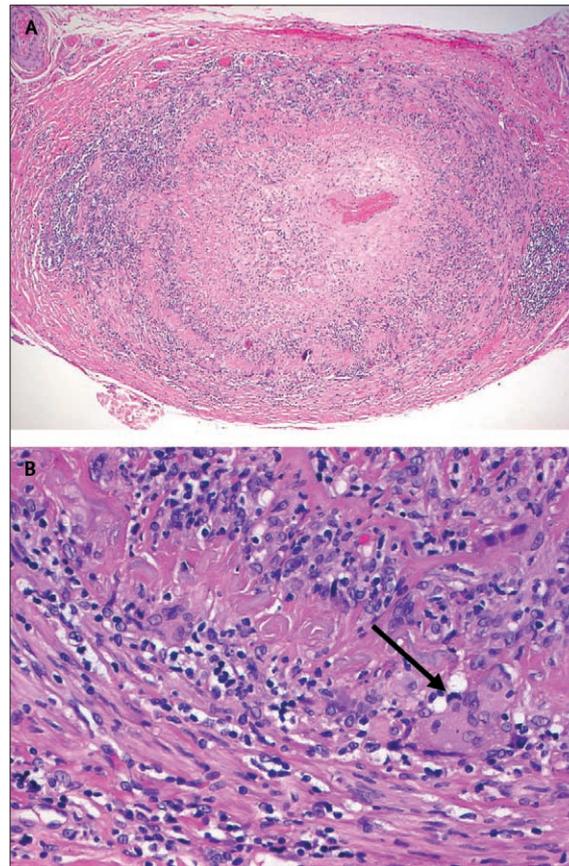


Figure 1: Cross section of the left temporal artery showing narrowing of the lumen and inflammatory changes (A) and lymphocytic infiltration and a giant cell (arrow) in the magnified section (B)

either side (mostly medial rectus). The disorder is characterised by acute or subacute pain in or around the eye with diplopia, ptosis, and ocular signs of inflammation.^{60,61} MRI shows enlargement and enhancement of the affected muscle and their insertions. Importantly, this disorder is steroid responsive.

Another unspecific (granulomatous) inflammation is the so-called idiopathic inflammatory pseudotumour of the orbit. Several presentations are possible and depend on the structure concerned (uvea, sclera, eye muscles,

Panel 3: Diagnostic criteria of temporal arteritis

- Age at onset of the disease ≥ 50 years
- New headaches
- Abnormalities of the temporal artery at clinical examination
- Raised ESR (≥ 50 mm/h)*
- Abnormal findings on biopsy of temporal artery

Three or more criteria: diagnosis of temporal arteritis with 91.2% specificity and 93.5% sensitivity. *Raised concentration of C-reactive protein (> 5 mg/L) is another, currently used, clinically useful laboratory parameter (not in these criteria).

Panel 4: Causes of painful ophthalmoplegia**Inflammatory***Unspecific*

Ocular myositis, Idiopathic inflammatory pseudotumour of the orbit, Tolosa-Hunt syndrome

Specific

Sarcoidosis, Wegener's granulomatosis, systemic lupoid erythematosus, rheumatoid arthritis

Infectious*Fungal*

Mucormycosis, aspergillosis ("fungus ball")

Bacterial

Pyogenic bacteria (eg, complication of sinusitis), syphilis, tuberculosis

Viral

Herpes zoster, HIV

Parasital

Cysticercosis

Vascular

Aneurysms of internal carotid, posterior communicating, posterior cerebral artery

Arteriovenous malformations (orbit, cavernous sinus)

Fistula (orbit, cavernous sinus)

Carotid-cavernous thrombosis

Pituitary apoplexy

Ischaemia (oculomotor nerve, brainstem)

Neoplastic*Primary tumours*

Meningioma, pituitary adenoma/adenocarcinoma, craniopharyngioma, neurofibroma, sarcoma, chordoma, chondroma

Metastases

Melanoma, lymphoma, myeloma, breast tumours, nasopharyngeal tumours

Traumatic

Skull base fractures with lesion of the ocular motor nerves

lacrimal glands, optic nerve, ocular motor nerves). Acute or subacute orbital and periorbital pain, exophthalmus, and ocular motor palsies are the most common characteristics.⁶² Again this disorder is steroid responsive.⁶³ Specific inflammation of the orbit and eye muscles includes systemic lupus erythematosus, rheumatoid arthritis, dermatomyositis, Wegener's

Case 2: Ocular myositis

A 73-year-old lady presented to the neurologist in the emergency room because of left-sided periorbital pain, which worsened over a few days. She complained about painful eye movements and double vision. She noticed that the left eyelid was swollen. Physical examination revealed in the left eye conjunctival infection, some degree of exophthalmus, and a diminished range of eye movements for abduction and elevation of the left eye. ESR was 38 mm/h, while CRP, routine blood count, and vasculitis screen were normal. Brain MRI showed swelling and gadolinium enhancement of the left lateral rectus muscle (figure 2). The diagnosis of an ocular myositis was made. On steroids, she became asymptomatic within 2 weeks. MRI control examination after a few months showed normal findings.

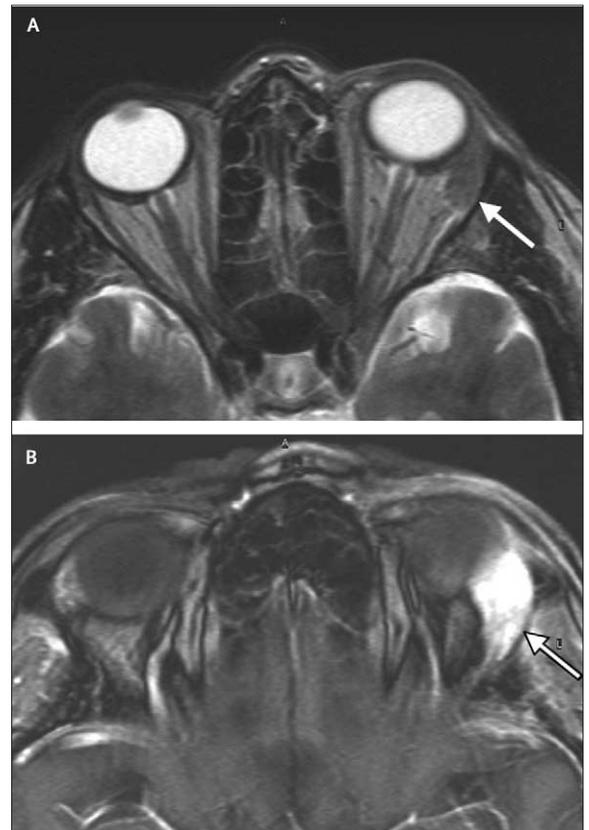


Figure 2: T2-weighted MRI image showing a focal enlargement of the left lateral rectus muscle (A; arrow) and T1-weighted MRI image with gadolinium showing a focal enhancement of the left lateral rectus muscle (B; arrow)

granulomatosis, and sarcoidosis. In these disorders, facial pain associated with ocular motor palsies tends to be part of the syndrome rather than the presenting complaint.

Infections of the orbit can be caused by fungi (eg, mucormycosis, aspergillosis, the so-called "fungus ball"), pyogenic bacteria (eg, secondary effects on the orbit by sinusitis), parasites (ie, cysticercus), herpes zoster, HIV, syphilis, or tuberculosis,⁵⁹ and primarily occur in immunocompromised individuals. Vascular lesions of the orbit typically consist of arteriovenous malformations or arteriovenous fistulae, leading to conjunctival infection, eyelid oedema, pulsating exophthalmus, and chemosis. Neoplastic lesions can present with diplopia, diminished visual acuity, exophthalmus, and pain. They are most often caused by metastases, but also by tumours in structures next to the orbit, or rarely by primary tumours such as sarcomas. Endocrine orbitopathy, which is more frequent than the above-mentioned disorders, is usually not painful.

Pathologies localised at the tip of the orbit or cavernous sinus can also lead to painful ophthalmoplegia. The Tolosa-Hunt syndrome^{64,65} is a

rare unspecific granulomatous inflammation of the cavernous sinus or the superior orbital fissure. Pain in and around the eye together with visual, pupillary, and ocular motor abnormalities are typically accompanied by sensory impairment in the first or second trigeminal division.⁶⁶ MRI shows diffuse signal abnormalities with enlargement and enhancement of the cavernous sinus.⁶⁷ Importantly, this disorder readily responds to steroids.⁶⁸

The so-called ophthalmoplegic migraine is a very rare disorder that includes migraine-type headache of long duration and ocular motor palsy. It is now regarded as a recurrent demyelinating neuropathy rather than a form of migraine.⁶⁹⁻⁷¹ Specific inflammatory conditions, such as sarcoidosis, or infections of the cavernous sinus or superior orbital fissure, can lead to similar symptoms and signs as described above, and should be considered in the differential diagnosis.

Vascular causes of facial pain include aneurysms of the internal carotid, posterior communicating, or posterior cerebral artery, and result in impaired function of upper cranial nerves (mostly II, III, IV, V, VI). Arteriovenous malformations between the carotid artery and the cavernous sinus or fistulas are also possible causes, with a pulsating exophthalmus as a hallmark.

Pituitary apoplexy is a very rare, but severe and potentially life-threatening disorder. Fever, reduced level of consciousness, and endocrine characteristics are associated with headache or facial (mainly retro-orbital) pain. Further features include cranial nerve symptoms and signs (deterioration in vision or visual field defects, unilateral or bilateral ocular motor nerve palsies, sensory disturbances in the face) as well as nausea and photophobia.⁷²

Metastases (ie, nasopharyngeal carcinoma, melanoma, breast carcinoma, lymphoma) or primary tumours (ie, meningioma, craniopharyngioma, pituitary adenoma) in the orbital apex or in the cavernous sinus can also lead to painful ophthalmoplegia. If the cause of painful ophthalmoplegia is in the subarachnoid space, the oculomotor nerve is most commonly affected. This cause is, within the whole group of painful ophthalmoplegia, one of the most frequent ones. In disorders in which the oculomotor nerve is compressed, such as aneurysms (internal carotid, posterior communicating, posterior cerebral, and basilar artery) or tumours, pupillary involvement is frequent, whereas pupillary function is often preserved when the underlying mechanism is ischaemia (eg, in diabetes mellitus), but pain is often associated.⁷³

Brainstem disorders associated with involvement of the ocular motor system are usually not painful, except when the trigeminal system or the thalamus is affected.

A further disorder to be discussed in this section is carotid dissection (case 3), which is frequently seen in neurology. The lesion is mostly in the wall of the extracranial segment of the carotid artery, but pain is referred to the face (jaw, teeth, eye), often mimicking

Case 3: Carotid dissection

A 45-year-old health professional, suffering from migraine without aura since his early twenties, presented to the emergency room. He had taken a transatlantic flight from the USA to Zürich, Switzerland, over night, and woke up with a headache that he described as a "typical migraine attack", with periorbital, left-sided, moderate pain, and photophobia and phonophobia, but no nausea. While shaving, he noticed a smaller pupil on the left side and a drooping left eyelid. In the clinical examination, Horner's syndrome was identified. A carotid artery dissection was diagnosed by means of MRI, which revealed a haematoma in the wall of his left internal carotid artery with narrowing of the lumen. An anticoagulation treatment was undertaken. He recovered completely without any further neurological complications.

migraine or a trigeminal autonomic cephalalgia. The clinical presentation is variable. Pain might have unusual characteristics and can be associated with Horner's syndrome because of local compression or ischaemia of the sympathetic nerve fibres in the carotid wall. Ipsilateral cranial nerve lesions (often hypoglossal nerve), ipsilateral amaurosis, or contralateral sensorimotor deficits (the so-called opticocerebral syndrome⁷⁴), occur if impaired blood flow or secondary emboli result in ischaemic cerebrovascular infarction.⁷⁵ In migraine patients, the presentation of a carotid artery dissection can sometimes mimic a typical migraine attack (case 3). MRI including fat saturation sequences together with MR angiography is diagnostic in most patients and has largely replaced conventional angiography in clinical practice.

Horner's syndrome (oculosympathetic palsy with ptosis, miosis, enophthalmos, hypohidrosis or anhidrosis) can be associated with facial pain, depending on the underlying cause (typically in patients with carotid artery dissection⁷⁶ or brainstem infarction⁷⁷). Exceptionally, lesions of the sympathetic fibres at the level of the proximal portion of the first dorsal root or in the cervical sympathetic chain can lead to Pourfour du Petit's syndrome (oculosympathetic hyperactivity with mydriasis, lid retraction, exophthalmos, hyperhidrosis), which can be also accompanied by facial pain.^{78,79}

Disturbed sensation in the face

In this group of disorders the sensation in the trigeminal distribution is altered in addition to facial pain, which tends to have a neuropathic character. Hypaesthesia, hyperalgesia, or allodynia are possible findings. The underlying pathological changes can be localised at any level of the trigeminal pathway, including the trigeminal nerve, the ganglion, the roots, the nuclei, as well as trigeminothalamocortical tracts. There can be many underlying causes, including inflammation or infection (eg, painful trigeminal neuropathies caused by herpes), demyelination (eg, trigeminal neuropathy in multiple sclerosis), tumours, vascular diseases, trauma, and operations (eg, anaesthesia dolorosa after surgical intervention for trigeminal neuralgia⁸⁰).

Case 4: Acute herpetic trigeminal neuropathy

A 42-year-old lady noticed a continuous, strong, burning, and strictly right-sided pain developing within a few hours in the lower half of her face, the gingiva of her upper and lower jaw, and her tongue, radiating to her ear. The pain was also characterised by short-lasting lancinating attacks in addition to the continuous burning pain and was accompanied by tingling and numbness on the right side of the tongue and lower and upper lips. About 10 days after the facial pain had started, a rash in the entire distribution of the 2nd and 3rd division of her right trigeminal nerve appeared, including the mucosa of the oral cavity and the tongue. She presented with this clinical picture to our emergency department. The neurological examination showed reduced sensation for touch in the same distribution. The diagnosis of an acute herpetic infection with involvement of the second and third right trigeminal division was made. Treatment with aciclovir and carbamazepine was initiated. An MRI was unremarkable. After 3 weeks, when the skin rash remitted, the patient became pain free.

Head or facial pain attributed to acute herpes zoster infection (case 4) is a common clinical problem and can be constant or paroxysmal. It occurs in 10–35% of patients with herpes zoster infection of the face and is mainly localised in the first trigeminal division. The pain can be associated with sensory impairment in the same area or with other cranial nerve lesions. Typically, pain precedes herpetic eruptions by less than 7 days and resolves within 3 months.^{71,81} Up to 25% of patients develop persistent pain, which is then called postherpetic neuralgia,^{82–84} although the pain is typically constant and not neuralgiform. Very rarely, but distinctly, and sometimes as a premonitory symptom, patients have a sharp facial pain of sudden onset (“salt and pepper on the face”) in temporal association with paramedian pontine ischaemia, which is mainly localised in the eye, nose, or around the mouth, and is associated with ipsilateral facial numbness or contralateral ataxic hemiparesis.^{85,86} Therefore, subtle accompanying symptoms and signs might be essential characteristics to differentiate peripheral from central trigeminal pain. In up to 1% of the patients, facial and oral pain or

Case 5: Herpes zoster oticus (Ramsay Hunt syndrome)

A 32-year-old lady was put on a course of antibiotics by her family practitioner because of a very painful inflammation of the left ear and external ear canal. After 10 days, the patient's left palpebral fissure was widened and the left side of her mouth was slightly drooping. She had intense pain behind the left ear and left-sided hypoacusis. On examination, apart from a red ear and external ear canal with skin changes suggesting subacute herpes zoster infection and a peripheral facial palsy, we found a nystagmus to the right, sensory hearing loss on the left side, and a head impulse test localising the pathology to the left.⁹⁰ MRI showed gadolinium enhancement in the left vestibulocochlear nerve (figure 3). The triad facial palsy, cochleovestibular dysfunction, and skin changes of the ear and external ear canal were fulfilled, and the diagnosis of a Ramsay Hunt syndrome (herpes zoster oticus) was made. Treatment with steroids and aciclovir was given. After 2 weeks she had transient recurrent attacks of vertigo and nausea for a few days. The other symptoms and signs improved gradually over 3 months and finally resolved completely.

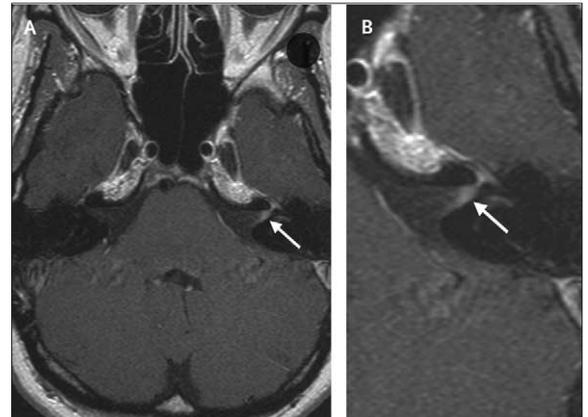


Figure 3: T1-weighted MRI of the head with gadolinium showing an enhancement in the distal portion of the VIII cranial nerve (arrow) as expression of a herpes zoster infection with Ramsay Hunt syndrome

discomfort can occur in the context of Parkinson's disease, especially during the pain-free phases.⁸⁷

Facial palsy, hypoacusis, or disturbed balance

Idiopathic (Bell's) palsy is a common disorder and is often associated with facial pain localised around the ear, jaw angle, and neck. Pain is usually the first symptom, starting hours to days before the motor deficits occur.^{88,89} Symptomatic facial palsy due to different underlying conditions (most often inflammatory, infectious, compressive, infiltrative), which can present in a similar way, is much less common. Although usually painless, parotid tumours should be considered in patients presenting with painful swelling in the respective region and slowly progressive facial palsy. In Ramsay Hunt syndrome (case 5),⁹⁰ the combination of peripheral facial nerve palsy and a rash (localised ipsilaterally in the ear, hard palate, or anterior two-thirds of the tongue) is often accompanied by pain. Associated symptoms and signs of vestibulocochlear, glossopharyngeal, or vagal nerve involvement can occur.⁹¹ Diagnosis can be challenging if the syndrome arises without the typical skin rash (herpes sine herpette).

Lesions in the cerebellopontine angle, such as tumours like acoustic neuroma,²⁷ meningioma, or cystic lesions, as well as aneurysms tend to be associated with hypoacusis, vertigo, or facial palsy. Pain in the face, however, is a rather unusual characteristic in this context.

Red flags suggestive of a symptomatic cause are bilateral facial palsy,⁹² involvement of other cranial nerves, signs of raised intracranial pressure, systemic symptoms, and signs (especially fever, skin changes, muscle and joint pain, weight loss). Bilaterally intact innervation of the frontal portion of the facial muscles as well as less pronounced mimetic (involuntary) than voluntary involvement suggests a central origin of the facial palsy.⁸⁸

Dysphagia, dysphonia, or dysarthria

Occasionally, lesions of the caudal cranial nerves can be accompanied by pain in the face. The causes can be of various kinds, including inflammation, infection, neoplastic disorders at the base of the skull or in the subarachnoid space,⁹³ and vascular diseases such as aneurysms or a dissection of the internal carotid artery.⁹⁴ Hence, radiological examination is mandatory.

Cerebrovascular disorders that affect the lower brainstem (medulla oblongata), such as lateral medullary infarctions, might be associated with ipsilateral facial pain due to involvement of the spinal trigeminal tract or nucleus.⁹⁵ Ipsilateral Horner's syndrome, dysphagia, dysphonia, and loss of pain or temperature sensation in the face as well as hemiataxia of the limbs and contralateral loss of pain or temperature sensation are commonly associated. This is best known as Wallenberg's syndrome.

Trigeminal autonomic cephalalgias

The so-called trigeminal autonomic cephalalgias—cluster headache, paroxysmal hemicranias, and short lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome—represent a group of relatively uncommon primary headache syndromes characterised by short lasting, unilateral attacks mainly localised in the first trigeminal division (fronto-orbital region), associated with signs of ipsilateral cranial autonomic (parasympathetic) activation, such as lacrimation, conjunctival injection, eyelid oedema, rhinorrhoea, miosis, and ptosis.^{96–100} Activation of the posterior hypothalamic grey was shown to be present in cluster headache, SUNCT, and hemicrania continua.^{101–104} Table 1 summarises the most important clinical characteristics of trigeminal autonomic cephalalgias. The clinically most important entity cluster headache, is a very distinct disorder and occurs mostly in men. The disorder is called cluster headache because it typically occurs in clusters of daily attacks during a few weeks, once or twice per year, in spring or autumn. It has a circadian rhythm and tends to wake patients up in the early morning, with a headache lasting 15 or 30 min, rarely up to 180 min, and it occurs in the setting of smoking and is triggered by alcohol. This type of headache syndrome requires investigation because cases with a secondary origin have been described in some of the rare forms.^{105,106}

Pure facial pain without neurological signs

Rhinosinus-related headache

Pain caused by sinusitis (but also by other abnormal changes of the nasal sinuses, such as tumours) can project to different parts of the head. Whereas frontal sinusitis projects to fronto-orbital regions, maxillary sinusitis projects to the cheek, the palate, and the maxilla (including the teeth). Pain from ethmoid sinusitis is usually localised between the eyes or in the orbit, and may be aggravated by eye movements. Sphenoid sinusitis, the

	Cluster headache	Paroxysmal hemicrania	SUNCT
Ipsilateral autonomic signs	+	+	++
Attack duration	15–180 min	2–30 min	5–240 s
Attack frequency per day	1–8	1–40	3–200
Pain localisation	Unilateral, orbital, temporal	Unilateral, orbital, temporal	Unilateral, orbital, temporal
Pain intensity	+++	+++	++/+++
Indomethacin efficacy	+/-	+	–
Triggering by alcohol	+	(-)	–

For pain intensity +=mild; ++=moderate; +++=severe. For all other categories –=absent; +/-=sometimes present; +=present; ++=pronounced.

Table 1: Clinical features of trigeminal autonomic cephalalgias

least common acute sinusitis (<5%), can project to different localisations of the head, such as forehead, occipital or temporal region, or vertex.^{107,108} Pain exacerbation by chewing, standing, walking, Valsalva manoeuvres, or by bending forward is common. Fever, nasal discharge, postnasal drip, and hyposmia or anosmia, are helpful diagnostic characteristics. Cranial nerve involvement (II, III, IV, V, VI), mostly due to inflammation or infection of the orbit or the trigeminal nerve, could be a rare complication. Because of the similarity in pain localisation, frontal sinusitis and migraine might be confused. Migraine, however, is accompanied by sensory hypersensitivity, such as phonophobia and photophobia, but no purulent discharge or fever. However, there is the possibility of diagnostic overlap—eg, when migraine is triggered by sinusitis.¹⁰⁹ Clinical examination can provide hints—ie, for frontal and maxillary sinuses—but imaging is often needed. The best diagnostic yield is obtained with CT¹¹⁰ rather than MRI, which is mandatory in patients with signs of intracranial complications.¹¹¹ Standard radiographs are false negative in about a quarter of patients.

Disorders of the temporomandibular joint

Disorders of the temporomandibular joint can sometimes cause diagnostic difficulties because they are prevalent in the population and can mimic primary headaches such as persistent idiopathic facial pain or tension-type headache, especially the subtypes associated with pericranial tenderness.⁷¹ Diagnosis of a temporomandibular-joint disorder is mostly in the domain of dentists and maxillary surgeons. The clinical picture and the association with bruxism^{112,113} can help neurologists to make a probable diagnosis. In practice, however, the distinction between pain originating from the muscle or from the temporomandibular joint can be difficult and the importance of muscular structures in pain generation has to be kept in mind, including the therapeutic consequences.¹¹⁴ Pain from a disorder of the temporomandibular joint is usually of variable severity, and can be described as dull or throbbing, lasting minutes to hours. The pain is typically triggered by jaw movements or palpation of the joint or the masticatory muscles. The pain may be bilateral or unilateral, is

Panel 5: Persistent idiopathic facial pain—diagnostic criteria of the International Headache Society (ICHD-II classification)

- A. Pain in the face, present daily and persisting for all or most of the day, fulfilling criteria B and C
- B. Pain is confined at onset to a limited area on one side of the face, and is deep and poorly localised
- C. Pain is not associated with sensory loss or other physical signs
- D. Investigations including radiograph of the face and jaws do not demonstrate any relevant abnormalities

localised mostly in the preauricular region, and sometimes radiates to the temples or to the neck.¹¹⁵ Noise on jaw opening, tinnitus, or vertigo might be associated. Examination can show a tender temporomandibular joint, reduced opening, lateral deviation of the jaw, and tenderness of the masticatory muscles.^{116–118}

Disorders of oral structures or salivary glands

In most cases, pain arising from oral structures is localised in the mouth and not the face. These disorders, if regarded as a source of facial pain, should be investigated in a straightforward way by the respective specialist. Pain character and duration include the whole range of possibilities and can show some degree of diagnostic overlap with trigeminal neuralgia.¹¹⁹ Inflammatory disorders of the oral mucosa and tongue usually manifest with sharp, burning pain, often precipitated by ingestion of sour and sharp foods. Changes in taste can occur. Burning sensation of the oral mucosa, especially of the tongue, can be caused by Sjogren’s syndrome or associated with systemic disease, such as chronic iron deficiency anaemia, and accompanied by trophic changes; a small fibre neuropathy may be associated. However, burning sensations of the tongue (glossodynia) or the oral mucosa (burning mouth syndrome¹²⁰) are also reported without trophic changes or without associated systemic disease, and can sometimes be explained in a psychiatric context. Pain arising from salivary glands is usually well localised and can be more pronounced by increased saliva production—ie, before or during a meal. Local swelling, tenderness to palpation, reduced salivary flow, and fever might be associated symptoms.

Referred pain

Facial pain can rarely be referred from thoracic or cervical structures, mimicking a local effect and leading

to diagnostic difficulties. Importantly, pain due to ischaemic heart disease radiates to the neck, jaw, or teeth. As described above in detail, carotid dissection is a clinically important example of pain referred to the face. Diseases of the hypopharynx or larynx can be referred to the ear. Unilateral facial pain, probably due to invasion or compression of the vagus nerve, can be a presenting complaint of neoplastic disorders of the lung.^{121–123}

Rare facial pain syndromes of miscellaneous causes

Recently, primary trochlear headache has been proposed as a new diagnostic entity.¹²⁴ It was described as pain focused in the trochlear region without any accompaniment, worsened by palpation, and with negative paraclinical examinations. Local injection of corticosteroids were described to be helpful. Sometimes pain in the face can result from continuous stimulation of cutaneous nerves—eg, by swimming goggles—and is then called external compression headache.¹²⁵ The rare red ear syndrome was first described by Lance¹²⁶ and is characterised by attacks of unilateral burning sensations in the ear associated with redness of the skin and might be associated with facial or head pain.¹²⁷ Local mechanical and thermal stimuli are possible triggers. A dysregulation of autonomic outflow in the upper cervical segments is discussed as a possible mechanism.^{128,129} An overlap with trigeminal autonomic cephalalgias¹³⁰ and with migraine¹³¹ has been reported. The so-called Eagle syndrome (stylohyoid syndrome) is due to local pressure of an abnormally elongated styloid process or calcified stylohyoid ligament, and can lead to temporomandibular pain mimicking glossopharyngeal neuralgia.¹³² Carotidynia has been a diagnostic entity for decades; however, recent studies suggest that there may be many underlying causes, and it has even been removed from the second edition of the International Headache classification.^{71,133}

Persistent idiopathic facial pain

Previously called atypical facial pain, persistent idiopathic facial pain is a common, but poorly defined entity, which is diagnosed by exclusion (panel 5).⁷¹ The disorder is defined as continuous facial pain, typically localised in a circumscribed area, present all or most of the day, which is not accompanied by any neurological or other lesion, in terms of clinical examination or investigations.^{134–136} The cause is unknown, but surgery or injury in the

	Idiopathic	Symptomatic	Imaging (mostly MRI)	Specialist assessment by
Neuralgias	Mostly	Possible	Recommended if new onset	Neurologist
Facial pain with cranial nerve symptoms/signs	Very rarely	Very often	Mandatory (early)	Neurologist
Trigeminal autonomic cephalalgias	Mostly	Rare	Recommended if new onset or change of clinical picture	Neurologist
Pure facial pain	Sometimes	Often	Recommended if underlying cause after clinical examination still unclear	ENT physician/dentist/dental surgeon

Table 2: Facial pain syndromes—synopsis of aetiology and investigations

Search strategy and selection criteria

References for this review were identified by searches of MEDLINE up until December, 2005, as well as references from relevant articles and book chapters. The search terms were: "headache", "migraine", "ophthalmoplegic", "cluster", "trigeminal-autonomic", "SUNCT", "vascular", "malformation", "arteritis", "dissection", "neoplasm", "neuralgia", "Tolosa", "Hunt", "herpes", "zoster", "post-herpetic", "trigger", "trigeminal", "glossopharyngeal", "tension", "type", "facial", "pain", "cephalalgia", "sinusitis", "temporo", "mandibular", "joint", "tmj", "arteriovenous", "bradycardia", "geniculate", "intermedius", "nasociliary", "Charlin", "sphenopalatine", "Sluder", "supraorbital", "cephalalgias", "optic", "neuritis", "pseudotumor", "orbit", "SLE", "rheumatoid", "arthritis", "dermatomyositis", "Wegener", "granulomatosis", "sarcoid", "endocrine", "orbitopathy", "painful", "ophthalmoplegia", "pituitary", "apoplexy", "idiopathic", "Bell", "palsy", "Ramsay", "Hunt", "hemicrania", "continua", "paroxysmal", "Costen", "glossodynia", "burning", "mouth", "Sjogren", "syndrome", "trochlear", "red", "ear", "external", "compression", "Eagle", "stylohyoid", "carotidynia", and their combinations. Abstracts and reports from meetings were not included. Furthermore, articles were identified through searches of the extensive files of the authors. Only original and review papers have been included. The final reference list was generated based on originality and relevance to the topics covered in the review.

distribution of the trigeminal nerve could be an initiating event. A comorbidity with depression is frequently found. Treatment is often unsatisfactory.

Conclusion

In the clinical situation, a systematic approach dividing the facial pain syndromes into neuralgias, facial pain accompanied by cranial nerve symptoms and signs, trigeminal autonomic cephalalgias, and pure facial pain could provide a differential diagnostic tool that helps to determine the investigations necessary to substantiate the diagnosis. Although urgent investigations are needed when cranial nerve symptoms and signs are found, the diagnostic yield of a careful history and a complete neurological examination is larger in neuralgias and pure facial pain syndromes, and imaging, if needed, can often be done with less time pressure (table 2).

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Authors' contributions

MS proposed and worked-up the classification of facial pain syndromes. MS and PSS drafted the paper and did the reference search. The cases were patients seen by any of the three authors. All three authors contributed to the review at its various stages.

Conflicts of interest

We have no conflicts of interest.

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