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Midfacial pain

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Abstract: Midfacial pain is not a diagnosis per se but rather describes an anatomical region of pain manifestation of various origins. The midface is built of cavities (nose, sinuses), calcified structures (teeth, bone) and soft tissues (nerves, muscles, mucosa, salivary glands, cartilage, skin). Since midfacial bones form the nose, sinuses and the alveolar ridge containing the upper teeth, the following three specialties are commonly consulted by patients experiencing midfacial pain

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Midfacial pain

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Midfacial Pain

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Introduction / Background

Midfacial pain is not a diagnosis per se but rather describes an anatomical region of pain manifestation of various origins. The midface is built of *cavities* (nose, sinuses), *calcified structures* (teeth, bone) and *soft tissues* (nerves, muscles, mucosa, salivary glands, cartilage, skin). Since midfacial bones form the nose, sinuses and the alveolar ridge containing the upper teeth, the following three specialties are commonly consulted by patients experiencing midfacial pain: dentists, maxillofacial surgeons, as well as ear, nose and throat (ENT) specialists. The exciting challenge for clinicians - called diagnostic process - is to match the patients' complaints in combination with clinical, imaging and/or laboratory findings to sets of diagnostic criteria defined by expert committees. Clinicians diagnosing midfacial pain need to be aware of the following:

- Mucosal alterations readily visible on imaging rarely explain pain complaints, as these generally evoke minimal or no pain (e.g. seasonal allergies).
- Discreet nerve or muscle alterations invisible on imaging may evoke disabling pain.
- Neural sensitization processes frequently blur the clinical picture.
- Primary headaches can present as midfacial pain.
- Cranial artery obstructions may present as midfacial pain.

Consequently, although a broad spectrum of midfacial pain can be confirmed by imaging, a large proportion relies solely on history taking and palpation. Cautious interpretation of image findings cannot be overemphasized. Irreversible dental or surgical treatment is justified only when a documented pathology explains the midfacial pain.

Diagnostic classification of orofacial pain - a project in progress

Diagnostic criteria for facial pain were established and repeatedly revised by the International Headache Society (IHS). The current third version of the International Classification of Headache Disorders (ICHD) is available online: www.ichd-3.org. Yet, additional nomenclature emerged in parallel, so that no uniform classification exists at this point in time. Efforts are ongoing to establish a consensus based International Classification for Orofacial Pain (ICOP). The international group working on this project is composed of experts from the IHS, the American Academy of Orofacial Pain (AAOP), the International Network for Orofacial Pain and Related Disorders

Methodology (INfORM) and the International Association for the Study of Pain (IASP) [1]. The current Version 1.0 beta is available on www.ihs-headache.org.

Differential diagnosis form a pragmatic clinical perspective

Main features of pain are its location, quality, intensity, time pattern, triggers, modulators, and accompanying symptoms. Most commonly, the nociceptive signal is generated in facial structures where the pain is felt. Confusingly however, even when nociceptive signaling signal originates in more centrally located tissues, the pain is still experienced in peripheral structures. The mnemonic “**DAMN-ODD**” may serve for remembering some of the more common causes in the form of a differential diagnosis. It is briefly described in Table 1 and in more detail in Table 2. The first letter “D” stands for *dental* pain, which may result from pulpal or periodontal pathology. The entities *arthralgia* (“A”) of the temporomandibular joint and *myalgia* (“M”) of masticatory muscles are commonly grouped under the non-specific umbrella term temporomandibular disorders. *Neuropathic pain* (“N”) may be due to a pathology located peripherally or along the primary afferent neuron (e.g. neuroma), or alternatively due to a central nervous system dysfunction (e.g. primary headache). *Obstructions* (“O”) of arteries may lead to pain as a result of tissue hypoxia, whereas sialolithiasis and sinus obstructions cause pain by tissue expansion and/or neural irritation. *Distension* (“D”) may further be caused by various benign or malignant tumors. Due to the anatomical complexity of the midface region and the broad differential diagnoses, inappropriate invasive procedures by *doctors* (“D”) may induce sensitisation processes that change the original pain phenotype.

Table 1

Table 2

Next, we discuss the following entities that are not addressed by other authors, namely midface pain caused by migraine, cluster headache, nose and sinus disorders, and cardiovascular disorders.

Migraine with midface pain

Etiology and pathophysiology

Migraine is the most common disabling headache disorder. The global prevalence is 10% in men and 22% in women [2]. Peak prevalence increases to the age of 40 years and declines after in both genders [3].

Migraine is defined as a recurrent headache disorder manifesting in attacks lasting 4–72 hours. The postulated pain mechanism includes neurogenic inflammation within the trigeminovascular system and possible links to metabolic factors [4, 5].

Neuropeptides such as CGRP, Substance P, and Neurokinin A, are thought to be involved [6]. It has been hypothesized that the activation of a feed-forward neurovascular dilator mechanism is functionally specific for the first (ophthalmic) division of the trigeminal [7]. Clinical data indicate that this mechanism might not be restricted to the dura and the frontotemporal area, and therefore the first trigeminal branch, but may also extend to the 2nd and 3rd division involving maxillary and mandibular fibers [8]. In line with the above, nociceptive nerve fibers exhibiting Substance P- and CGRP-positive immunoreactivity have been demonstrated in human dental pulp tissue [9].

Presentation and diagnosis

Migraine has two major types: migraine without and with aura. The latter is characterized by transient focal neurological symptoms that usually precede or sometimes accompany the pain. Additionally, prodromal and postdromal symptoms may occur such as hyper- or hypoactivity, depression, cravings for particular foods, repetitive yawning, fatigue and neck stiffness and/or pain (www.ichd-3.org). Typical migraine features are unilateral location, pulsating quality, moderate to severe intensity, aggravation by routine physical activity and accompanying symptoms such as nausea and/or photophobia, phonophobia, cutaneous allodynia cranial autonomic symptoms [10].

Pain location of migraine can vary inter- and intraindividually between attacks [11, 12]. Occasionally, patients report distinctive type of episodic dental pain, lasting hours to days, sometimes associated with headache episodes and accompanying symptoms comparable to migraine and sometimes even with aura [8]. Precisely because of the pain location, these patients primarily seek help from their dentist. Imaging of the affected region will show no abnormality and the neurological examination is normal, at least during pain free intervals. Due to the experience of burdening pain in peripheral tissues, patients often seek and/or risk receiving

unnecessary dental treatment, especially during an acute pain episode. The term orofacial migraine has been proposed to classify this migraine subtype, analogous to retinal or abdominal migraine [13]. There is evidence that more severe forms of temporomandibular disorders are associated with increased headache frequency, which applies namely for migraine [14].

Management

Migraine management options include behavioral and pharmacological interventions that are best combined. Pharmacotherapy can be implemented preventively and/or therapeutically. Preventive treatment should be offered to patients who suffer several migraine days per month that cause significant disability. Regularly updated guidelines for proper migraine treatment are listed on the website of the international headache society: www.ihs-headache.org.

Future directions and conclusion

Migraines and midfacial pain share common trigeminal nerve pathways. Future investigation on facial representations of migraines will hopefully shed light on the connection between the two. Future prevalence studies on midface pain could clarify the proportion of migraines and stimulate investigations on related mechanisms.

Cluster headache with midfacial pain

Etiology and pathophysiology

Cluster headache is defined as a severe or very severe unilateral pain in the orbital, supraorbital or temporal region. It is commonly accompanied by autonomic features [10]. It has a prevalence of about 0.1%, four times more common in men. The peak age of onset is between the 3rd and 4th decades. Cluster headache sufferers are often smokers

Presentation and diagnosis

Pain attacks are typically severe, strictly unilateral, last 15-180 minutes and occur from once every other day to eight times a day. The pain is associated with ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis and/or eyelid edema, and/or with restlessness or agitation. Patients are typically pacing around during the headache phase. Characteristic is a

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3 circadian rhythmicity with attacks predominantly at night and additional circannual
4 rhythmicity with clusters of attacks in spring and/or autumn. In the episodic form,
5 cluster headache attacks occur in periods lasting from 7 days to one year, separated
6 by pain-free periods lasting at least 3 months. Cluster episodes usually last between
7 2 weeks and 3 months, yet may extend longer in the chronic form (www.ichd-3.org).
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12 Cluster headaches have been described as presenting in the second and third
13 branches of the trigeminal nerve as toothache and jaw pain [15, 16]. In patients who
14 have already been diagnosed with a cluster headache, facial involvement was
15 reported in 14.8% [17]. In 31% of these, the pain was predominantly perceived in the
16 midface. Pain with neurovascular characteristics in the midface includes local
17 hypersensitivity, episodic, unilateral throbbing pain, often waking up patients from
18 sleep. The similarity to pulpitis is obvious and may mislead to an assumed dental
19 diagnosis and subsequent treatment with frustrating results. Patients should actively
20 be questioned regarding for secondary symptoms such as lacrimation, facial
21 redness, rhinorrhea, even if these symptoms are mild [16].
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30 *Management*

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32 Acute therapy approaches include high flow oxygen for 15-20 minutes and or
33 Triptans intranasally or subcutaneously. Regularly updated guidelines for proper
34 cluster treatment are listed on the website of the international headache society:
35 www.ihs-headache.org.
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40 *Future directions and conclusion*

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42 Analogous to migraines with midface pain manifestation, cluster headaches and
43 midfacial pain share common trigeminal pathways. To prevent inappropriate
44 procedures, there is a need to disseminate information about cluster headaches
45 among different specialists providing care in this anatomical region (e.g. neurologists,
46 ENT, dentists).
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51 *Midfacial pain attributed to nose and sinus disorders*

52 *Etiology, pathophysiology, presentation and diagnosis*

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55 Patients with mid facial pain and predominantly sinonasal complaints like rhinorrhea,
56 nasal congestion, sinus pressure or pain are usually referred to an otolaryngologist.
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59 Pain presumably attributed to a diagnosis of rhinosinusitis doesn't seem to be as
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prevalent as assumed. More than 80% of patients with purulent secretions have no facial pain [18, 19]. Patients with nasal polyposis do not complain about facial pain [20, 21]. Patients with “only” midfacial pain receiving endoscopic sinus surgery risk to have symptoms that persist postoperatively [22, 23]. Studies on selected facial pain patients that had a normal computed tomography and nasal endoscopy identified migraine as the most common cause of pain [24]. Also, many epidemiological studies revealed migraine as the most common cause for so called “sinus headaches”. 42% of patients experiencing migraine type pain in the midface are misdiagnosed with rhinosinusitis [25], likely, because symptoms of migraine and rhinosinusitis overlap [26, 27]. In self-diagnosed or physician diagnosed “sinus headache” 86% suffered from some migraine subtype [28]. Conversely, in non-otorhinolaryngological settings, studies revealed that migraine pain is frequently misdiagnosed as sinusitis [29]. According to radiological signs, 28.7% of 1,235 patients diagnosed with a primary headache showed radiological signs of rhinosinusitis, septal spur, concha bullosa, isolated sphenoid lesion or osteoma [30]. Conversely, individuals with chronic rhinosinusitis had a 9-fold increased risk of suffering from a chronic headache. Allergic rhinitis was observed in 54% of patients with migraine [28]. It has been hypothesized that rhinosinusitis increases the risk of comorbid migraine via irritation of trigeminal nerve receptors [31].

Management

Proper diagnosis is the key to proper management of nose and sinus disorders.

Future directions and conclusion

In conclusion, rhinosinusitis rarely presents with facial pain. Research is needed that elucidates the reasons why inflammation of the maxillary sinuses is generally painless. When in doubt, observe the therapeutic principle of do no harm.

Midfacial pain attributed to cardiovascular disorders

Giant cell arteritis (GCA):

Etiology and pathophysiology

GCA is a T-cell-dependent autoimmune disease with vasculitis and genetic predisposition that affects medium and large arteries. It comprises overlapping

phenotypes of cranial arteritis and extracranial GCA. Infections are discussed in triggering a disease outbreak, in particular viruses (e.g. HBV, influenza viruses and VZV) and bacterias (e.g. Borrelia, Klebsiella) [32]. There is a close connection with polymyalgia rheumatica.

Presentation and diagnosis

GCA should be suspected in patients older than 50 years who experience unilateral or bilateral jaw muscle tenderness, jaw claudication, visual disturbances, and tenderness in the area of the temporal arteries [33]. Elevated erythrocyte sedimentation rate (>50 /h) and C-reactive protein (>50 mg/L) increases the probability of GCA. Biopsy of the GCA is the gold standard diagnostic test and should be considered when GCA is suspected. Imaging can also aid in the diagnosis, namely duplex sonography, high-resolution magnetic resonance imaging, and positron-emission tomography [33, 34].

Management

GCA is a medical emergency. High doses of corticosteroids (40 – 60 mg) are indicated when there is an urgent suspicion of the disease. In case of spread to ocular or cerebral vessels (threat of blindness or life-threatening stroke) 500 mg – 1 g of methylprednisolone applied intravenously three times daily are indicated. Biological agents are effective and safe corticosteroid-sparing agents in treating GCA.

Carotid artery dissection (CAD):

Etiology and pathophysiology

CAD can occur spontaneously or as a result of trauma or defect with intimal wall damage. The splitting of the arterial wall forms a new lumen with secondary thrombosis, which can lead to pseudoaneurysm, vessel occlusion, embolisms with the risk of consecutive cerebral apoplexy. The carotid wall is innervated by the trigeminal nerve so the pain is attributed to a stimulation of the trigeminovascular system.

Presentation and diagnosis

Due to new imaging techniques we have evidence, that CAD and vertebral artery dissections show an annual incidence rate of 5 per 100,000 [35]. 95% of the patients

describe new unilateral steady or throbbing pain in the head, face, eye, neck, and toothache ipsilateral to the defect [35–37]. A Horner's Syndrome may be present if adjacent sympathetic nerve fibers are compressed. An ischemic stroke due to CAD may manifest with disturbance of consciousness (e.g. confusion) and severe focal neurological signs (e.g. unilateral numbness or facial weakness, difficulties to speak or understand, or to see on or both eyes, as well as loss of coordination).

Management

Timely and appropriate diagnostic strategies permylay the ground for early and effective treatment strategies [38].

Conclusion

When a patient presents with stroke symptoms in combination with a severe orofacial pain, a carotid artery dissection or similar vascular conditions should be suspected [10].

Ischemic heart disease (IHD)

Etiology and pathophysiology

IHD accounts for one third of all deaths annually, and approximately 2–3% of acute myocardial infarctions are missed in the emergency department [39, 40]. Pain manifestation in the orofacial region are thought to be mediated by afferent fibers of the vagus nerve transmitting nociceptive information to cervical neurons [41–43].

Presentation and diagnosis

Pain due to IHD typically refers to the shoulder or arm. Yet, it can also affect the face, jaw and ear [44, 45]. A systematic review indicated that midface pain was the sole symptom of cardiac ischemia in approximately 6% of cases [46, 47]. Patients often described their midface pain as “pressure” or “burning”. The following situation should trigger a screening electrocardiogram: bilateral midfacial pain that is evoked by exercise, or associated with chest discomfort, shortness of breath, nausea or fatigue [48].

Management

Management ought to be directed towards the underlying cause.

Conclusion

Midface pain due to IHD carries the risk of misdirected dental treatment and more importantly, delay of urgent medical care.

For Peer Review

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Table 1

The mnemonic of midfacial pain etiologies “**DAMN-ODD**” serves the dentist or specialist for remembering the directions of the more common causes in the diagnostic process.

Table 2

Midfacial pain diagnosis grouped by the mnemonic DAMN-ODD with ICHD-3 classification codes and the referral to topics discussed in this issue by other authors.

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Table 1:

D	–	Dentogenic
A	–	Arthrogenic
M	–	Myogenic
N	–	Neurogenic (primary, secondary)
O	–	Obstruction of arteries, salivary glands, sinuses
D	–	Distension by tumors
D	–	Doctor induced (sensitisation processes)

For Peer Review

Etiologi

[illegible]