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INVITED REVIEW

Midfacial pain

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Abstract

The midface anatomy includes a variety of structures and pain may therefore originate from different tissues. Several medical specialties are often involved in its management. Criteria that define a specific pathology guide the diagnostic process. Namely, reported symptoms require careful verification by the clinical examination. Where appropriate, imaging can offer supplemental information. However, there is mostly no image correlate for myogenic and neuropathic pain. Hence, the medical images need to be interpreted with caution to avoid an inadequate attribution of pain aetiology. The mnemonic "DAMN-ODD" may serve for remembering the more common differential diagnoses. Specific entities such as migraine, cluster headache, nose and sinus disorders, and cardiovascular disorders are discussed.

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 and sinuses), *calcified structures* (teeth and bone) and *soft tissues* (nerves, muscles, mucosa, salivary glands, cartilage and 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 sensitisation 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 overemphasised. 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,

Table 1 The mnemonic of midfacial pain aetiologies '*DAMN-ODD*' serves the dentist or specialist for remembering the directions of the more common causes in the diagnostic process

D – Dental pain
A – Arthralgia
M – Myalgia
N – Neuropathic pain (primary, secondary)
O – Obstruction of arteries, salivary glands, sinuses
D – Distension by tumours
D – Doctor-induced (sensitisation processes)

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 signalling 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 tumours. Due to the anatomical complexity of the midface region and the broad differential diagnoses, inappropriate invasive procedures

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

Aetiologies	ICHD-3 codes	Diagnoses	Topics discussed by other authors
*D*entogenic *D*ental pain	ICHD-3: 11.6	Inflammation (e.g. pulpitis, periodontitis, abscess)	Odontogenic pain by Maria Pigg & Simon Stone
	ICHD-3: 11.9	Trauma (e.g. cracked tooth)	
*A*rthrogenic *A*rthralgia	ICHD-3: 11.7	Temporomandibular disorders	Temporomandibular disorder by Justin Durham
*M*yogenic *M*yalgia	ICHD-3: 11.7		
*N*eurogenic *N*europathic pain	ICHD-3: 13.1.1:	Trigeminal neuralgia (various types)	Trigeminal Neuralgia and Cephalgias by Joanna Zakrzewska
Peripheral	ICHD-3: 13.1.2:	Trigeminal neuropathy (various types)	
	ICHD-3: 13.12:	Persistent idiopathic facial pain	
Central	ICHD-3: 1.1 to 1.3:	Migraine (various types)	Localised non-odontogenic pain (formerly known as PDAP/atypical odontalgia) by Don Nixdorf
	ICHD-3: 3.1 to 3.5:	Trigeminal autonomic cephalalgias (various types)	
	ICHD-3: 13.13.1:	Central neuropathic pain attributed to multiple sclerosis	
	ICHD-3: 13.13.2:	Central post-stroke pain	
*O*bstruction (arteries, salivary glands, sinuses)	ICHD-3: 6.3.4:	Arteritis (various types)	
	ICHD-3: 6.3.5:	Carotid artery disorders (various types)	
	ICHD-3: 10.6:	Myocardial ischemia	
	ICHD-3: 11.9:	Sialolithiasis, Salivary gland disorders (various types)	
	ICHD-3: 11.9:	Paranasal sinus disorders (various types)	
*D*istension (tumors)	ICHD-3: 11.9:	Tumours (various types)	Temporomandibular disorders by Justin Durham
*D*octor-induced (iatrogenic)	ICHD-3: 13.1.2.3:	Painful post-traumatic trigeminal neuropathy	Surgical nerve injuries by Tara Renton

by *doctors* ('D') may induce sensitisation processes that change the original pain phenotype.

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

Aetiology 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 h. 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 hypothesised that the activation of a feed-forward neurovascular dilator mechanism is functionally specific for the first (ophthalmic) division of the trigeminal nerve[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 second and third division involving maxillary and mandibular fibres[8]. In line with the above, nociceptive nerve fibres 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 characterised 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 behavioural 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 IHS: 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

Aetiology 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 third and fourth decades. Cluster headache sufferers are often smokers.

Presentation and diagnosis

Pain attacks are typically severe, strictly unilateral, last 15–180 min 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 oedema and/or with restlessness or agitation. Patients are typically pacing around during the headache phase. Characteristic is a circadian rhythmicity with attacks predominantly at night and additional circannual rhythmicity with clusters of attacks in spring and/or autumn. In the episodic form, cluster headache attacks occur in periods lasting from 7 days to 1 year, separated by pain-free periods lasting at least 3 months. Cluster episodes usually last between 2 weeks and 3 months, yet may extend longer in the chronic form (www.ichd-3.org).

Cluster headaches have been described as presenting in the second and third branches of the trigeminal nerve as toothache and jaw pain[15,16]. In patients who have already been diagnosed with a cluster headache, facial involvement was reported in 14.8%[17]. In 31% of these, the pain was predominantly perceived in the midface. Pain with neurovascular characteristics in the midface includes local hypersensitivity, episodic, unilateral throbbing pain, often waking up patients from sleep. The similarity to pulpitis is obvious and may mislead to an assumed dental diagnosis and subsequent treatment with frustrating results. Patients should actively be questioned regarding for secondary symptoms such as lacrimation, facial redness and rhinorrhea, even if these symptoms are mild[16].

Management

Acute therapy approaches include high-flow oxygen for 15–20 min and or triptans intranasally or subcutaneously. Regularly updated guidelines for proper cluster treatment are listed on the website of the IHS: www.ihs-headache.org.

Future directions and conclusion

Analogous to migraines with midface pain manifestation, cluster headaches and midfacial pain share common trigeminal pathways. To prevent inappropriate procedures, there is a need to disseminate information about cluster headaches among different specialists providing care in this anatomical region (e.g. neurologists, ENT, dentists).

Midfacial pain attributed to nose and sinus disorders

Aetiology, pathophysiology, presentation and diagnosis

Patients with mid facial pain and predominantly sinonasal complaints like rhinorrhea, nasal congestion, sinus pressure or pain are usually referred to an otolaryngologist. Pain presumably attributed to a diagnosis of rhinosinusitis does not seem to be as 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 post-operatively[22,23]. Studies on selected facial pain patients who 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'. Forty-two per cent 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 1235 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 ninefold increased risk of suffering from a chronic headache. Allergic rhinitis was observed in 54% of patients with migraine[28]. It has been hypothesised 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 "first, do no harm".

Midfacial pain attributed to cardiovascular disorders

Giant cell arteritis

Aetiology and pathophysiology
Giant cell arteritis (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 bacteria (e.g. *Borrelia*, *Klebsiella*)[32]. There is a close connection with polymyalgia rheumatica.

Presentation and diagnosis
Giant cell arteritis 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) increase 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
Giant cell arteritis 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

Aetiology and pathophysiology
Carotid artery dissection (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 and 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]. Ninety-five per cent of the patients describe new unilateral steady or throbbing pain in the head, face, eye, neck and toothache ipsilateral to the defect[35,36,37]. A Horner's syndrome may be present if adjacent sympathetic nerve fibres are compressed. An ischaemic 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 lay 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 *CAD* or similar vascular conditions should be suspected[10].

Ischaemic heart disease

Aetiology and pathophysiology
Ischaemic heart disease (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 is thought to be mediated by afferent fibres of the vagus nerve transmitting nociceptive information to cervical neurons[41,42,43].

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 ischaemia 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.

References

1. Benoliel R. Editorial: let's adopt ICOP: speaking the same language. J Oral Facial Pain Headache 2019;33:245–6.
2. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton RB, Scher AI *et al*. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 2007;27:193–210.
3. Lipton RB, Silberstein SD, Stewart WF. An update on the epidemiology of migraine. Headache 1994;34:319–28.
4. Bolay H, Reuter U, Dunn AK *et al*. Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. Nat Med 2002;8:136–42.
5. Gross EC, Lisicki M, Fischer D, Sándor PS, Schoenen J. The metabolic face of migraine — from pathophysiology to treatment. Nat Rev Neurol 2019;15:627–43. https://doi.org/10.1038/s41582-019-0255-4.
6. May A, Büchel C, Turner R *et al*. Magnetic resonance angiography in facial and other pain: neurovascular mechanisms of trigeminal sensation. J Cereb Blood Flow Metab 2001;21:1171–6.
7. Rodd HD, Boissonade FM. Comparative immunohistochemical analysis of the peptidergic innervation of human primary and permanent tooth pulp. Arch Oral Biol 2002;47:375–85.
8. Gaul C, Sándor PS, Galli U, Palla S, Ettlin DA. Orofacial migraine. Cephalalgia 2007;27:950–2.
9. Hargreaves KM, Bowles WR, Jackson DL. Intrinsic regulation of CGRP release by dental pulp sympathetic fibers. J Dent Res 2003;82:398–401.
10. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. Cephalalgia 2018;38:1–211.
11. Kelman L. Migraine pain location: a tertiary care study of 1283 migraineurs. Headache 2005;45:1038–47.
12. Hussain A, Stiles MA, Oshinsky ML. Pain remapping in migraine: a novel characteristic following trigeminal nerve injury. Headache 2010;50:669–71.
13. Gaul C, Sándor PS, Ettlin DA. Neurovascular orofacial pain: authors' reply. Cephalalgia 2008;28:305. https://doi.org/10.1111/j.1468-2982.2008.01548.x.
14. Gonçalves DAG, Camparis CM, Speciali JG, Franco AL, Castanharo SM, Bigal ME. Temporomandibular disorders are differentially associated with headache diagnoses: a controlled study. Clin J Pain 2011;27:611–5.
15. Gaul C, Gantenbein AR, Buettner UW, Ettlin DA, Sándor PS. Orofacial cluster headache. Cephalalgia 2008;28:903–5.
16. Benoliel R, Sharav Y, Eliav E. Neurovascular orofacial pain. J Am Dent Assoc 2010;141:1094–6.
17. Ziegeler C, May A. Facial presentations of migraine, TACs, and other paroxysmal facial pain syndromes. Neurology 2019;93:e1138–47.
18. West B, Jones NS. Endoscopy-negative, computed tomography-negative facial pain in a nasal clinic. Laryngoscope 2001;111(4 Pt 1):581–6.
19. Walliczek-Dworschak U, Diogo I, Strack L, Mandapathil M, Teymoortash A, Werner JA *et al*. Indicazioni all'esecuzione di una TC cone beam del distretto testa e collo nei bambini. Acta Otorhinolaryngol Ital 2017;37:270–5.
20. Fahy C, Jones NS. Nasal polyposis and facial pain. Clin Otolaryngol Allied Sci 2001;26:510–3.
21. Gelardi M, Iannuzzi L, De Giosa M, Taliente S, De Candia N, Quaranta N *et al*. Trattamento medico della rinosinusite cronica con poliposi naso-sinusale sulla base del sistema di grading clinico-citologico per un approccio medico personalizzato. Acta Otorhinolaryngol Ital 2017;37:38–45.
22. Tarabichi M. Characteristics of sinus-related pain. Otolaryngol Head Neck Surg 2000;122:842–7.
23. Jones NS, Cooney TR. Facial pain and sinonasal surgery. Rhinology 2003;41:193–200.
24. Perry BF, Login IS, Kountakis SE. Nonrhinologic headache in a tertiary rhinology practice. Otolaryngol Head Neck Surg 2004;130:449–52.
25. Graff-Radford SB. Facial pain. Curr Opin Neurol 2000;13:291–6.
26. Barbanti P, Fabbrini G, Pesare M, Vanacore N, Cerbo R. Unilateral cranial autonomic symptoms in migraine. Cephalalgia 2002;22:256–9.
27. Schreiber CP, Hutchinson S, Webster CJ, Ames M, Richardson MS, Powers C. Prevalence of migraine in patients with a history of self-reported or physician-diagnosed "sinus" headache. Arch Intern Med 2004;164:1769–72.
28. Eross E, Dodick D, Eross M. The Sinus, Allergy and Migraine Study (SAMS). Headache 2007;47:213–24.
29. Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache 2001; 41:638–45.
30. Lee J-H, Kim H-J, Hong Y-H, Kim KS. Underestimation of rhinogenic causes in patients presenting to the emergency department with acute headache. Acta Neurol Taiwan 2015;24:37–42.
31. Aaseth K, Grande RB, Kvaerner K, Lundqvist C, Russell MB. Chronic rhinosinusitis gives a ninefold increased risk of chronic headache. The Akershus

study of chronic headache. Cephalalgia 2010;30:152–60.
32. Lavi E, Gilden D, Nagel M, White T, Grose C. Prevalence and distribution of VZV in temporal arteries of patients with giant cell arteritis. Neurology 2015;85:1914–5.
33. Veldhoen S, Klink T, Geiger J, Vaith P, Glaser C, Ness T *et al*. MRI displays involvement of the temporalis muscle and the deep temporal artery in patients with giant cell arteritis. Eur Radiol 2014;24:2971–9.
34. Schmidt WA. Ultrasound in the diagnosis and management of giant cell arteritis. Rheumatology (Oxford) 2018;57(suppl_2):ii22–ii31.
35. Mokri B. Headaches in cervical artery dissections. Curr Pain Headache Rep 2002;6:209–16.
36. Biousse VMP. Carotid or vertebral artery disease. In: Carotid or Vertebral Artery Disease., Hrsg.: Carotid or Vertebral Artery Disease. Philadelphia: LippincottWilliams and Wilkins, 2006:911–8.
37. Abbott JJ, Newman AC, Schievink WI. Maxillary tooth pain as a symptom of internal carotid artery dissection: case series. J Am Dent Assoc 2017;148:399–403.
38. Benoliel R, Svensson P, Evers S, Wang S-J, Barke A, Korwisi B *et al*. The IASP classification of chronic pain for ICD-11: chronic secondary headache or orofacial pain. Pain 2019;160:60–8.
39. Capewell S, Ford ES, Croft JB, Critchley JA, Greenlund KJ, Labarthec DR. Cardiovascular risk factor trends and potential for reducing coronary heart disease mortality in the United States of America. Bull World Health Organ 2010;88:120–30.
40. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR *et al*. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med 2000;342:1163–70.
41. Foreman RD. Neurological mechanisms of chest pain and cardiac disease. Cleve Clin J Med 2007;74(Suppl 1):S30. https://doi.org/10.3949/ccjm.74.Suppl_1.S30
42. Kreiner M, Okeson J, Tanco V, Waldenström A, Isberg A. Orofacial pain and toothache as the sole symptom of an acute myocardial infarction entails a major risk of misdiagnosis and death. J Oral Facial Pain Headache 2020;34:53–60. https://doi.org/10.11607/ofph.2480.
43. Kreiner M, Alvarez R, Waldenstrom A, Michelis V, Muñiz R, Isberg A. Craniofacial pain of cardiac origin is associated with inferior wall ischemia. J Oral Facial Pain Headache 2014;28:317–21.
44. Myers DE. Toothache referred from heart disease and lung cancer via the vagus nerve. Gen Dent 2010;58:e2–e5.
45. Amirhaeri S, Spencer D. Myocardial infarction with unusual presentation of otalgia: a case report. Int J Emerg Med 2010;3:459–60.
46. Jalali N, Vilke GM, Korenevsky M, Castillo EM, Wilson MP. The tooth, the whole tooth, and nothing but the tooth: can dental pain ever be the sole presenting symptom of a myocardial infarction? A systematic review. J Emerg Med 2014;46:865–72.
47. Bakhshi M, Rezaei R, Baharvand M, Bakhtiari S. Frequency of craniofacial pain in patients with ischemic heart disease. J Clin Exp Dent 2017;9:e91–5.
48. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP *et al*. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation 2019;139:e56–e528.