ARTICLE

Facial presentations of migraine, TACs, and other paroxysmal facial pain syndromes

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Abstract

Objective

To assess the prevalence of facial pain (V2 and/or V3) presentations among nearly 3,000 patients with headache treated in a university tertiary care center.

Methods

Between 2010 and 2018, we routinely assessed the prevalence of facial pain presentations of all patients with primary headaches.

Results

Of 2,912 patient datasets, 291 patients reported facial pain either as an independent or as an additional symptom. Among patients with migraine, 2.3% (44 of 1,935) reported a facial involvement, most commonly in V2. Of these, 18 patients (40.9%) experienced the pain predominantly in the face. In patients with cluster headache, 14.8% (42 of 283) reported a facial involvement, of which 31.0% perceived the pain predominantly in the face. A facial involvement was seen in 45.0% of patients with paroxysmal hemicrania (9 of 20), 21.4% of patients with hemicrania continua (9 of 42), and 20.0% of patients with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing/short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (3 of 15). In addition, we present 6 patients who reported a constant side-locked facial pain with superseded well-defined facial pain attacks of 10- to 30-minute duration that appeared several times per day.

Conclusion

Our data suggest that a facial involvement in primary headaches is infrequent but not uncommon. A sole facial presentation of primary headache symptomatology seems to be exceptionally rare. We describe 3 different types of facial pain involvement and, in this context, distinguish patients with paroxysmal orofacial pain syndromes that have not been previously described. These patients may represent a new entity that could tentatively be called constant unilateral facial pain with added attacks.

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Glossary

CUFPA = constant unilateral facial pain with added attacks; **ICDH-3** = International Classification of Headache Disorders, 3rd edition; **ICOP** = International Classification of Orofacial Pain; **HC** = hemicrania continua; **IHS** = International Headache Society; **PIFP** = persistent idiopathic facial pain; **PH** = paroxysmal hemicrania; **SUNA** = short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms; **SUNCT** = short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing; **TAC** = trigeminal autonomic cephalalgia; **TN** = trigeminal neuralgia.

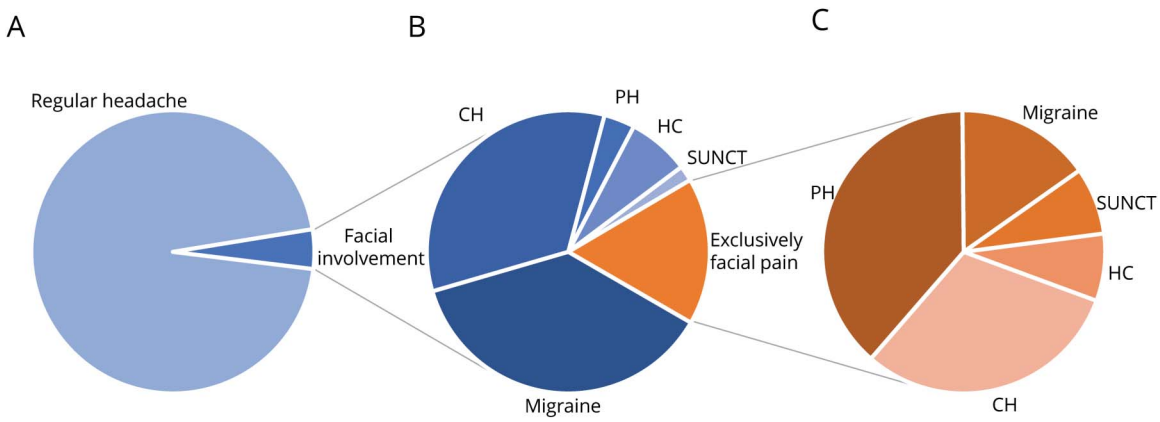
Headache is highly prevalent in the general population, affecting half or more of all adults and many children worldwide,[1] and is recognized to be in the top 5 of burdensome diseases.[2] In the current International Classification of Headache Disorders, 3rd edition (ICHD-3), the International Headache Society (IHS) distinguishes primary from secondary headaches,[3] with migraine being the most prominent primary headache syndrome. Although the name already implies that headaches are usually perceived in the head, it is recognized that some headache syndromes may have representations in the face.[4] Facial pain may be seen in patients with primary headache, either as a spread of pain or as a coactivation of the first and second divisions of the trigeminal nerve. Assuming that the clinical picture of a given headache biology should in principle not change, it is remarkable that the first cases have been reported only in the last few years[5–10] as either case reports or case series. Of note, the affection of limbs as part of the clinical spectrum of migraine and cluster headache is even more sparse but has been recently reported.[11–14]

For the sake of simplicity, (oro-)facial pain can be roughly distinguished into dental and nondental facial pain; dental includes intraoral pathologies and diseases of the masticatory organs. Chronic orofacial pain that usually has no morphologic cause, detectable by current diagnostic means, is usually either a constant burning or dull pain as seen in neuropathic pain syndromes (painful posttraumatic trigeminal neuropathy) and in persistent idiopathic facial pain (PIFP).

The literature on patients who report regular differentiated tooth pain or nonodontogenic orofacial pain attacks with complete remission between attacks is sparse at best. Few case reports exist that describe attacks that only occur in the face. Because most of these attacks are reported by patients with migraine or cluster headache and follow migraine or cluster headache attack duration, they have been called facial migraine[15] and facial cluster attacks.[16]

Such uncommon presentations of pain location present a considerable challenge to clinicians,[17] and patients often see many specialists before receiving a proper diagnosis and treatment. The fact that facial representations (figure) of headache are rather rare[4] underlines that the first division of the trigeminal nerve seems to be set apart from the rest of the trigeminal system, leading to important pathophysiologic and treatment considerations.[18] For a better pathophysiologic understanding and ultimately the development of adequate treatment regimens of facial pain syndromes, it is crucial that we understand whether facial presentations of primary headaches are the same disease with a different localization or whether they are in fact different syndromes.[19] A robust classification is hence key to a better general understanding of facial pain syndromes.[20] To add to the existing pool of data of

Figure Distribution of facial representations in our sample of 2,912 patients with headache and facial pain



(A) All patients with primary headache with the percentage of patients with headache with a facial involvement. (B) The separate entities of primary headache disorders with a facial involvement. (C) Pain syndromes exclusively affecting the face. CH = cluster headache; HC = hemicrania continua; PH = paroxysmal hemicrania; SUNCT = short-lasting unilateral neuralgiform headache with conjunctival injection and tearing.

facial pain syndromes, we systematically categorized the patients with facial pain seen in our specialized outpatient clinic and present in this article cases of primary headaches with facial affection and cases of pain syndromes not previously described.

Methods

The headache and facial pain outpatient clinic is a tertiary care center within the University Medical Center Hamburg-Eppendorf with ≈1,000 to 1,200 annual patient contacts. In addition to medical records, all patients were asked to fill out a custom-designed questionnaire about personal socio-demographic information, pain characteristics, and medical history, as well as other standardized questionnaires such as the Patient Health Questionnaire and the Migraine Disability Assessment.[21,22] Besides several dozen pain-related questions, we also routinely and actively asked all patients with headache specifically for facial involvement. Between 2010 and 2018, >2,900 datasets with a completed questionnaire plus the medical records were compiled and integrated in a structured extended database for research.

We mainly treated patients with primary headache syndromes such as migraine (59.6%), trigemino-autonomic cephalalgias (12.0%), medication-overuse headache (6.1%), and symptomatic headache syndromes (4.2%). Over the course of these nearly 10 years, we have also seen many patients with facial pain syndromes, of which ≈300 have provided a completed questionnaire.

Patients presenting with facial pain mostly had PIFP (31.6%), trigeminal neuralgia (TN), and rarely neuralgias of other cranial nerves (30.6%), as well as neuropathic or symptomatic pain syndromes (30.9%).

In this study, we present patients with primary headaches and a facial involvement (i.e., involvement of the second and/or third trigeminal branch [V2, V3]) and patients who consulted us exclusively regarding facial pain. Facial pain is defined as "pain below the orbitomeatal line, anterior to the pinnae and above the neck" by the ICHD-3 criteria.[3] For practical reasons, our definition of facial pain is stricter. Pain of the eye, which is below the orbitomeatal line, is extremely common both in migraine and especially in cluster headache, which is why we included the orbital area, but only if the patient positively excluded headache.[23,24] The inclusion criteria for patients with primary headaches were that the patient fulfilled the corresponding criteria specified in the ICHD-3, including probable cases.[3] Patients with orofacial pain who also had alveolar or dental problems that could explain the pain attacks were excluded. Patients consulting our clinic were typically referred by dentists. In the rare cases when patients with orofacial pain were not referred but consulted us as a first contact, we asked about their dentist's evaluation first.

We distinguished 3 types, with the first one being the most common:

1. Type I: pain is perceived in the head and face either concomitantly or independently, V1 and V2 and/or V3, respectively. type Ia, pain is perceived predominantly in V1 but also concomitantly or independently in V2 and/or V3; and in type Ib, pain is perceived in predominantly V2 and/or V3 but also concomitantly or independently in V1.
2. Type II: the focus of pain has shifted over time. The initial primary headache ceased to affect V1 and is now exclusively present in V2 and/or V3 (maintaining initial timing and characteristics of attacks and associated symptoms).
3. Type III: headache-naive patients develop de novo orofacial pain attacks that resemble one of the primary headache types in pain character, duration, and severity with or without associated symptoms of such headache types.

As part of our workup, our clinicians fill out a custom-designed questionnaire and, besides other clinical issues, specifically document which trigeminal branches are affected by the pain (left, right, V1, V2, V3) and specifically indicate whether there is also a facial involvement because it has been our experience that many patients do not report a facial involvement of their headache attacks when it is not primarily affected. The distribution patterns of the trigeminal branches are usually determined by reference of an acknowledged German anatomy atlas.[25] Whenever additional information besides the medical records and questionnaires was needed, we called the patients by phone to receive all required information.

Standard protocol approvals, registrations, and patient consents

The collection of data for this study was approved by the local ethics committee of the chamber of physicians of Hamburg, Germany (PV 3185). Patients gave written informed consent to participate in the study.

Data availability

Deidentified participant data and detailed tables for each syndrome will be shared on reasonable requests to the corresponding author.

Results

Facial presentations of migraine

Migraine is defined as a "recurrent headache disorder manifesting in attacks lasting 4–72 hours" accompanied by typical symptoms such as nausea and/or photophobia and phonophobia.[3] Facial affection in patients with migraine is rare[4,6,26–28] but not uncommon and is referred to as facial migraine[29] or lower-half facial migraine. It is noteworthy that these syndromes are explicitly not considered separate entities from regular migraine by the ICHD-3.

As a general rule, facial presentations of migraine seem to be associated with later age at onset,[30] and aura seems to be absent or at least less common in facial presentations of migraine.

Table 1 shows demographic data of 44 patients with migraine, corresponding to 2.3% of our database (n = 1935) who reported a facial involvement; 90.9% (n = 40) of these patients were female. The average age was 43.2 ± 14.4 years. The duration of migraine was 152.8 ± 142.3 months (range 7–576 months), and the average age at onset was 30.5 ± 15.8 years.

Twenty-six patients (59.1%) had pain localized mainly in V1 that also affected V2 or V3 (type Ia); 12 patients (27.3%) had pain localized mainly in V2 or V3 that also affected V1 (type Ib); 5 patients (11.4%) used to have a migraine in V1 but the focus shifted to V2 or V3 with no headache (type II); and only 1 patient reported an exclusive presentation of facial pain that otherwise resembled migraine symptoms and did not have any history of headaches (type III).

The most common facial involvement was reported in the maxilla, often also involving pain of the teeth. The mandible was affected in only 4 cases of facial involvement (9.3%).

Auras were reported in patients presenting with type Ia (n = 11) and type Ib (n = 2) but not in those with type II or III.

Table 1 Data of patients with facial presentations of migraine, cluster headache, PH, HC, and SUNCT following ICHD-3 criteria

Disease entity, % of facial presentation	Type	Patients (female/male), n	Age of onset (mean ±SD), y	Duration of disease at first consultation (mean ± SD), mo
Migraine, 2.3 (44/1,935)	Overall	44 (40/4)	30.5 ± 15.8	152.8 ± 142.3
	Type Ia	26 (23/3)	25.1 ± 13.1	189.1 ± 159.2
	Type Ib	12 (12/0)	33.7 ± 13.1	96.6 ± 83.9
	Type II	5 (4/1)	44.9 ± 18.5	93.0 ± 94.3
	Type III	1 (1/0)	59	180
Cluster, 14.8 (42/283)	Overall	42 (14/28)	38.7 ± 13.2	111.6 ± 133.1
	Type Ia	29 (9/20)	36.5 ± 12.4	100.7 ± 97.7
	Type Ib	9 (4/5)	40.9 ± 15.5	184.7 ± 205.5
	Type II	NA	NA	NA
	Type III	4 (1/3)	48.8 ± 4.4	26.5 ± 40.1
PH, 45.0 (9/20)	overall	9 (7/2)	45.4 ± 15.5	52.6 ± 49.6
	Type Ia	NA	NA	NA
	Type Ib	4 (3/1)	52.3 ± 10.8	99.0 ± 39.2
	Type II	NA	NA	NA
	Type III	5 (4/1)	39.9 ± 16.5	15.4 ± 9.2
HC, 21.4 (9/42)	Overall	9 (5/4)	38.3 ± 11.7	40.3 ± 25.8
	Type Ia	2 (1/1)	50 and 48.2	60 and 10
	Type Ib	6 (4/2)	32.6 ± 10.4	44.8 ± 26.8
	Type II	NA	NA	NA
	Type III	1 (0/1)	51	24 m
SUNCT, 20.0 (3/15)	overall	3 (1/2)	43.1 ± 8.8	27.3 ± 15.7
	Type Ia	NA	NA	NA
	Type Ib	2 (0/2)	31.2 and 46	10 and 48
	Type II	NA	NA	NA
	Type III	1 (1/0)	52	24

Abbreviation: HC = hemicrania continua; NA = not applicable; PH = paroxysmal hemicranias; SUNCT = short-lasting unilateral neuralgiform headache with conjunctival injection and tearing.

Four patients (2 with type Ib, 2 with type II) had probable migraine with facial involvement. They had episodic pain attacks of typical migraine duration, worsening with physical activity and triptan responsiveness but lacking the typical accompanying symptoms such as photophobia, phonophobia, nausea, or vomiting during the attacks.

One patient (patient 44) had menstruation-related migraine (following ICHD-3 criteria) for 20 years but also had independent facial migraine-like attacks in the maxilla for 5 years. These attacks did not occur simultaneously and differed in location (frontotemporal vs maxilla only) with significantly less prominent photophobia and phonophobia during the facial pain attacks. However, both types of attacks responded well to triptans (rizatriptan 10 mg), and physical exercise worsened the pain in both instances. The patient could clearly differentiate between the 2 types of attacks.

Facial presentations of trigeminal-autonomic cephalalgias

Facial representations of cluster headache

Cluster headache usually presents with severe periorbital stabbing pain. This pain may radiate to adjacent areas. A facial affection is very common in cluster headache, with up to 50% in the upper teeth, 45% in the jaw and cheek each, and 32% in lower teeth.[23] Sole presentation in the maxilla or mandible (V2 or V3 respectively) is less common, except that the cluster headache pain is sometimes described as toothache-like at the very beginning of an attack.[31,32]

Table 1 shows the demographic details of 42 of 283 patients (14.8%) with cluster headache in our database reporting a clear facial affection. Twenty-eight (66.7%) of these patients were male. The average age was 48.0 ± 11.3 years. The average duration of the cluster headache was 111.6 ± 133.1 months (range 1–720 months), and the average age at onset was 38.7 ± 13.2 years. A spread from V1 to V2 and/or V3 (type Ia) was present in 29 patients (69.0%). V2 was the area mainly affected, and a spread to V1 (type Ib) was reported in 9 cases (21.4%). Four patients (9.5%) had pain exclusively in V2 and/or V3 without any spread to V1 and no relevant history of comparable headaches (type III). Typical attacks with autonomic symptoms and a side-locked pain were seen in 3 of these patients. One patient (patient 9) presented with 1 to 2 severe pain attacks of 20 to 90 min/d that changed sides between episodes and did not have autonomic symptoms. This patient, however, had a distinct sense of restlessness and agitation during pain attacks.

Facial representations of paroxysmal hemicrania

While the ICHD-3 criteria describe paroxysmal hemicrania (PH) as "severe unilateral orbital, supraorbital and/or temporal pain,"[3] very rarely the involvement of V2, V3, the jaws, and teeth has been reported. [33] Table 1 shows 9 patients with a facial involvement and attacks that clinically appeared like PH or probable PH. This corresponds to a rate of 45.0% (9 of 20 of our database). The mean age at first consultation was 49.8 ± 16.7 years; the mean age at onset was 45.4 ± 15.5 years; and the mean duration of pain at first consultation was 52.6 ± 49.6 months (range 5–144 months). Seven patients were female. The pain was perceived mainly in V2 and/or V3 but also spread to V1 in 4 patients (type Ib) and was confined to only V2 and/or V3 without any spread or history of headache in 5 patients (type III).

Patients had pain attacks of typical length with typical autonomic features accompanying the pain and/or restlessness and agitation during the attacks. In addition, indomethacin was a successful treatment option for 6 patients. One patient did not respond to indomethacin; 1 patient had to discontinue the use of indomethacin before therapeutic doses were reached; and 1 patient declined to test indomethacin.

Some patients showed a typical length of attacks and indomethacin responsiveness but reported <5 attacks per day and did not have typical autonomic features or agitation during attacks. We note that patients with facial attacks may, for anatomic or physiologic reasons, show a different or no autonomic phenotype.

Six patients had a history of migraine. One patient (patient 9) with pain paroxysms located exclusively in the mandible (according to the World Dental Federation notation) did not have PH-typical autonomic symptoms but reported a tickling urge to cough in ≈25% of the attacks. These phenomena always started with the pain paroxysms and lasted for the whole attack and exclusively appeared during pain paroxysms. Another patient (patient 7) with the pain occurring mostly in the maxilla and mandible reported next to ipsilateral lacrimation, particularly hypersalivation, during attacks. The phenomena of an urge to-cough and the hypersalivation could represent vagal/parasympathetic symptoms of the lower half of the face in these patients.

Facial representations of hemicrania continua

Hemicrania continua (HC) usually affects the temporal, orbital, frontal, and/or parieto-occipital region. It is, however, also seen to a lesser degree in the distribution areas of V2 and V3 (infraorbital, maxillary, teeth, and jaw).[34,35]

The differential diagnosis of regular HC is challenging, and HC is often misdiagnosed as migraine, temporomandibular joint dysfunction, dental pain, sinus headache, or cluster headache.[7,36,37] Because of the rarity of HC and overlap of symptoms with other chronic pain syndromes, facial presentations of HC are even more difficult to diagnose. Furthermore, common autonomic symptoms such as lacrimation could be absent in V2 and V3 pain paroxysms, and autonomic symptoms could be different in presentation as mentioned above, further complicating a correct diagnosis.

Table 1 shows 9 patients (21.4% of 42 in our database) with a facial involvement in HC. Five patients were female. The

mean age at first consultation was 41.7 ± 11.5 years; the mean age at onset was 38.3 ± 11.7 years; and the mean duration of pain at first consultation was 40.3 ± 25.8 months (range 5–66 months).

Only 1 patient (patient 1) had a constant unilateral pain localized in the mandible without any referral to V1 or history of headache (type III). This patient experienced ipsilateral lacrimation during pain exacerbations but did not respond to indomethacin. The pain was often localized in the maxilla and radiated to V1 in 6 patients (type Ib) and predominantly localized in V1 radiating to V2 in 2 patients (type Ia). All patients had unilateral side-locked pain, but 1 patient with episodic HC (patient 4) reported a change of sides between episodes. Unremitting pain was observed in 7 patients, whereas 2 patients reported pain episodes. These 2 patients did not try indomethacin because both of them did not have pain when consulting us and did not experience new episodes until recently. A therapy with indomethacin was successful in 5 patients. Whether indomethacin was successful in patient 2 is unknown because he was lost to follow-up, and patient 1 did not respond to indomethacin.

Short-lasting unilateral neuralgiform headache attacks

According to the ICHD-3 classification, short-lasting unilateral neuralgiform headache attacks are currently divided into short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA).[3] It was proposed that SUNCT might constitute a subtype of SUNA.[38] However, it is also argued that the 2 entities may indeed be separate and not connected to each other.[39]

The first review of SUNCT mentioned occasional spreads to the second trigeminal branch, i.e., the cheek and the palate. However, these were not mentioned as the main areas of pain.[40] It was also stated there that a downward extension of the pain into maxillary and mandibular trigeminal divisions was absent.

A later review found affections of V2 in 33% and in the teeth of 21% of the documented patients with SUNCT.[41] For SUNA, an affection of V2 and V3 was described in 33% each and for the teeth in 22% in the patients.[41] Sole presentations in the areas of V2 or V3 without spreading to V1 were not reported.

The current ICHD-3 requires "moderate or severe unilateral head pain, with orbital, supraorbital, temporal and/or other trigeminal distribution" in its diagnostic criteria for SUNCT.[3] The clinical appearance of the short-lasting unilateral neuralgiform headache attacks, however, is very similar to that of TN, which makes the correct diagnosis difficult. This difficulty is further enhanced when the region of main affection is not the first but the second or third trigeminal branch, where the typical autonomic signs of SUNCT/SUNA might be less distinct, absent, or even different (as mentioned above). Important aspects of the differential diagnosis between TN and SUNCT have been discussed previously.[39] Prominent were the rarity of nightly attacks, the lack of a refractory postictal phase after pain paroxysms, and the need for rougher stimuli to trigger attacks in SUNCT.

Our database showed 3 patients (of 15) with short-lasting unilateral neuralgiform headache attacks and affection of V2 and/or V3 (table 1). Two patients had a typical SUNCT syndrome according to ICHD-3 criteria[3] that radiated from the maxilla in both cases. One patient presented with pain only in the second and third trigeminal branches accompanied by extensive autonomic symptoms and never had a relevant history of headache (type III). This patient had intracranial aneurysm bleeding 9 years before pain onset that was treated with coiling when the diagnosis was made and again 2 years before the first onset of facial pain symptoms.

To distinguish these patients from patients with ordinary SUNCT/SUNA and thus allowing us to study them, we propose the term short-lasting unilateral neuralgiform facial pain attacks, which could be adapted for patients with such pain attacks confined to the second and third trigeminal branch.

Constant unilateral facial pain with added attacks

In addition to the manifestations of primary headaches in the trigeminal maxillary and mandibular branches, we describe exclusive facial pain syndromes that do not fit well into any of the existing criteria for either primary headache or facial pain syndromes, specifically PIFP, which is defined as constant facial pain without any other positive or negative features and otherwise intact sensory perception (e.g., no hypoesthesia, dysesthesia, or anesthesia). Orofacial or dental causes were meticulously ruled out, including cone beam computed tomography when applicable. Magnetic resonance brain scan was done in all patients. There was no relevant medical history aside from hypothyroidism in 2 patients. The neurologic examinations showed no relevant abnormalities, and all patients were also seen by dental specialists. The main feature is a side-locked constant facial pain in the mandible and/or maxilla with additional pain attacks in the same region of intermediate lengths. The character of this facial pain is dull and pressing, and the pain may undulate over the day. Table 2 shows the demographic data of 6 female patients. The mean age at first consultation was 53.5 ± 9.6 years (range 41–67 years), and the duration of the pain was 15.7 ± 13.0 months (range 2–36 months).

The pain was always one-sided but in 1 patient (patient 1) changed sides over time and in another patient (patient 2) occurred very rarely on the other side. Headache was absent in all but 1 patient (patient 5) with typical episodic migraine attacks lasting 1 to 2 days since her youth that was independent from the facial pain.

Table 2 Demographic data of 6 patients with CUFPA

Patient	Sex	Age at first consultation, y	Duration of pain at first consultation	Remission? Duration overall?	Site of consistent pain	Intensity of chronic pain	Site of attacks	Length of attacks, min	Pain intensity; attacks	Attacks, n	Episodic character?
1	F	47	3 mo	No remission. Duration overall ≈1 y	Left mandible	Used to be ≈5/10, under pregabalin 1/10	Left mandible, radiating to maxilla, molar, not clearly localizable	30	Used to be 8/10, under pregabalin 3/10	3/d	Chronic
2	F	41	3 y	No remission, but less intense. Duration overall ≈4 y	Right mandible, seldom left side	Used to be 3/10, now 0–2/10	Same location, predominantly right	30	Used to be 6–7/10, now 3–5/10	Used to be 3-4/d, now 1–2/wk	Chronic
3	F	62	2 mo	No remission, but less intense. Duration overall ≈2 y	Left mandible and teeth	2/10	Left maxilla and mandible	15	9/10	Up to 20/d	Chronic
4	F	45	2 y	Unknown	Right maxilla, radiating to ear	5/10	Starting in right mandible, radiating to right maxilla and ear	15	10/10	5–10/d	Possible
5	F	59	2 y	Unknown	Right maxilla, radiating to eye, temporal and TMJ	4/10	Same location	10	8/10	10–20/d	Chronic
6	F	67	5 mo	Remission after a total of 1.5 y	Left mandible, radiating to maxilla, perceived as toothache	2/10	Same location	10–20	8/10	2–3/d	Episodic

Trigger?	Autonomic symptoms	Photo-, phono-, osmophobia or nausea/vomiting	Side-locked?	Restlessness or agitation	Headache history	Medication that helped	Indomethacin?	Trauma?	Relevant medical history	Imaging and neurologic examination
Possible mechanic trigger like chewing	No	No	Yes, but changed sides over time	No, petrifaction	None	Pregabalin 150 mg,	Not tried	Fractured larynx and mandible 30 y ago	None	w/o pathologic/ abnormal finding
None	No	No	Yes, but rarely changing sides	No	None	None (opioids, antidepressants, anticonvulsant, prednisolone tried)	Did not help	Dental extraction and infection before onset	None	w/o pathologic/ abnormal finding
Yes, warmth	No	No	Yes	No	None	Ibuprofen 400–800 mg	Not tried	none	None	w/o pathologic/abnormal finding
No	No	No	Yes	Possible		Carbamazepine 400 mg, Indomethacin 75 mg (unclear whether episode would have ended anyway)	Possible	None	Hypothyroidism	w/o pathologic/ abnormal finding

Continued

Table 2 Demographic data of 6 patients with CUFPA *(continued)*

Trigger?	Autonomic symptoms	Photo-, phono-, osmophobia or nausea/vomiting	Side-locked?	Restlessness or agitation	Headache history	Medication that helped	Indomethacin?	Trauma?	Relevant medical history	Imaging and neurologic examination
Possible, chewing	No	No	Yes	Unknown	Migraine	Metamizole	Not tried	Dental restorations before onset of pain	None	w/o pathologic/ abnormal finding
No	No	No	Yes	Yes	None	None	Did not help and discontinued (side effects)	Operations of sinus maxillaris of both sides	Hypothyroidism	w/o pathologic/ abnormal finding

Abbreviations: CUFPA = constant unilateral facial pain with added attacks; TMJ = temporomandibular joint; w/o = without.

In addition to the constant facial pain, all patients had distinct pain exacerbations (attacks) of 10- to 30-minute duration that occurred between 2 and 20 times per day during active episodes and without medication. No patient reported autonomic features or photophobia, phonophobia, or osmophobia during the constant pain or during the attacks. One patient (patient 1) reported that she was petrified during attacks but did not have restlessness or agitation typical for CH or PH. Another patient (patient 4) had a slight sense of unrest during attacks but not as distinct as is commonly seen in trigeminal autonomic cephalalgias (TACs).[42]

In 3 patients, the well-defined attacks occurred exclusively spontaneously without any triggers; in 2 patients, chewing was reported as a possible trigger of attacks; and 1 patient reported that warm drinks may sometimes trigger attacks. However, all patients had spontaneous attacks. Alcohol did not trigger attacks in any patient. The pain syndrome was chronic in 4 of 6 patients; 1 patient (patient 4) had episodic bouts of constant pain and attacks with intermittent episodes with nearly no pain at all, and 1 patient (patient 6) experienced a remission after ≈1.5 years.

Because of the length of attacks, we proposed the administration of indomethacin to all patients. Possible relief was reported by 1 patient (patient 4), but this patient also took 400 mg carbamazepine and had a possible episodic character of the syndrome. Three patients did not try indomethacin; in 2 patients, indomethacin had no effect on either the constant or the paroxysmal pain. Other successful or partially successful medications were pregabalin, ibuprofen, or metamizole in 4 patients. Two patients did not experience relief from any medication tried (including opioids, antidepressants, anticonvulsant, cortisone).

The striking feature of all these patients was the well-defined and distinct nonneuralgic attacks that superseded a side-locked dull featureless pain in the same facial region. All of these patients reported spontaneous attacks; none of these patients described associated symptoms. For these reasons, we believe that this could be a facial pain disorder not well described or researched yet. We propose the term constant unilateral facial pain with added attacks (CUFPA) that could be applied for patients with a constant unilateral facial pain with distinct pain attacks.

Discussion

Understanding facial involvement in primary headache syndromes could potentially provide decisive insights into headaches in general. A facial involvement seems to be rather infrequent but not uncommon. Interestingly, however, a sole presentation of primary headache symptomatology in the second or third trigeminal division without involvement of the first trigeminal branch or the head in general and without any relevant history of headaches seems to be exceptionally rare.

Even though it is the same nerve, the first trigeminal branch by itself seems to play a distinguished role in the pathophysiology of head pain.[18]

At this point, it is difficult to decide whether the exclusive presentation of orofacial pain that resembles the clinical primary headache syndromes in length of attacks and triggers or associated symptoms is just another representation of such headache syndromes or in fact a distinct facial pain syndrome. It seems that paroxysmal orofacial pain syndromes are distinct from paroxysmal headache syndromes in associated symptoms and response to medication. However, this distinction can be verified only when the pathophysiologic context, e.g., electrophysiologic, imaging, or genetic findings, are properly investigated. It therefore makes sense to list them as distinct entities to allow comparison of findings of such patients and patients with analogic headache syndromes.[43,44]

In a complex CNS disease such as migraine, it could be argued that it might not be feasible to focus on the region of pain alone when defining different forms of migraine. This seems fair enough in cases with a clear representation of migraine following ICHD-3 and an additional spread of pain to the neck or face. That being said, the mere fact that there seem to be only very few cases with a sole facial affection with migraine-like features makes these cases even more prominent, and investigating the pathophysiology of these extraordinary cases could ultimately help to form a better general understanding of migraine and TACs. Especially for this reason and in accordance with the upcoming integrated International Classification of Orofacial Pain (ICOP),[45] we support the notion of implementing facial migraine or orofacial migraine as a *terminus technicus*. For the same reason, we also propose classifying facial presentations of primary headache syndromes into the 3 different subtypes (types I, II, III) mentioned above. This will be the only way to directly compare such representations of orofacial pain and answer the question of whether any of them indeed qualifies as a separate pathophysiologic entity. Of note, patients who can be categorized as type II were found only in the migraine group. The implications of this, however, are not clear. Interestingly, a shift in the opposite direction from V2/V3 to V1 has never been documented but may well have been neglected until now (by patients and clinicians alike). In addition, the variance of age between groups is rather large in our sample, which needs to be prospectively investigated because it was described previously that facial presentations can be associated with a later age at onset.[30]

We note that the clinical representation of patient 44, who clearly distinguished attacks of migraine from independent attacks in the maxilla with no overlap of pain location whatsoever, supports this concept: both phenotypes (headache attacks and facial pain attacks) coexist independently from each other, exhibiting slightly different extents of accompanying symptoms, but both respond well to triptans.

There is no question that further studies (i.e., functional and structural imaging, therapeutic interventions) are needed to provide more robust evidence for this case. Nonetheless, it is especially important to raise awareness for atypical presentations of primary headaches to provide better and faster care to the affected patients. Cooperation and combined scientific efforts between head and facial pain specialists are crucial in that respect. A landmark cooperative endeavor involving the Orofacial and Head Pain Special Interest Group of the International Association for the Study of Pain, the International Network for Orofacial Pain and Related Disorders Methodology, the American Academy of Orofacial Pain, and the IHS is currently working on a first ICOP.[45]

A limitation of our study and a possible factor of underrepresenting facial affection of primary headaches lies in its retrospective nature. It is possible that, due to the lack of clinical implications, a facial spreading of pain in headache either might not have been mentioned by the patient or might not have been explored explicitly by the consulted physician. It is therefore likely that we underestimate a facial affection in primary headaches, and previous studies indicate this.[24] The patients described as having CUFPA would theoretically fit into the criteria of PIFP as defined by the IHS,[3] which momentarily allows sharp exacerbations without more detailed information and possibly referring to neuralgiform stabs, which are not uncommon in neuropathic pain. It is widely accepted that the diagnostic criteria of PIFP are far from ideal, and it has been proposed that PIFP very likely includes different pain syndromes.[46] While there may be subclinical neuropathic pain syndromes misdiagnosed as PIFP, the nature of prominent and very distinct attacks in our CUFPA cohort strongly suggests a clinical subgroup of its own right. These syndromes show similarities in attack length with paroxysmal headaches but absolutely lack autonomic features and instead are superimposed on a constant dull background pain. We note that all of our patients were referred to us because of the constant pain, and attacks were not noted by the referring dentists. Indomethacin does not seem to have an effect in CUFPA, but this need to be properly studied. Following ICHD-3 logic, we propose the following diagnostic criteria for CUFPA to homogenize further research:

1. Mild to moderate unilateral facial pain fulfilling criterion 2
2. Lasting for >3 months
3. Additional attacks of moderate to severe intensity fulfilling criteria 4 and 5
4. Attack length of 10 to 30 minutes
5. Between 2 and 20 attacks per day
6. Normal clinical neurologic examination, and a pathologic cause excluded by appropriate investigations
7. Not better accounted for by another ICOP or ICHD diagnosis

Patients with chronic facial pain are often in a diagnostic and therapeutic trap, leading to an average pain history of

a decade.[17] Because we know so little about these syndromes, such entities have been called atypical facial pain in the past, which is now called PIFP, and facial pain experts unanimously agree that this oversimplifies a complex disorder. The last 20 years has seen tremendous efforts, and as a consequence, the field of facial pain has advanced greatly. Perhaps the most success so far has been achieved regarding overriding conceptual models for orofacial pain.[46,47] Cross talk between the disciplines is important, and a concrete achievement out of such collaborations is perhaps that we are at the brink of a new and generally accepted facial pain classification.[18] Now is the right time to join forces to eventually provide patients with ever-improving therapeutic strategies.

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Appendix Authors

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Christian Ziegeler, MD	University Medical Center Hamburg-Eppendorf, Hamburg, Germany	Author	Acquisition of data; interpreted the data; analyzed the data; drafted the manuscript for intellectual content
Arne May, MD, PhD	University Medical Center Hamburg-Eppendorf, Hamburg, Germany	Author	Design and conceptualized study; interpreted the data; analyzed the data; revised the manuscript for intellectual content

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