Unilateral headaches and their relationship with cervicogenic headache

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ABSTRACT

The concept of headache originating/ starting in the neck is revised and considered in the light of previous descriptions of syndromes and entities and with reference to the current diagnostic systems for the classification of headache and other head pain. Cervicogenic headache (CEH), a clinical picture recently described by Sjaastad and coworkers and listed in the International Association for the Study of Pain (IASP) Classification, is analyzed, also taking into consideration its diagnostic criteria in terms of sensitivity and specificity.

The problem of a differential diagnosis with migraine, tension headache and other well defined forms of unilateral headaches is discussed with reference to a case series of 114 patients who were selected based on their adherence to two fundamental criteria: (i) side-locked unilaterality of pain; and (ii) pain starting in the neck and spreading to the frontoorbital area. Based on the results, these simple criteria can contribute to a preliminary identification of possible CEH cases that may then undergo a sequence of clinical and instrumental procedures in order to confirm the diagnosis and, possibly, to localize the level(s) of dysfunction in the cervical spine which may be the target for therapeutic investigations, whether invasive or non-invasive.

Introduction

The clinical phase of the diagnostic process in headache, as in any other disorder, is invariably based upon the identification and the weighted analysis of a few fundamental clinical variables as they emerge from the patient's history. A side-locked unilaterality of symptoms in the presence of short-lasting attacks, is often enough to address the diagnosis towards some particular forms of primary headache such as Cluster Headache (CH) (13-26) and Chronic Paroxysmal Hemicrania (CPH) (13-14). Unilaterality is also a mandatory criterion for cranial

neuralgias and other head pain with organic causes, but the relevance of this factor becomes very weak among other episodic and more or less chronic headaches, namely Migraine without aura (M) and Tension Headache (TH). This low to negligible importance of unilaterality as a distinctive feature is clearly evident when considering the Diagnostic Criteria of the International Headache Society (IHS) (13) and is supported by epidemiological studies reporting unilaterality of pain in percentages of 16 to 21% for M and 4.1 to 12.5% for TH, respectively (15-18).

However, it is well known that the sensitivity and specificity of the IHS criteria may vary for different forms of headache, with the result of an accordingly variable number of unclassified headaches, as well as possible diagnostic overlap. Furthermore, the unilaterality factor is simply not included for the identification of the many conditions listed in Section 11 of the IHS, even if it is taken as a general assumption in the diagnostic criteria that "headache is located to the affected facial or cranial structure and radiating to surroundings" (13). But it is also clear that many of the conditions listed in Section 11 are commonly recognized as being capable of contributing to a side-locked unilateral presentation of M and TH for variable periods of time in many cases - disorders of the head and neck as causes of a prevalently unilateral presentation of symptoms in primary headache patients.

Finally, regarding IHS subgroup 11.2 (headache or facial pain associated with disorders of the neck), it should be noted that the low specificity of the criteria for M and TH may have reduced to a minimum the epidemiological consistency of head and neck (unilateral) pain of cervical origin, one of the most common features among spinal pain syndromes. In fact, although reliable epidemiological studies are limited, the estimated prevalence of cervical pain in the general adult

population is 13.8% (cervical complaints lasting over 6 months), and it is among these patients that cases with unilateral symptoms of head and neck pain should be selected for further investigation and more accurate classification (30).

A practical approach to this matter, i.e. pain of cervical origin starting in the neck and back of the head, currently the object of various diagnostic and therapeutic procedures (often conceived and developed by pain-specialists, within and outside official medical circles), tend to distinguish between localized cervical pain, cervical pain with radicular radiation to the shoulder/arm, cervicogenic headache as a distinct and definite entity, plus some referred pain syndromes such as atypical facial (neuralgiform) pain of cervical origin (20-22). In this context, the contribution of the Trondheim group is worth mentioning; from the early 1960s they have dedicated much work to the description and definition of various new categories of unilateral headaches including cervicogenic headache (CEH), a new syndrome now acknowledged by the medical literature (IASP) (14). Without this contribution from O. Sjaastad and co-workers, we would still be looking at the heterogeneous group of unilateral headaches in the absence of evidence-based principles and criteria for a reliable diagnosis and appropriate treatment (23, 27, 29).

The aim of the present paper will be therefore the description of the main general characteristics of those headaches presenting with a strict unilateral expression of symptoms and sign, giving particular emphasis to CEH, a now welldefined clinical entity already described by several authors (4-6), who have underlined the cervical origin of the pain symptoms and of some of the local associated phenomena. These authors had been observing for the most part patients with unilateral pain involving the head and neck, frequently presenting with head/neck trauma in their history and with diffuse degenerative changes in the cervical spine (10). At least some of these patients can now be considered for a diagnosis of possible/probable CEH based on a well defined set of validated diagnostic criteria that make this entity recognizable on clinical grounds (31).

Definition and characteristics of CEH

The list of headaches (Table I) and other head pain (vascular, neuralgiform, pure neuralgic) characterized by frequent, prominent or constant unilaterality includes some primary disorders, namely M with or without aura, CH, short-lasting paroxysmal attacks with local autonomic phenomena (CPH and SUNCT [short-lasting unilateral neuralgiform attacks with conjunctival ingectia and tearing]) as well as chronic/fluctuating and more or less continuous forms, namely hemicrania continua (HC) and CEH, which are extremely different with regard to the age at onset, gender, mode of autonomic involvement, severity, evolution and prognosis. Some forms seem to be relatively stable over time, others tend to evolve or change; different patterns of response to specific treatment and procedures, the presence/absence of precipitating mechanisms, and variable interference with physiological functions are also aspects contributing to the definition of the respective entities in clinical, pathophysiological and therapeutical terms.

Apart from these similarities and differences, a general concept must be kept in mind when investigating unilateral headaches, i.e. the need for a complete diagnostic work-up in order to rule out organic causes. In this field and for some particular forms, symptomatic cases are, in fact, far more frequent than among unilateral headaches of the migraine and tension type. On the other hand, even when a major pathology has been excluded by appropriate investigation, functional or morphological abnormalities and alterations may still frequently be found, which are difficult to correlate with the clinical picture in a causeeffect relationship.

This may be particularly true for CEH,

which has been essentially described and defined as a primary form of (unilateral) headache with identifiable characteristics and requisites, even if in the broad sense (CEH syndrome) it may include a still unidentified number of symptomatic cases.

CEH as originally described and more recently confirmed by the observation of large case series, is in principle any headache having its origin in the neck (or back of the head), at different segmental levels, with the involvement of one or more structures: skeletal muscle, joints, intervertebral discs, ligaments, nerves, roots, vessels and other deep somatic structures (11-12).

Trauma, overload, posture and other factors may induce, precipitate, or aggravate some functional (reversible) alterations or damage (sometimes pre-existing, as a predisposing condition) at the cervical level up to a critical level beyond the threshold of clinically relevant phenomena, thus initiating the symptomatology. In this respect CEH is indeed an acquired condition and its evolution - from the pain episodes typical of the early phase to an almost continuous pain - points to a combination of mechanisms, including the persistent activation and sensitization of deep somatic afferents, central sensitization, and other mechanisms common to neuropathic pain with the correlated local autonomic involvement. Indirect evidence of these mechanisms comes from the observations of various authors who described the pain patterns evoked by stimulation of the cervical zygapophyseal joints, as well as by cervical discography, and the possibility of inducing, at the symptomatic level (in cases with positive provocative tests) long-lasting anaesthetic blocks or radiofrequency lesions (7-8-30).

Besides its origin from the neck, CEH is

Table I. Headaches and related disorders with unilateral expression, i.e. cluster headache, chronic paroxysmal hemicrania, hemicrania continua, SUNCT (short-lasting unilateral neuralgiform attacks with conjunctival ingectia and tearing), and cervicogenic headache.

- · Migraine with and without aura
- Trigeminal V_1 neuralgia and Reader's syndrome
- Carotidynia; spontaneous dissection of neck arteries; neck-tongue syndrome; post endo-arterectomy and post-traumatic dysautonomic cephalalgia; Tolosa (Hunt) syndrome.

defined as a rule by the unilaterality of the pain and other accessory symptoms, which contribute to separate it from the symptoms produced by congenital or acquired diseases and disorders of the neck, including early and (at least in part) late whiplash-associated disorders (9). Even if unilaterality is by definition required as side-locked, pain may eventually also spread across the midline, particularly in cases with a severe and longlasting picture. The unilaterality factor is also associated in CEH with the possibility of precipitating the attacks mechanically and of observing (in 50 to 70% of cases) a non-radicular, ipsilateral, shoulder/arm pain, thus confirming the existence of an ipsilateral focus where pain is generated.

Diagnostic aspects of CEH

As demonstrated by our group, a significant number of patients may be identified as possible cases of CEH based on the presence of the two factors described above: unilateral pain without side-shift and pain starting from the neck and spreading to the fronto-ocular area (once CH, CPH and HC have been excluded by their respective criteria) (1). Among this population, shown by the 114 cases we have followed so far, 24% fit the IHS criteria for M without aura and 16% those for headache associated with neck disorders (HN), while over 60% remain unclassified. As seen in Figure 1, when the criteria for CEH are instead applied, 47% of the cases may be allocated to this diagnostic group, with the possibility of diagnostic overlap between CEH and M or HN in 15% of the cases.

In 53% of the population studied (62/114 cases) both of the inclusion criteria (unilaterality and neck origin of the headache) were satisfied, and the frequency of adherence to the other major and minor diagnostic criteria proposed for CEH diagnosis (31) was as follows:

- pain episodes of varying duration or a fluctuating continuous course (61%);
- moderate, non-excruciating pain, usually non-throbbing (73%);
- provoked pain (neck movements/ sustained awkward position/external pressure over the greater occipical nerve (GON) or the ipsilateral upper, posterior neck region C2-C3) (52%);
- ipsilateral shoulder-arm pain (non-radicular) (52%);
- reduced range of movement (ROM) (84%);
- history of head/neck trauma (remote) (51%);
- cervical spine X-ray abnormalities (26%).

The mean age of these patients was 35 ± 11 years, with a range of 19 to 70; the mean age at headache onset was 2913 years; symptoms lasted from at least 1 year (range 1.8 - 6.7 years); and the mean interval from previous trauma was more than 24 months.

In this group of probable CEH patients, 46/62 cases (74.2%) satisfied 5 or more

of the diagnostic criteria for CEH while less than 3 of these criteria were met in those cases (n = 8) classified by the IHS system as having common M (24, 25). Migraineurs symptoms (such as nausea, vomiting, photo- and phonophobia), dizziness, blurred vision and other minor signs were recorded with a frequency of less than 25%, in the absence of clinically significant local autonomic disturbances.

The diagnostic power of the criteria for CEH was also evaluated in the present series in the comparison with the subgroup of patients not fulfilling the unilaterality criterion (Antonaci *et al.*, in press), with the aim of evaluating the frequency of diagnostic overlap with IHS group 11.2 (neck) and the contribution of trauma (whiplash injury) as a predisposing factor for CEH (9).

Higher levels of diagnostic probability may be achieved by evaluating the response to appropriate anaesthetic blocks (2-7), although the sensitivity and specificity of these procedures, when adopted for the screening of large series of possible CGH patients, gave poor or inconclusive results. In our study data were available only for a subgroup of 32 cases (M/F: 11/21, 14 with a history of trauma), due to the fact that maximal or sub-maximal pain at observation was required for the investigations.

Block procedures were performed, according to current guidelines (2) proceeding from SON to GON, at the C2 and C3 occipital nerves, at intervals of at least 24 hrs, using small amounts of lidocaine (0.5 ml 2%) and evaluating the visual analogue score (VAS) every 10 minutes for 90 minutes. Blocks were considered unequivocally positive in cases with the complete or near-complete abolition of pain (VAS score < 15), also showing sensory loss in the pertinent nerve territory. Facet joints were blocked in a subgroup under fluoroscopic control (lateral approach), followed in a few cases by a long-term therapy.

As reported in Table II, VAS score reductions of more than 50% from baseline were obtained for SON, GON, C2 and C3 blockade in over 50% of the cases, and C2-C3 joint block in 9/16 cases, with a positive correlation (Chisquare test) between the GON and C2

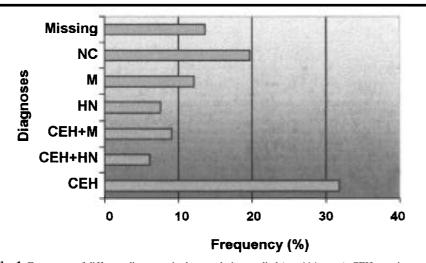


Fig. 1. Frequency of different diagnoses in the population studied (n = 114 cases). CEH: cervicogenic headache; HN: headache with neck disorders; M: migraine (without aura); NC: not classifiable; Missing: missing data for the final diagnosis.

Table II. Blockade response in cervicogenic headache.

Block	Responders *	Non-responders
SON	22	10
GON	23	9
C2	22	10
C3	16	16
C2-C3	9	7 **

 ^{*} over 50% reduction in baseline pain within 30 mins after injection

response (Pearson's coefficient p < 0.003). A positive correlation was also demonstrated between C3 (p < 0.043) and SON (p = 0.046) blocks and the presence of continuous non-episodic pain, while a negative correlation emerged between the effectiveness of SON block and a positive history of trauma (p = 0.052).

The data point to a good sensitivity of these procedures, but with low specificity, particularly considering the results in terms of an absolute (unequivocal) response: SON 21%, GON 53%, C2 41%, C3 37%, facet joint 7 out of 9 positive cases selected for their complete positive response to C2 and C3 procedure. The low resolution of the SON block supports the indication for a priority of GON and C2/C3 procedures in the diagnostic sequence, which should then proceed to explore the lower levels in all cases with negative or equivocal results. Cases with shoulder-arm pain could also be directly addressed by investigation at the intermediate/low levels of the cervical spine, based on the poor correlation obtained between this variable and the results of C2 block (p = 0.033).

As a general rule, the outcome after longlasting blocks might also be relevant for the choice of other therapeutic proce-

Table III. Conditions to be considered in the differential diagnosis of CEH.

- · Migraine without aura
- Tension type headache
- · Headache associated with neck disorders
- Hemicrania continua
- · Occipital neuralgia
- · Cluster headache

dures, which should be considered in sequence from the least to the most invasive (28).

Other characteristics of CEH remain under investigation, namely its interference with daily activities and the quality of life, psychological aspects, the profile of responses to pharmacological treatments, as well as the long-term outcomes after the different procedures proposed so far.

Another relevant aspect discussed in this issue by various authors covers methodological aspects of the clinical and functional investigations aimed at obtaining objective measurements: manual palpation (tender points), muscle contraction (surface EMG), activation levels of cervicocephalic reflexes (EMG), range of movement (ROM) (X-ray and analysis of movements), vascular and autonomic activity, and pain and sensory thresholds (respective techniques) (19).

CEH and other unilateral headaches

The list of headaches and other head and neck pain with possible/prominent or side-locked unilaterality to be considered for a differential diagnosis with CEH is reported in Table III and includes members of the migraine family, CH and related disorders with attacks of shorter duration, and other vascular, pure neuralgic and neuralgiform head pains.

The pathogenetic implications of the unilaterality of pain and associated phenomena vary largely in this group from form to form, according to the structures involved in pain generation and control, the different expression of the underlying changes (functional/structural), the interplay with physiological functions, the different correlates of predisposition (genetic versus acquired forms, defined central generators versus variable peripheral triggers or foci).

The above components will therefore contribute to the background characteristics of unilateral headache, that will be identified in terms of their temporal pattern (recurrent attacks versus continuous; episodic versus chronic), the severity and duration of pain and autonomic involvement, the evolution and prognosis, and the stability of the clinical picture or its tendency to transform or overlap with other disorders (pre-stages; subclinical

phases; variant forms).

In the comparison of CEH versus M without aura, the similarities are very weak and the differences very great and relevant for a clinical diagnosis (Table IV). In M without aura the pain may be bilateral or unilateral, but can change sides or become bilateral during the same or in subsequent attacks. The age at onset, genetic susceptibility, systemic autonomic involvement, and facilitating and trigger factors are distinctive features for M, without considering the specific response to triptans and the absence of shoulder-arm even in those cases with a cervical component.

CH, the prototype of periodic headaches, is invariably unilateral but highly recognizable for its temporal pattern, the extreme severity of pain and ipsilateral autonomic involvement, its male preponderance and possible family aggregation (12% in first-degree relatives). In the presence of typical features (diagnostic criteria completely fulfilled) the probability of a primary (benign) disorder is very high; resistance to treatment instead must be considered for other diagnoses. CPH, a very rare disorder, exhibits a female predominance (3:1) and migrainelike behaviour during attacks, which are shorter-lived than in CH (2 to 45 mins) and associated with minor (or subclinical) signs of parasympathetic activation. The mechanical provocation of attacks is a feature that it shares with CEH, but the stimuli and the duration of triggered phenomena are different in most cases (fast movements / short duration). Besides its clinical characteristics. CPH is defined by a dramatic response to indomethacin, a feature that it shares with HC. Patients with a diagnosis of possi-

Table IV. Differential diagnosis of CEH versus migraine without aura.

Similarities	Differences
• Unilaterality of pain	•Reduced ROM
• Throbbing pain	• Lack of precipitating mechanism
• Moderate to severe pain	•Ergot/sumatriptan response
Autonomic symptoms	•Blockade response
• Temporal pattern	

^{**}performed in 16 patients

Table V. CEH: differential diagnosis versus Hemicrania Continua.

Similarities	Differences
•Unilaterality of pain	•Reduced ROM
•Temporal pattern	•Lack of precipitating mechanism
	•Indomethacin response
	•Blockade response

ble/probable CEH should therefore undergo a standard indomethacin test (3) in order to exclude the diagnosis of HC, a form included in the differential diagnosis with other chronic or fluctuating continuous headaches (drug overuse), which is often recurrent in the initial phase, with moderate pain and poor autonomic oculocephalic phenomena, usually absent in CEH.

The main similarities and differences between CEH and HC are reported in Table V. Among the unilateral headaches, SUNCT (19) must also be considered, although its similarities and differences with CEH have to be kept in mind, as reported in Table VI.

Conclusion

Patients with headache originating from the neck constitute a heterogeneous group requiring thorough clinical and instrumental investigation in order to determine the appropriate treatment. Their classification using the IHS system may allow a correct diagnosis as either common migraine, tension headache, a subgroup of Section 11 (11.2 Neck) or a late (chronic) post-whiplash disorder. Many cases, however, remain unclassifiable

Table VI. Similarities and differences between SUNCT and CEH.

Similarities	Differences
•Male preponderance •Autonomic phenomena	•Pain severity •Temporal pattern •Precipitation of attacks •Treatment responses

and the diagnosis of CEH, a newly defined syndrome recognized by the IASP, should be considered. Candidates for this category are these patients presenting with a side-locked unilaterality of symptoms and other criteria presently under validation. The definition of its similarities and differences with other unilateral headaches may contribute to a better understanding of the pathophysiological underpinings of this condition.

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