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Review

Epileptic seizures and headache–migraine: A review on types of association and terminology

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ABSTRACT

Purpose: There are different possible temporal associations between epileptic seizures and headache attacks which have given rise to unclear or controversial terminologies. The classification of the International League Against Epilepsy does not refer to this type of disorder, while the International Classification of Headache Disorders (ICHD-2) defines three kinds of association: 1. migraine-triggered seizure (“migrralepsy”), 2. hemicrania epileptica, and 3. post-ictal headache.

Methods: We performed an extensive review of the literature, not including “post-ictal” and “inter-ictal” headaches.

Results: On the basis of well-documented reports, the following clinical entities may be identified: (A) “epileptic headache (EH)” or “ictal epileptic headache (IEH)”: in this condition headache (with or without migrainous features) is an epileptic manifestation *per se*, with onset, and cessation if isolated, coinciding with the scalp or deep EEG pattern of an epileptic seizure. EH maybe followed by other epileptic manifestations (motor/sensory/autonomic); this condition should be differentiated from “pure” or “isolated” EH, in which headache/migraine is the sole epileptic manifestation (requiring differential diagnosis from other headache forms). “Hemicrania epileptica” (if confirmed) is a very rare variant of EH, characterized by ipsilateral location of headache and ictal EEG paroxysms. (B) “Pre-ictal migraine” and “pre-ictal headache”: when a headache attack is followed during, or shortly after, by a typical epileptic seizure. The migraine attack may be with or without aura, and its seizure-triggering role (“migraine-triggered seizure”) is still a subject of debate. A differentiation from occipital epilepsy is mandatory. The term “migrralepsy” has not been used univocally, and may therefore led to misinterpretation.

Conclusions: On the basis of this review we suggest definitions and a terminology which may become the basis of a forthcoming classification of headaches associated with epileptic seizures.

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The temporal association between a headache attack and an epileptic seizure is an interesting phenomenon, which may occur in various ways, and has recently been the subject of debate^{1–5} and revisitation.⁶ The classification of the International League Against Epilepsy does not refer to this type of disorder, while the International Classification of Headache Disorders, 2nd edition (ICHD-2)⁷ defines three kinds of association, synthetically reported in [Table 1](#).

According to their temporal occurrence, four types of association between headache and epileptic seizure are recognized: 1.

pre-ictal headache, 2. headache as the expression of an epileptic manifestation, 3. post-ictal headache, and 4. inter-ictal headache.

Apart from *post-ictal headache*, which has recently been reviewed by Ekstein and Schachter⁸, and from *inter-ictal headache*, the patterns of expression of the other two associations is complex, and terminology has been widely discussed. The aim of this review is therefore to update information reported in the literature on pre-ictal and ictal epileptic headache, searching for unification or differentiation criteria, and suggesting relative terminology.

1. Pain as an epileptic phenomenon

Although infrequently, ictal pain may be the initial symptom of an epileptic seizure; it can be distinguished as lateralized peripheral, abdominal and cephalic.^{9,10} The parietal lobes appear to be involved in most cases of *cephalic ictal pain*, while in other cases epileptic activity occurs in a different location, as there are multiple site representation of pain in the brain.^{11,12} Cephalic pain

Abbreviations: GTC, generalized tonic-clonic; MA, migraine with aura; MO, migraine without aura.

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may assume the characteristics of migraine or of other types of headache; it may involve the face alone, or facial pain may be followed by other epileptic manifestations⁹ (case no. 10) or be isolated.¹³

The literature reports episodes of headache, sometimes with migrainous features, not followed or accompanied by other manifestations of a clear epileptic nature, with paroxysmal EEG features beginning simultaneously with the headache, and ceasing with it if not followed by other epileptic manifestations. This is a true epileptic seizure manifesting itself with headache, therefore an “*epileptic headache*”.

2. Epileptic headache (ictal epileptic headache^a, ictal headache^b)

2.1. Not followed by other epileptic manifestations (pure epileptic headache)

In this condition a cephalic pain (headache), with or without migrainous features, with concomitant EEG paroxysms, is not followed by other epileptic phenomena.

We recently described¹⁵ a new case with video-EEG report, and briefly illustrated the cases available in the literature regarding this condition, for which we suggested the term of “*pure (or “isolated”)* epileptic headache”. To meet the criteria for this condition, at least some of the headache episodes experienced by the patients should be isolated episodes, without other manifestations of a clearly epileptic nature, and in particular should not be immediately followed by motor and/or sensory and/or autonomic manifestations. This is relevant, since it may pose the problem of a differential diagnosis with headaches due to other causes.

The main features of 15 published cases affected by “pure epileptic headache”^{15–25} are reported in Table 2. In the table, no data are provided for the first patients reported with epileptic headaches,^{26–29} as the full text articles are unavailable. Among the cases described by Isler et al.¹⁷ and by Beauvais et al.¹⁸, due to the paucity of data available, only those more likely to be “pure epileptic headache” have been included.

In the cases reported in Table 2, head pain lasted from seconds to days. Headache was reported as having the characteristics of migraine without aura (MO) in 4 cases, migraine with aura (MA) in 3 (one both), “tension-type” in one and not defined or not classifiable in the other cases. Pain location varied: frontal, temporal, vertex, hemicranial. In some cases, mild symptoms accompanying headache were reported: agitation, dyspnea, confusion, difficulty to talk, hypersensitivity to noise. EEG abnormalities contemporary with pain were of various types (spikes, spike-and-waves, sharp-waves) and location: in 2 cases generalized, in 4 (3 MO, 1 both MO and MA) monolateral occipital, and temporal or frontal or central or parietal in the others. Occasionally, as may occur for seizure of deep origin, a scalp EEG did not show paroxysmal activity during the headache episode, which revealed its epileptic origin only on performing a deep-electrode EEG: Laplante et al.¹⁶ (case 2), Isler et al.¹⁷ (case 2) and Dainese et al.²³ (case 1). As shown in the table, neuroimaging findings and etiologies varied widely, with location of the probable causative focus in different brain areas, although prevalently in the occipital and temporal.

Thus, all cases listed in Table 2 represent examples of pure (or isolated) epileptic headache: only head pain, sometimes accom-

^a “Ictal epileptic headache”, used for the first time by Parisi,¹ appears repetitive, since *per se* ictal signifies “relating to a seizure” (Oxford dictionary), “relating to a seizure or convulsion” (Farlex dictionary), “relating to or caused by a stroke or seizure” (The American Heritage® Medical Dictionary). Moreover, an “epileptic headache” is “*per se*” ictal.

^b “Ictal headache”, first used by Piccioli et al.,¹⁴ could be confused with headache due to an “ictus”.

panied by with minor manifestations. However, in some cases, episodes of pure epileptic headache alternate with episodes of headache followed by other epileptic manifestations, as illustrated in the variant described in Section 2.2.

2.2. Followed by other epileptic manifestations (epileptic seizure beginning with headache)

Headache with concomitant EEG paroxysms, with or without migrainous features, developing along with other epileptic manifestations, was reported by Isler et al.¹⁷, Marks and Ehrenberg³⁰ (MA, cases 1, 2, 5), Walker et al.³¹ (migraine with visual aura), Velioglu and Ozmenoglu³² (migraine with visual aura, cases 1, 2, 4, 6), and possibly some cases by Verrotti et al.³³. These situations are clearly *epileptic seizures beginning with (epileptic) headache*, which is actually an “aura”.

Epileptic headaches followed by other more habitual epileptic manifestations, particularly the motor ones, are probably underdiagnosed, since both the physician and the patient tend to emphasize the latter, not giving importance to the initial headache. On the other hand, it should be considered that only the episodes of “pure” epileptic headache have a clinical relevance, requiring a diagnostic differentiation from other types of headache, particularly when no other types of seizures occur and no epileptic abnormalities are present in the interictal EEG.

Isler et al.¹⁷ used the term “*hemicrania epileptica*” to describe the occurrence, in 5 of their patients, of unilateral migraine attacks coinciding with EEG (scalp and/or deep) epileptic activity, localized homolaterally to migraine pain. The term “*hemicrania epileptica*” has been accepted by the ICHD-2, as shown in Table 1. Apart from the peculiar characteristic of homolaterality between the epileptic focus and hemicranial pain location (also reported by others although referring only to interictal EEG^{6,34–36}) Isler’s cases clearly appear to be epileptic headaches. Data from the report by Isler et al.¹⁷ are not sufficiently detailed to establish whether headache episodes are isolated or not. At least 2 patients (cases 1, 2, reported in Table 2) appear to have had “pure” epileptic headache, while in the other cases headache appears to be part of or followed by other epileptic manifestations.

Although interictal EEG abnormalities may be ipsilateral to periictal headache, particularly in temporal lobe epilepsy,^{6,34–36} in the literature no other cases have been reported in relation to the ictal EEG. In any case, this correlation does not seem to bear any speculative interest in relation to headache mechanisms, since the causative foci in the reported cases of epileptic headaches were all located in different brain areas.

On the basis of the aforementioned data, the following suggestions for terms and definitions in view of a new classification may be put forward:

“**Epileptic headache (EH)**” (or “**Ictal epileptic headache**”, or “**Ictal headache**” – see note ^a). *Headache (whether migraine or not) with onset, and cessation if isolated, coinciding with an EEG pattern of epileptic seizure (rarely EEG alterations may only be detectable using deep electrodes), featuring two variants: A) “Pure” or “isolated”, e.g. “Isolated epileptic headache” (IEH), or B) headache followed without discontinuity by other epileptic manifestations thus actually being an epileptic seizure beginning with headache (as an “aura”).*

To this definition a comment could be added, that this form is usually of short duration (seconds to minutes, like epileptic seizures), although comprising a long-duration variant (more similar to migraine attack or tension-type headache), considered as a status epilepticus. When lacking an ictal EEG, the immediate stopping of headache by intravenous benzodiazepine is diagnostic. In the condition B) headache actually is to be considered an “aura”

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