Case Report

The Clinical Concurrence of Migraine and Transient Global Amnesia: “Migramnesia”?

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The Clinical Concurrence of Migraine and Transient Global Amnesia: "Migramnesia"?

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Abstract: Complaint of transient impairment or loss of memory as an attendant feature in some migraine attacks has long been recognised. In some cases, migraine may be a trigger or precipitating factor for the syndrome of transient global amnesia (TGA). However, the exact frequency of this concurrence is unknown, perhaps related to the absence from the International Classification of Headache Disorders (ICHD3) of amnesia or memory loss symptoms in association with migraine, unlike the situation with epileptic seizure (migralepsy) or stroke (migrainous infarction). Similarly, headache has generally been regarded as an incidental feature of TGA, reported in about 10% of cases. We present further examples of TGA in the context of migraine headache; consider possible reasons why this concurrence might be under-recognised, such as the retrograde amnesia characteristic of TGA; review possible shared pathogenetic mechanisms; and suggest a new terminology, "migramnesia", which may encourage clinicians to address the possible significance of migraine in the context of an episode of TGA.

Keywords: migraine; transient global amnesia

Introduction

Transient global amnesia (TGA), a self-limiting episode of dense anterograde amnesia often characterised by repetitive circular questioning and with a variable duration of retrograde amnesia, was first described as such in the 1950s.[1] The exact pathophysiology of TGA remains undefined.[2] However, an association between migraine diathesis and the predisposition to TGA is long-established and robustly confirmed, extending from initial individual case reports and case series to more recent population-based studies.[3,4] In addition to acting as a predisposing factor for TGA, typical amnesic episodes have sometimes been described in the context of an episode of migraine headache, suggesting that migraine might also on occasion act as a precipitating or triggering factor for TGA. The frequency and symptomatology of this concurrence is ill-defined, in part because classification schemata such as the International Classification of Headache Disorders 3rd edition (ICHD3) do not recognise amnesia or memory loss symptoms in association with migraine,[5] and TGA criteria accept headache as a common "non-focal" incidental feature in TGA episodes.[6]

In order to reappraise the clinical phenomena of migraine and TGA occurring in close temporal association, we present three illustrative cases, in light of which the aims of the discussion are to review the previous literature on migraine as a precipitating factor for TGA, and for other paroxysmal events such as epilepsy and stroke; to consider possible shared pathophysiological mechanisms which might explain why in these circumstances subsequence is indeed consequence; and hence to suggest the term "migramnesia" as an appropriate way to denote this clinical scenario.

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Case Reports

Case 1

A 75 year-old lady was referred to the neurology clinic following an episode in which she lost her memory for about an hour. The history from the patient and her daughter was that they were together at her home one morning. She chatted on the phone with a relative, mentioning her anxiety about an upcoming hospital appointment. She also complained of some head pain for which she took paracetamol. Thereafter she was forgetful, could not recall things that had happened in the previous week, and subsequently had no recall of her conversations either with her daughter or the telephone call made during this time period. When seen in the neurology clinic about 3 months later, this event was judged to conform to the clinical diagnostic criteria for TGA,[6] as there was evidence of both anterograde and retrograde amnesia.

About fourteen years earlier, aged 62, the patient had had an episode of amnesia lasting several hours; this occurred on Boxing Day and she was unable to recall events of the previous Christmas Day. Brain imaging (MR) and EEG performed about one month after this episode showed no abnormalities. The neurologist who assessed the patient at this time had made a diagnosis of TGA.

Her past medical history also included a thirty-year history of episodic 'sinus trouble' above the right eye, symptoms judged retrospectively to be typical of migraine.

Case 2

A 57 year-old lady who suffered about 3 episodes of migraine each year, usually responsive to paracetamol, was referred for assessment of an amnesic episode following a typical migraine. The day after returning from an overseas holiday, the flight arriving in the early hours of the morning, she developed a headache for which she took paracetamol and went to bed. About 3 hours later, she woke and was asking repetitive questions about what was going on; she had no recall of the flight, and could not remember her current car, naming one that she had owned thirty years previously. The memory symptoms improved after about 3 hours but she was left with an amnesic gap of about 24 hours, although she could recall details of the holiday. Brain imaging (MR) performed about six months after the amnesic episode showed no abnormalities. Subsequent neurological opinion judged the episode to conform to the clinical diagnostic criteria for TGA.[6]

Case 3

A 65 year-old lady who had suffered from episodic migraine with aura since young adulthood was referred following an episode of memory loss occurring in the context of prolonged constant headache. This was more severe than her usual episodic migraines and was associated with phonophobia and occasional episodes of her typical visual aura. About four weeks after headache onset, for most of one day she had no clear recollection of her activities, including getting up, washing and dressing, driving, or attending a job interview. Collateral history from the interview noted she gave short responses to questions, a behaviour recognised to be out of character. She was able to drive home thereafter, where her daughter observed repetitive questioning but no other symptoms. By the time the patient attended the local A&E department in the evening, the memory symptoms were improving. Although she could recall no headache that day, the medical staff treated her with a triptan. Brain imaging (CT) was normal. Interval MR brain imaging, about 3 weeks later, was also unremarkable. Subsequent neurological opinion judged the amnesic episode to conform to the clinical criteria for TGA.[6]

Discussion

These three patients experienced criterial episodes of TGA occurring in the temporal context of migraine headache.

Transient impairment or loss of memory has long been recognised as an attendant feature in some migraine attacks: they were mentioned, for example, in Liveing's monograph of 1873 which

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also referred to earlier cases described by Tissot and by Parry.[7] Moersch in 1924 emphasized amnestic dysfunction occurring in migraine attacks,[8] and Nielsen in 1958 wrote of the "amnesia of migraine" although none of the five cases he described (nos. 29-33) had a clinical phenotype now recognisable as that of TGA.[9] Frank in 1976 compared amnesic episodes in migraine, which he termed "Migranedammerattacken", with reports of TGA and suggested that they seemed to be identical.[10] A syndrome of acute confusional migraine in children has been noted to have clinical features similar to TGA,[11] prompting the idea of "cognitive migraine".[12]

Whilst the association between migraine and TGA is robustly established for a history of migraine tendency, hence as a predisposing factor,[13] TGA occurring in the context of a migraine episode, hence migraine as a precipitating or triggering factor, is less frequently noted. There are occasional case reports and series describing patients in whom an episode of migraine was followed by TGA,[14,15] some in apparently familial cases of TGA.[16,17] Cases are also described wherein TGA is followed immediately by a typical migraine headache such that TGA is considered to be migraine aura,[18,19] some with the typical MR imaging signature of hippocampal CA1 area punctate hyperintensities seen in many TGA cases.[20] However, both of these categories are relatively infrequently reported, so might possibly be ascribed to nothing more than chance concurrence. The only study in a defined population, a retrospective analysis of a cohort of 8821 new patients seen over an 11-year period in a dedicated migraine clinical centre in France, reported only 6 cases of TGA "triggered" by a migraine attack.[21] These data prompted the view, in a recent monograph devoted to TGA, that "TGA occurring during a migraine attack … is probably a very rare occurrence".[22]

However, a number of confounding factors may be operating here which might negate, or modify, this conclusion. There may be under-reporting, and possibly underascertainment, of TGA: as a transient self-limiting condition, patients may not present to neurological attention (or only very late, as in our cases) and/or the absence of reliable collateral history may render the clinical diagnosis unavailable since the clinical diagnostic criteria are by application binary ("definite or pure TGA" or "not TGA"). But even if TGA is reported and ascertained, there may be under-reporting and possibly underascertainment of migraine occurring as a feature of TGA. This may be simply a consequence of accepting headache as an incidental feature in TGA episodes, which reportedly occurs in around 10% of cases.[6,23,24]

In addition to these considerations, one also needs to consider the nature of TGA itself. If a *sine qua non* of TGA is a period of retrograde amnesia (although not criterial[6]), then patients will by definition not recall events such as migraine aura and/or headache occurring immediately before the onset of anterograde amnesia (see, for example, our Case 3), as these events may fall within the resulting amnesic gap. Hence one is dependent on the collateral history from a reliable informant, which may understandably focus on the memory symptoms, as more dramatic, unfamiliar, and hence concerning (e.g., of a stroke) rather than headache symptoms, particularly if the patient is already known to have a tendency to migraine. Thus, if not specifically enquired for, migraine as a precipitating or triggering factor for TGA may be easily overlooked.

Migraine as a trigger for other neurological phenomena is well recognised, albeit relatively uncommon. For example, in 1960 the American epileptologist William G. Lennox (1884-1960) coined the term "migralepsy" to describe a clinical scenario in which "ophthalmic migraine with perhaps nausea and vomiting was followed by symptoms characteristic of epilepsy".[25] The concept of migralepsy has proved controversial, with some authorities advocating abolition of the term in favour of "ictal epileptic headache",[26] although migralepsy is enshrined in ICHD3 as a "seizure triggered by an attack of migraine with aura" with specific diagnostic criteria.[5] It is also recognised that migraine features may sometimes be followed by stroke. Denoted as migraine stroke or, as per ICHD3 terminology, migrainous infarction, this is defined as "one or more migraine aura symptoms occurring in association with an ischaemic brain lesion in the appropriate territory demonstrated by neuroimaging, with onset during the course of a typical migraine with aura attack".[5]

Could a mechanistic explanation of migraine followed by TGA, or of TGA as a migraine aura, be posited? Just as shared mechanisms have been postulated to explain the differing clinical features in migralepsy[27] and in migrainous infarction,[28] the same may be the case for migraine and TGA.

Specifically, the mechanism of cortical spreading depression, also known as spreading depolarization, has long been suggested as the cause of both migraine aura and TGA,[29] and this remains a favoured explanation for the observed clinical phenomena of TGA.[2,30] Spread of depolarization from occipital to temporal cortex might explain the sequential clinical phenomena of migraine and amnesia, or from temporal to occipital cortex to explain TGA as a migraine aura.

In light of such considerations we suggest, following Lennox's characterisation of "migralepsy",[25] that the term "migramnesia" be used to denote this particular concatenation of neurological events. Rather than coining a needless neologism, a key advantage of this proposed nomenclature is that it characterises headache as potentially integral, rather than merely incidental, to episodes of TGA. If this term is used in the differential diagnosis of any episode of transient amnesia, it will remind clinicians to consider, and hence ask for the relevant clinical features of, migraine as a possible cause, in the same way that features of epilepsy are sought for the differential of transient epileptic amnesia. This will obviously have implications both for ongoing investigation and management of these patients.

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Availability of Data and Materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflict of interest relevant to this paper.

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