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LETTER TO THE EDITOR

Migralepsy: a new case confirming the existence of this migraine complication and proposing therapy

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Dear Sir,

We describe the case of a 43-years-old, right handed woman, who suffered from migraine with aura and epilepsy. Co-morbidity of migraine and epilepsy is a well known condition since more than 100 years ago [1]. Although it is a rare phenomenon, migraine attack may trigger an epileptic seizure. ICHD II (International Classification of Headache Disorders) [2] classified migralepsy (migraine triggered seizures) as a complication of migraine (coded 1.5.5) if two diagnostic criteria are fulfilled: (1) migraine fulfilling diagnostic criteria for coded 1.2 migraine with aura and (2) a seizure fulfilling diagnostic criteria for one type of epileptic attack developing during or within 1 hour of a migraine aura. Despite the fact that the term migralepsy (attributed to Lennox and Lennox) [3] was coined in 1960 both to define an "ophtalmic migraine with perhaps nausea and vomiting followed by symptoms characteristics of epilepsy" and to describe three specific cases, the migraine-epilepsy sequence (migralepsy) seems to be less common than epilepsy-migraine (hemicrania epileptica coded 7.6.1) and post-ictal headache (coded 7.6.2). A review of the literature suggested that migralepsy as coded by ICHD II is quite infrequent but not indeed inexistent [4].

A 43-years-old woman referred to the ER Department of San Raffaele Hospital, Milano, because of a generalized tonic seizure. She was born full term with a normal delivery and had normal developmental milestones. She has a family history positive for migraine with aura (mother) but no family member suffered from epilepsy. At age 9 years she developed migraine with visual and sensitive aura. Aura consisted of flickering flashing lights, developing gradually in 15 min with a global duration of 45 min, followed by sensitive symptoms (paresthesia of hand and face) and finally by headache with migraine features (frequency of 1 attack/month in the past; in the last months they rapidly increased to 8 attacks/month). In 21 September 2011, at 10:30 a.m. she experienced her typical visual aura (photopsia) for 15 minutes. After few minutes she noted the appearance of clonic palpebral movements in her right eye. She eventually lost consciousness, felt to the ground and had a generalized seizure (lasting 5 min). She was rapidly admitted at the Hospital, being unresponsive and confused during the transport. At Neurological examination (11:30 a.m.), patient was responsive to pain stimulus with no other signs. At general examination, blood pressure was 140/80, Heart rate 98 and O_2 saturation 96 %. A slight metabolic acidosis was detected at blood gas analysis. Brain CT scan (12:00) was normal. She was treated with Diazepam i.v. (10 mg). A second neurological examination (1:30 p.m.) was normal, but patient reported the onset of a severe migraine attack (9/10 VAS) localized on the left parietal and temporal side with nausea, vomiting and photo-phonophobia. EEG (2:30 p.m.) revealed epileptiform discharges in right temporal hemisphere. Brain MRI was normal and when she performed EEG again, a normalization of the previously described epileptiform features was noted, with only residual theta slowing over the left hemisphere. A therapy with topiramate was started at the initial dose of 50 mg (after one week the dose was increased to 100 mg). At follow-up (3 and 6 months), she reported only three migraine attacks without aura in the first month of therapy (VAS 5/10) and no more migraine with aura attacks or epileptic seizures. EEG was normal.

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Despite the skepticism by several authors about the real nosological existence of migralepsy, few cases were anyway published confirming the diagnostic consistence of this entity [5]. Our case confirms the sequence migraine with aura-epilepsy supporting the diagnosis of migraine triggered seizure according to ICDH II. The same term is not considered by ILAE (International League Against Epilepsy) classification, generating confusion among neurologists subspecialized in headache or epilepsy treatment. In this clinical context, terminology such as ictal epileptic headache is increasingly used to define an event in which headache represents the only ictal epileptic feature [6]. In our patient the diagnosis of migralepsy is definitely confirmed by the classical characteristics of visual aura similar to previous episodes (photopsia, expanding from center to periphery of visual hemifield, not circular nor colored, duration of 15′), and different from occipital seizures characteristics. The same is true for the features of the eventual pain (throbbing, severe in intensity, associated with nausea and vomiting, phonophobia, aggravated by movement) fulfilling the diagnosis of migraine. Considering the clinical data, this case is perfectly coherent with ICHD II classification of migraine triggered seizure fulfilling the published criteria (oded 1.5.5) [2], supporting the nosologic entity as a migraine with aura complication "per se".

There is a clear evidence from randomized controlled clinical trials that topiramate is useful both in migraine and in epilepsy, and is approved for these indications [7]. Topiramate is a Glutamate receptor antagonist and GluK1 kainate receptor antagonist, acting both on hypersyncronous firing in epilepsy and in hypersynchronous activity (voltage-gated Na^+ channel-dependent) in migraine [8]. In our case, therapeutical approach with topiramate was able, in a short period of follow-up, to reduce the frequency of migraine and stop both the aura phenomenon and seizures. The pharmacological result is similar to Sances's patient [4], with confirmed reduction in frequency of visual aura and no further seizures at follow-up. Admittedly, due to the small number of treated patients, we cannot state a definite efficacy of topiramate for patients suffering from migralepsy. Nevertheless, further studies on a larger group of well-selected patients are necessary to consider topiramate as a first line approach for treatment of migralepsy cases.

Thus, in our opinion, the call for a revision of the definition of migralepsy [9] could not be supported considering the clinical existence of this entity according to ICHD II criteria, albeit in few well-described cases. Further studies are warranted to better understand the fascinating link between migraine and epilepsy, as well as the therapeutical approach in this specific and well-defined area named as migralepsy.

Conflict of interest Prof. Comi has received consulting fees for participating on advisory boards from Novartis, Teva Pharmaceutical Ind. Ltd, Sanofi-aventis, Merck Serono, Bayer Schering, Actelion and lecture fees from Novartis, Teva Pharmaceutical Ind. Ltd, Sanofi-aventis, Merck Serono, Bayer Schering and Biogen. All other authors declare no conflict of interest.

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