Ophthalmoplegic migraine and juvenile myoclonic epilepsy: two side of the same coin?

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Received: February 06, 2013
Published online: March 05, 2014

Migraine and epilepsy have a proven and established association with the prevalence of migraine in populations of individuals with epilepsy estimated to be between 8-24%. Vice versa, the prevalence of epilepsy in individuals with migraine is estimated to be in the range of 1-17%, median being roughly 5.9% [1-3]. This association is not confined to adult population only. As per available literature, even the paediatric population with migraine had a 3.2-fold increased risk of epilepsy. Ophthalmoplegic migraine is an unusual and rare form of migraine headache, with an incidence estimated to be as low as less than 0.7 per million [4-6].

Ophthalmoplegic migraine is a unusual and rare form of migraine. It is epitomized by multiple, recurrent attacks of ophthalmoplegia. Based on our current clinical experience of treating migraine patients at our tertiary level hospital we feel that migraine may have a certain role in the pathological genesis of Ophthalmoplegic Migraine [7-10]. We have observed ophthalmoplegia in majority of patients with Ophthalmoplegic Migraine develop while they have a severe migraine attack. Cranial nerve palsies are well documented in this condition with the involvement of either/or third, fourth and sixth cranial nerves. However isolated cranial neuropathy is rare. The above observation has been made by us in patients of various ages, sex with or without cranial nerve involvement [11-14].

Most patients of Ophthalmoplegic Migraine have a past history of typical migraine. There seems to be an increase in severity of migraine headaches antecedently, before the onset of ophthalmoplegia in majority of patients we have monitored. The hemi cranial migraine headache being ipsilateral to ophthalmoplegia is almost a rule [13, 16].

Based on the available literature, there seems to be release of neuropeptides in the vessel wall on activation of trigemino-vascular system during an attack of migraine. As a result, it is hypothesized that a sterile
inflammation of the wall of vasa nervosa causes breach in the blood nerve barrier leading to nerve edema and injury. As a result post Gadolinium Magnetic Resonance Imaging may show enhancement, however it is not a rule. The postulation is that there no difference in migraine headaches in patients with and without enhancement. On the attack of Ophthalmoplegic Migraine reduces in its severity, there is a reduction in neurogenic inflammation of the wall of the vessel, leading to restoration of the BNB(Blood Nerve Barrier) and decrease in edema of the nerve and its enhancement. In addition, recurrent attacks may have long term repercussions such as infarction of the nerve and its aberrant regeneration. There is a mention Ophthalmoplegic Migraine variants in the form of (i) Childhood variant (ii) Adult variant in the literature. Childhood variant has its onset in childhood, and is characterized by migraine, which is severe along with recurrent third nerve palsy with involvement of the pupil, and enhancement on Gadolinium MRI in most of the patients. The adult variant is characterized by onset of symptoms in adult life. It also has characteristically severe migraine with a worsening in severity of migraine antecedently, prior to the ophthalmoplegic attack. The peculiar thing noted about this form of Ophthalmoplegic Migraine is that it characteristically has a single attack of sixth nerve palsy. The involvement of third cranial nerve with pupillary sparing is less common. However Gadolinium enhancement is rare despite third nerve involvement.

Juvenile myoclonic epilepsy (JME) is one of the generalized epilepsy syndromes and has a prevalence of roughly 4-10%. It is common in the ages between 10 & 20 years (2nd decade). The main seizure types are myoclonic jerks. Other important forms such as generalized tonic-clonic seizures and absence seizures may also co-exist, they however are far less common.

The association between migraine and epilepsy (especially JME) is well established but uncommon. The high prevalence of Migraine with aura in JME is hypothesized to be due to the Cortical Spreading Depression (CSD) starting more often in patients with JME than otherwise. There seems to be scientific evidence in literature, that epileptic foci and CSD might facilitate each other.

Grafstein proposed that the phenomenon of Cortical Spreading Depression (CSD) has a molecular basis to it, which was induced experimentally by inducing elevated glutamate, potassium in extracellular fluid and Na+/K+ adenosine tri phosphatase (ATPase) channel inhibition. The basis for these similarities could be genetic. These can be seen in mutations of various genes responsible for different forms of epilepsy and familial hemiplegic migraine. One of the important neuronal P/Q type calcium channels (pore-forming subunit-associated with episodic ataxia syndrome-type 2) is encoded by CACNA1A. It has also been associated with 2 other important conditions, namely the spinocerebellar ataxia syndrome-type 6 and idiopathic generalized epilepsy. ATP1A2 finds itself being strongly associated with migraine without aura along with other conditions such as alternating hemiplegia of childhood, basilar-type migraine and benign familial infantile convulsions. SCNA1 gene mutation has been known to be associated with myoclonic epilepsy in patients with familial hemiplegic migraine. It seems real that epileptiform discharges which may be with or without cortical epileptic signs additionally or symptoms, might trigger the onset of CSD, resulting in an activation of the trigeminovascular system and, finally, in headache. Hence both migraine attacks and epileptic seizures are postulated to be triggered by cellular excitability of the neocortex, which is in excess at that point of time. The hyperexcitability leading to CSD (cortical spreading depression) characterizes migraine whereas hypersynchronous activity characterizes seizures.

Acknowledgements

I would like to express my deep gratitude to Professor K Radhakrishnan, my mentor during my Neurology residency and Dr Dariush Dowlatshahi, my present mentor & research supervisor for their patient guidance, enthusiastic encouragement in my research.

Conflict of interest

The author declares that they have no conflict of interest.

References


To cite this article: Deshpande A, et al. Ophthalmoplegic migraine and juvenile myoclonic epilepsy: two side of the same coin? Mol Cell Epilepsy 2014; 1: e70. doi: 10.14800/mce.epilepsy.70.