Autonomic Symptoms and Allodynia in Migraine

Esme EKİZOĞLU

Department of Neurology, İstanbul University, İstanbul Faculty of Medicine, İstanbul

Migraine is a common headache disorder causing severe disability by worsening the quality of life. It is thought to develop due to the hyperexcitability of the central nervous system, and the interaction of genetic and environmental factors have a role in the pathophysiology. Migraine seems to be a heterogeneous headache disorder, given the variability of its pain characteristics and associates. Therefore, the definition of homogeneous subgroups showing same features with careful clinical evaluation, as well as migraine types determined according to the presence of aura or pain frequency, seems to be necessary to establish the most appropriate treatment and follow-up plan.

Autonomic symptoms, hallmark of trigeminal autonomic cephalalgia, may also accompany typical migraine attacks. In migraine patients experiencing autonomic symptoms, it was reported that the pain was mostly unilateral, more severe, and frequent, with a longer attack duration and better response to triptans in comparison to migraineurs without autonomic features (1-3). Furthermore, photophobia and phonophobia were present in these patients at a higher rate, and allodynia was developed much more frequently when compared with migraineurs without autonomic manifestations (4).

Allodynia denotes the perception of pain or discomfort induced by a nonnoxious stimuli such as touching, combing hair, or wearing eyeglasses which are not expected to elicit pain. This phenomenon is accepted as the clinical result of the central sensitization in pathophysiology of headache. The neurogenic inflammation leading to migraine attack firstly activates the peripheral trigeminovascular neurons, and this condition is defined as peripheral sensitization. Ongoing pain signals cause an increased excitability of second-order neurons in the trigeminal nucleus caudalis, converting them into an independent state in which they themselves become the pain generator. Cephalic cutaneous allodynia is known to reflect the clinical presentation of this neuronal hyperexcitability. The presence of allodynia is important because it is found to be correlated with unresponsiveness to triptans and chronification of migraine. Therefore, the early administration of attack therapy before the development of central sensitization and allodynia has a determinative role in the pain recovery (5).

The prolonged peripheral sensitization seems to trigger the trigemino-autonomic reflex in some migraineurs leading to the development of autonomic symptoms. It has been suggested that the parasympathetic outflow further increases the sensitization of the perivascular sensory trigeminal fibers, and causes a higher hyperexcitability of second-order neurons in comparison to migraineurs without autonomic symptoms (4). This may explain the electrophysiological basis of the frequent presence of allodynia and other migraine associated features in migraineurs experiencing autonomic symptoms.

The observations that triptan therapy is ineffective after allodynia has developed, and triptans are fairly well tolerated in migraineurs with autonomic symptoms; and besides, the higher risk of the development of allodynia and the chronification of migraine in this subgroup are quite remarkable. These data suggest that a careful investigation of autonomic symptoms and allodynia in migraineurs in clinical practice will be a suitable approach to predict the disease course, define treatment strategies, and evaluate drug response.

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