Movement Disorder and Epilepsy in Subependymal Nodular Heterotopia

Anurag Lohmror¹, Richa Choudhary¹

Abstract

Context: Subependymal nodular heterotopia is a cortical development malformation that is commonly associated with refractory epilepsy. Patients with heterotopia show a wide spectrum of clinical manifestations, from being asymptomatic to presenting with intractable seizures and intellectual impairment.

Case Report: We report a case of refractory epilepsy with normal intelligence, having bilateral subependymal heterotopic nodules in brain, presenting to us with a movement disorder in the form of myoclonus of bilateral lower limbs which is an unusual manifestation of gray matter heterotopias.

Conclusion: Though rare, gray matter heterotopias may present as movement disorder and should be considered in differential diagnosis while work up of movement disorders.

Introduction

Subependymal nodular heterotopias (SNH) are one of the most frequent malformations of cortical development.¹ Gray matter heterotopias are best divided into three categories: subependymal, sub cortical, and band heterotopia. According to the classification system developed by Barkovich et al, updated in 2012, SNH are classified as malformations due to abnormal neuronal migration (Group II).² The main presenting feature in most patients with nodular heterotopias is focal drug resistant epilepsy³ with onset in second decade of life; development and neurological examination is otherwise normal. Here, we present a patient with generalized epilepsy and movement disorder in the form of myoclonus, whose MRI was consistent with bilateral subependymal nodular heterotopias.

Case History

A 19 year old female with a previous history of convulsions for last nine years presented to our department with myoclonus of bilateral lower limbs for three months. The onset of convulsions was at the age of ten years occurring with a frequency of 2 to 3 episodes per month. The convulsions were preceded by aura, described by the patient as heaviness in head, and were generalized tonic clonic in nature, each episode lasting for 1 to 2 minutes followed by 15 to 20 minutes of post ictal confusion. Medically she was initially treated with valproic acid with partial success. Clobazam and levetiracetam were added to control the convulsions and the family reported improvement. Her perinatal history was unremarkable and developmental milestones were achieved at appropriate ages. Although she was unable to complete her schooling after primary school level due to her medical condition, on examination her intellectual ability was within normal range. There was no family history of seizures. Neurological examination was unremarkable except for the presence of myoclonus in bilateral lower limbs. No evidence of neurocutaneous markers was present.

Investigations revealed normal haemogram and serum biochemistry. Concomitant congenital abnormality was present during screening for associated anomalies in the form of left ectopic (left iliac fossa), malrotated and small sized kidney.

Magnetic Resonance Imaging (MRI) of the brain was performed using spin echo and fast spin echo pulse sequences. Serial T1 and T2 weighted images were obtained in the sagittal,coronal and axial planes. Special fast FLAIR images were also obtained. The study revealed nodular lesions isointense to gray matter on all pulse sequences seen along lateral margins of bodies, frontal and occipital horns of bilateral lateral ventricles consistent with subependymal gray matter heterotopias (Figure 1).

Fig. 1: Subependymal Heterotopia- Magnetic Resonance images (a) T1-weighted axial section showing multiple subependymal nodules (arrows), isointense to cortical gray matter, symmetrically lining the lateral walls of the lateral ventricles; (b) T2- weighted coronal section demonstrating heterotopic nodules along the para-trigonal region of both ventricles; (c) Axial inversion-recovery magnetic resonance (MR) image showing bilateral nodules indenting the walls of ventricles (arrows)

¹Senior Resident, SMS Medical College, Jaipur, Rajasthan

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**Discussion**

Subependymal Nodular Heterotopia (SNH) was initially thought to be a neuronal migration disorder characterized by nodules of neurons due to arrested migration or failure of neuroblasts to undergo apoptosis but according to recent research, neuroependymal injury, rather than an intrinsic motility defect of the cell, is thought to be an important pathogenic factor in the development of SNHs. The denuded ventricular epithelium in periventricular/subependymal nodular heterotopia may cause disengagement of radial glia, resulting in an inability of young neurons to migrate away. The subependymal nodules are the most common form of grey matter heterotopias, which are located close together and form irregular lumps adjacent to the lateral ventricles, bilaterally or unilaterally.

The true prevalence of nodular heterotopias in the general population and in patients with epilepsy is unknown. Subependymal heterotopias usually present sporadically, however some cases are familial and demonstrate an X linked pattern of inheritance. Mutations in FILAMIN 1 gene, located on chromosome Xq28, have been associated with both sporadic and familial SNH.

Clinically, patients with subependymal heterotopias not associated with other types of cortical or cerebral malformations generally have normal development and motor skills. In a long term follow up, monitoring the course of epilepsy in 16 SNH patients d’Orsi et al found that isolated SNH patients without any associated cortical or cerebral malformation have a comparatively ‘benign’ course with seizures beginning during the second decade of life and rare in frequency at onset. The seizure type in these patients is usually partial with secondary generalization and drug responsive, without mental retardation. EEG may be normal or with focal abnormalities. During life, seizures may temporarily increase, but without reaching a high frequency and usually disappear or become very rare. A kidney malformation (ectopia) was evident in one of their patients. In the present case, a similar congenital anomaly in the form of left ectopic (left iliac fossa) and malfixed kidney was present.

In our case, the subject had onset of seizures in her second decade of life which were partially controlled and myoclonus of bilateral lower limbs. This was similar to two cases reported by J. P. Mullin et al in pediatric age group, both patients manifested as movement disorders as presenting features of heterotopias. Both patients experienced significant improvements following resection of their heterotopias.

MRI is far more sensitive than CT in the detection of subependymal heterotopias. On MRI subependymal heterotopias appear as ovoid lesions within the subependymal region. Neither perilesional edema nor contrast enhancement is seen. Donkol RH et al reported three types of heterotopia detected by MRI in a study of 20 patients (female to male ratio 14:6), all having a history of seizures. SNH was the commonest type, followed by Subcortical Heterotopia, while Band Heterotopia was the least common type. The heterotopic tissue was isointense with grey matter on all MR pulse sequences. Several studies revealed that most of the heterotopic nodules experience epileptic activity of their own accord at seizure onset, which is synchronous with the overlying neocortex or ipsilateral hippocampus. The heterotopia can generate not only normal EEG activity but also interictal and ictal epileptic discharges, usually synchronous with, but sometimes independent from the surrounding allo or neocortex.

In conclusion, heterotopias are a rare subgroup of cortical malformations characterized by abnormal neuronal migration, usually presenting as refractory epilepsy. In literature very few cases of heterotopic gray matter associated with movement disorders have been reported. Hence, the case above is reported to emphasize the unusual manifestation of subependymal nodular heterotopias as movement disorders.

**References**