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Case Report

# Sub-Ependymal Nodular Cortical Heterotopia Associated with Cerebellar Hypoplasia in a Nigerian Man with Epilepsy: A Case Report

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## Abstract

**Background**: Bilateral sub-ependymal nodular cortical heterotopia associated with unilateral cerebellar hypoplasia has been infrequently reported in literature and there has been no report in association with cleft palate. It is a recognised cause of intractable epilepsy and there is no previous report in literature from Nigeria.

**Case Presentation:** 21-year old Nigerian man, presented with a 3-year history of occasional visual hallucination and 1-year of recurrent focal onset unaware to generalised tonic-clonic epilepsy. The physical examination findings revealed a previous cleft lip repair and subtle spastic paraparesis. Electroencephalogram (EEG) was unremarkable with posterior dominant alpha rhythm (8 Hz-9 Hz) phase reversal in the right anterior temporal region. Brain Magnetic Resonance Imaging (MRI) showed bilateral sub-ependymal nodular cortical heterotopia, right cerebellar hemispheric hypoplasia, right parieto-occipital polymicrogyri and bilateral temporal sclerosis.

A diagnosis of multiple congenital malformations with epilepsy was made and seizures have so far been controlled with antiepileptic medications.

**Conclusion:** This case report of bilateral sub-ependymal nodular cortical heterotopia associated with unilateral cerebellar hypoplasia manifesting with epilepsy in adulthood is rare and often underreported. A high index of suspicion is required by the clinician. Brain Magnetic Resonance Imaging (MRI) should be performed in young adults with epilepsy to screen for structural malformations.

**Keywords: Cortical heterotopias; Epilepsy; Case report; Cerebellar hypoplasia**

## Introduction

Malformations of the Central Nervous System (CNS) are of major clinical significance because they lead to considerable morbidity and mortality in both prenatal and post-natal periods [1]. The term 'malformation' refers to any morphological abnormality that dates back to the embryonic or foetal period, regardless of the mechanism of it origin [1].

Cortical heterotopia is a group of neurological malformations characterised by the ectopic position of neurons. The cause is not clearly known, however, it is proposed that they arise from defects in genetic factors that control radial migration of neuroglia cell to the cortical region [2]. They can be classified as periventricular nodular/subependymal nodular, focal subcortical or subcortical band/double cortex heterotopias [2]. Subcortical band heterotopia has been shown to have a sex-linked inheritance and affect females in over 90% of cases [3].

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Periventricular Nodular Heterotopia (PNH) is the most common form of cortical developmental malformation and mostly seen in adulthood. Mutation in the FLNA gene on Xq28 has been found in 100% of familial X-linked bilateral and 26% of sporadic patients [2]. PNH is also been reported to be associated with other congenital CNS malformations such anterior encephalocoele [4] and megalencephaly [5]. Cortical malformations are a significant cause of epilepsy and may account for as much as 40% of drug-resistant epilepsy with varying levels of cognitive impairment [2].

## Case Presentation

The patient is a 21-year-old right-handed African male, who is the second child of healthy middle-aged non-consanguineous parents. He presented at the neurology outpatient clinic with a 3-year history of occasional visual hallucinations and 1-year of recurrent tonic-clonic seizures starting with both hands the later involving all his limbs and lasts for 2 minutes to 3 minutes. Prior to onset, he recounts being unaware of familiar environment. There is associated up-rolling of his eyes, however, no foaming of saliva from the mouth, urinary incontinence nor postictal confusion. He had 3 episodes of this seizures and the last was 2 months prior to presentation.

There was no history of head trauma, headache or differential limb weakness. There is no past medical history of seizure in childhood or febrile seizures and no family history of seizure disorder. He does use psychoactive substance(s). His mother had a threatened miscarriage in the first trimester and was hospitalised for a 1-month period; however there was no history of prenatal Toxoplasma, Rubella, Cytomegalovirus, Herpes Simplex or Syphilitic (TORCHS) infection. He was delivered via a spontaneous vaginal delivery at term and cried

immediately after birth. A unilateral cleft of the upper lip was noticed at birth and was repaired at age of 2 years. He attained neck control, sat without support and walked at 3, 6 and 11 months respectively. He completed all immunisations. His academic performance was average, however he had a progressive decline in his university Cumulative Grade-Point Average (CGPA) from 4.00 (1st year) to 2.16 (2nd year). During this period, his seizures were poorly controlled. He is the second born child in a monogamous non-consanguineous family and with 2 siblings (male and female) who are alive and in good health. His parents are also both alive and in good health and there is no known 1st or 2nd generation family member with a seizure disorder or related condition.

On general physical examination he was conscious, alert, in no obvious distress and not pale. His vital signs were within normal limits. His occipito-frontal circumference was 52 cm and body mass index 22.5 kg/m$^2$. His Glasgow coma scale score was 15, cranial nerves and fundoscopic examination were within normal limits. Motor system examination showed subtle spastic paraparesis. Sensory, posterior column and cerebellar functions were also examined and within normal limits. Cardiovascular, respiratory, gastrointestinal and dermatological systems examination were unremarkable.

A diagnosis of focal onset unaware to bilateral tonic-clonic epilepsy was made. He had an electroencephalogram done.

### Electroencephalogram

Findings:

- Background: Posterior dominant alpha rhythm (8 Hz-9 Hz), symmetrical and reactive to eye opening.
- Post-hyperventilation: Phase reversal noted in the right anterior temporal region (F8).
- Photic stimulation: No abnormality detected (Figure 1).
- A brain MRI was done after a time lag of 3 months due to financial constraint and the findings noted below (Figures 2-6). He was also started on tabs Carbamazepine 200 mg BD and further reviewed to 200 mg mane and 400 mg nocte with good seizure control, however, with occasional minor episodes.
- A diagnosis of congenital bilateral sub-ependymal nodular cortical heterotopia associated with unilateral cerebellar hypoplasia with epilepsy was made. His seizures have been satisfactorily controlled with 600 mg of tabs Carbamazepine daily. He has been compliant with his medications from enquiry at his last follow-up visit and evidenced by less frequent minor epilepsy episodes and he admits to have had remarkable seizure control. Genetic testing was not available.

## Discussion

The development of the cerebral cortex involves a complex sequence of events which include neuronal proliferation, migration and cortical organisation [2]. Cortical malformations account for majority of cases of epilepsy [2].

There has been a previous report of epilepsy associated with certain congenital CNS malformations as hemi-megalencephaly in a 3-month old male infant [6] and a 12-year old boy with tuberous sclerosis [7]. Ogunbiyi et al. [8] also reported a 5-month old infant with nevus sebaceous syndrome associated with facial hemi-hypertrophy, hemi-megalencephaly and epilepsy; however, no published report

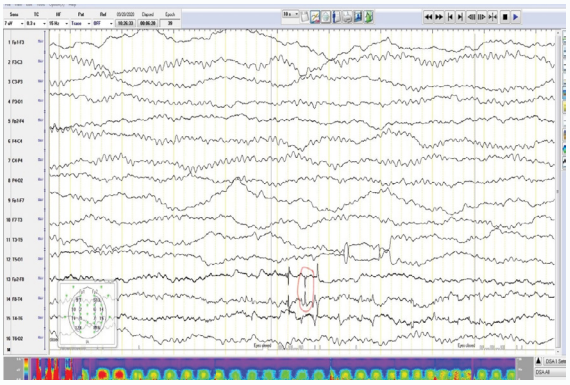

**Figure 1**: Electroencephalogram.

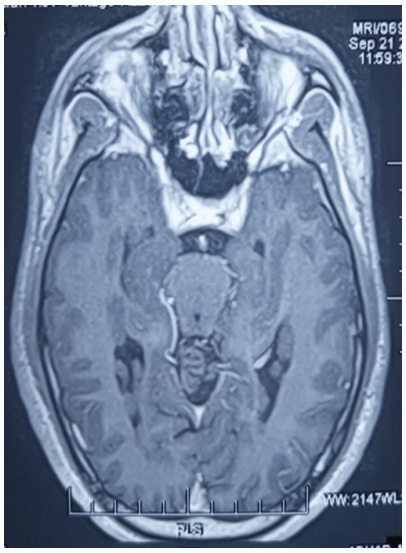

**Figure 2**: T1+C brain MRI, axial slice, showing bilateral subependymal/ periventricular gray matter within the occipital horns of the lateral ventricles, polymicrogyri (cortical dysplasia) involving the right parieto-occipital region.

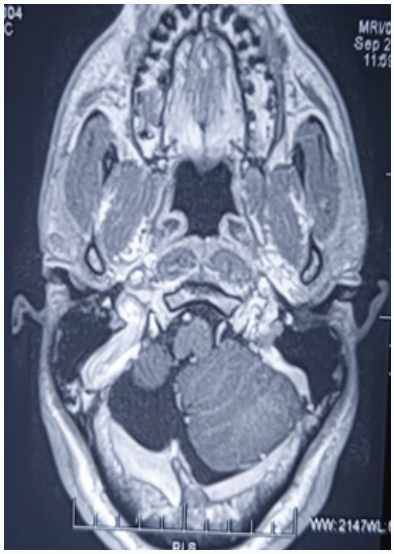

**Figure 3**: T2W brain MRI, axial slice, showing a hypoplastic right cerebellar hemisphere, increased cisterna magna and an asymmetric posterior fossa.

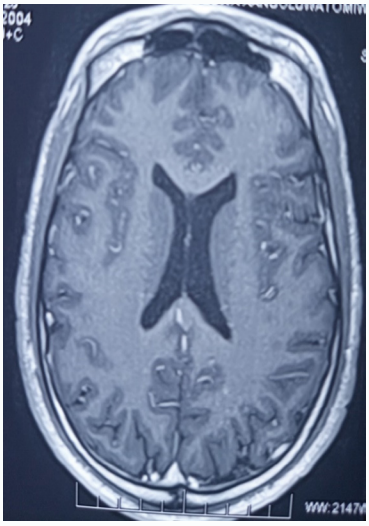

**Figure 4**: T1+C brain MRI, axial slice, showing bilateral periventricular gray matter.

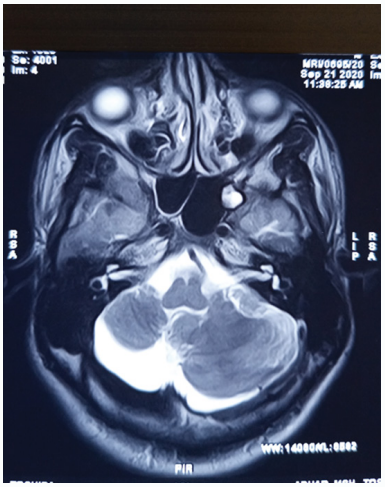

**Figure 5**: T2W brain MRI, axial slice, showing as asymmetric posterior fossa and right cerebellar hemispheric hypoplasia.

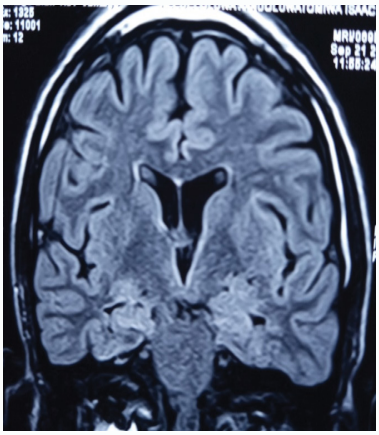

**Figure 6**: T1+C brain MRI, coronal slice, showing bilateral temporal sclerosis.

with cortical heterotopia in the West African sub-region.

In the case reported here, the striking feature was that of a young male adult with a clinical history suggestive of focal onset unaware to bilateral tonic-clonic epilepsy (International League against Epilepsy, 2017 classification) and some lower limb neurological signs of an upper motor neurone lesion. He also had congenital isolated cleft lip. Most individuals with bilateral periventricular nodular heterotopia present with epilepsy, normal intelligence and have no other associated congenital anomaly; however, it has been reported to be associated with cerebellar hypoplasia, severe mental retardation and syndactyly in 3 unrelated boys [9]. Mental retardation was not a feature in this index case. This may further suggest a similar genetic-based multiple congenital malformation syndrome with a less severe phenotype.

Periventricular nodular cortical heterotopia has also been reported to be associated with anterior encephalocoele [4] and megalencephaly [5]; however, epilepsy was not reported in these cases.

Individuals with multiple congenital CNS malformations and epilepsy commonly have significant mental retardation and learning disabilities; intellectual impairment was mild in the case presented. Detailed cognitive testing was not carried out and this may have documented specific areas of deficit. Certain associated phenotypes may account for the disparity in severity of clinical presentation; hence, genetic testing would be imperative.

In summary, this case highlights some of the brain malformations associated with cerebral cortical heterotopia which may only be seen in post-mortem specimens. It also highlights the fact that certain associated non-CNS congenital defects (cleft lip, syndactyly, facial hemi-hypertrophy, nevus sebaceous syndrome, etc.) may also coexist in patients. Clinicians should carry out detailed clinical examination and routinely request brain MRI for young individuals with epilepsy. This would be imperative in detecting these CNS malformations. Genetic studies would also play key roles in determining the molecular basis for the possible epilepsy phenotypes and would also be important for patient counselling and follow up.

## References


1. Greenfield's Neuropathology, 9th Edition, Volume 1; Adams and Duchen. 2015;270-300.
2. Watrin F, Manent JB, Cardoso C, Represa A. Causes and consequences of gray matter heterotopia. CNS Neurosci Ther. 2015;21(2):112-22.
3. Hemorrhage G, Syndromes M, Myeloid A. Case Report Case Report. 1999;5:33-5.
4. Rojas L, Melvin JJ, Faerber EN, Valencia I. Anterior encephalocele associated with subependymal nodular heterotopia, cortical dysplasia and epilepsy: Case report and review of the literature. Eur J Paediatr Neurol. 2006;10(5-6):227-9.
5. Abe Y, Kobayashi S, Wakusawa K, Tanaka S, Inui T, Yamamoto T, et al. Bilateral periventricular nodular heterotopia with megalencephaly: A case report. J Child Neurol. 2014;29(6):818-22.
6. Ugboma E, Agi C. Hemimegalencephaly in a 3-month-old male infant: A case report from port harcourt and review of the literature. West African J Radiol. 2017;24(1):79-81.
7. Altraide DD, George IO, Otike-Odibe B. Tuberous sclerosis: a rare cause of seizure in Nigeria. Niger J Med. 2010;19(3):326-8.
8. Nuova SM, Emilia R. Genetic-unit C. 428 Pediatric Dermatology. 2007;24(4):428-9.
9. Dobyns WB, Guerrini R, Czapansky-Beilman DK, Pierpont MEM, Breningstall G, Yock DH, et al. Bilateral periventricular nodular heterotopia with mental retardation and syndactyly in boys: A new X-linked mental retardation syndrome. Neurology. 1997;49(4).