Case Report

Alternating Hemiplegia of Childhood: Report of Two Cases

Kanij Fatema[1], Md Mizanur Rahman[2], Shaheen Akter[3], Suraiya Begum[4], Md Tanvir Islam[5]

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Abstract

Alternating hemiplegia of childhood (AHC) is a rare disorder which presents before 18 months of age characterized by repeated attacks of hemiplegia involving either side of the body, paroxysmal disturbances,developmental delay and learning disability. The cause of AHC remains largely unknown and treatment evidence is less available. AHC is unreported in Bangladeshi literature. We report two cases of AHC. Our first case is a 16-month-old girl who presented with hemiplegia in alternate side for four episodes. She also had abnormal body movement and irritability during awakening. Every episode subsided spontaneously after 2 to 5 days. All investigations were normal except iron deficiency anemia. She was treated with flunarizine. Our second case, a 7 year and 10 month-old boy presented with recurrent alternate hemiplegia since 3½ years of age with epilepsy. His attacks were precipitated in high temperature. His EEG was abnormal. He was treated with multiple antiepileptic drugs and flunarizine. These are first two cases reported from Bangladesh. AHC remains undiagnosed in many cases. So a detailed history and diagnostic evaluation is very important for early counseling and treatment.

Key words*: Alternating hemiplegia; Flunarizine; Children*

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Introduction

Alternating hemiplegia of childhood (AHC) is rare with an incidence of 1 in 1 million.[1] The clinical features of AHC were first described more than three decades ago. Children with AHC often have a delay in diagnosis or are misdiagnosed. Major features of AHC are — onset before 18 months of age, repeated attacks of hemiplegia involving either side of the body, paroxysmal disturbances including tonic or dystonic spell, nystagmus, strabismus, dyspnea and autonomic phenomena occurring during hemiplegic episodes or in isolation, episodes of bilateral hemiplegia either during attacks that start unilaterally or from the beginning of attacks, disappearance of all symptoms while sleeping, reappearance on awakening after 10 to 20 minutes in children having long attacks, evidence of developmental delay and learning disability.[2] The cause of AHC remains largely unknown and there is little treatment evidence available.[3] So far we know, AHC is unreported in our country. Here we report two cases of AHC.

Case 1

A 16-month-old immunized girl, 1st issue of her consanguineous parents presented with hemiparesis of left side of body for one day in the department of Pediatric Neurology in a tertiary care hospital. She had similar type of episodes three times previously. First time the weakness was on left side, then on other side subsequently. In each episode, onset of weakness was sudden, associated with irritability and abnormal body movements after awakening from sleep. The symptoms were absent during sleep. There was no relationship with temperature, water exposure or activities. She was fully conscious, but half of her body was paralyzed. Every episode persisted for 2–5 days and resolved spontaneously. In between attacks,

1. *Associate Professor, Department of Pediatric Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka*
2. *Professor, Department of Pediatric Neurology, BSMMU, Dhaka*
3. *Professor, Department of Pediatric Neurology, BSMMU, Dhaka*
4. *Associate Professor, Department of Pediatrics, BSMMU, Dhaka*
5. *MD Resident (Phase B), Department of Pediatrics, BSMMU, Dhaka*

Correspondence *Kanij Fatema, Email: mailmonami@gmail.com*

she was quite normal. There was no history of fever, seizure, headache or unconsciousness. None of her family members had this type of illness. She achieved normal developmental milestones during the first year of life. At 12 months of age she was walking independently and could speak few words. She was well alert and moderately pale. Vital signs were within normal limit with appropriate length and weight. Eye examinations revealed normal findings. Higher psychic functions were normal with normal muscle bulk, but hypotonia and weakness were present on left side, reflexes were normal with bilateral planter flexor response. Cranial nerves and pain sensation were intact. Examination of other systems was normal. Her complete blood count and peripheral blood film showed features of iron deficiency anemia. Her CT scan of brain, MRI (Fig 1) and MRA (Fig 2) of brain and EEG were normal. Laboratory tests including lipid profile, ANA and echocardiogram were within normal limit.

Based on the clinical history, normal neurologic examination findings between episodes, and normal investigation reports, the patient was diagnosed as a case of AHC. The patient was treated with flunarizine as prophylaxis for her attacks, but only a modest improvement could be achieved. She was also treated with iron preparation for iron deficiency anemia.

Case 2

A 7 years and 10 month-old boy came to a specialist chamber with history of recurrent episodes of paralysis of one side of body since three and half months of age, which at first persisted for about one hour and resolved after sleep. He had similar episodes of attack recurrently on either side alternately lasting for one hour to several days with intervals of one week to several months. Her mother noticed that exposure to sunlight or even bathing often initiated these hemiplegic episodes. The boy also had recurrent attack of seizure since 2nd day of life which was initially partial tonic in nature lasting for several minutes, then from three months of age he developed frequent atonic seizures. Subsequently, seizure was tonic clonic in nature, sometimes associated with dystonia. This boy had history of perinatal asphyxia and his development was delayed. There was no history of head trauma, fever with unconsciousness, congenital heart disease or similar episodes among family members. Hemiplegia did not occur following a seizure.

Physical examination revealed a cooperative, conscious, alert child without any dysmorphic features. He had squint in left eye. The vital signs were normal. Muscle power was normal with normal reflexes and flexor plantar response in between episodes and classic hemiparetic features during episodes. During attack patient was areflexic and plantar response was flexor bilaterally. Examination of fundus and cranial nerves were normal. Routine blood count, liver and renal function tests were within normal range. EEG were done two times. The first one was normal, but the second one showed generalized epileptic discharge. MRI and MRA of brain were done but none showed significant abnormality. For epilepsy, initially phenobarbitone was given. Then subsequently, sodium valproate, carbamazepine, clonazepam, oxcarbazepine, levetiracetam were given. But seizure did not remit completely although frequency decreased.

Considering the clinical profile and investigations a diagnosis of AHC was made. Flunarizine was given without any significant improvement of clinical features.

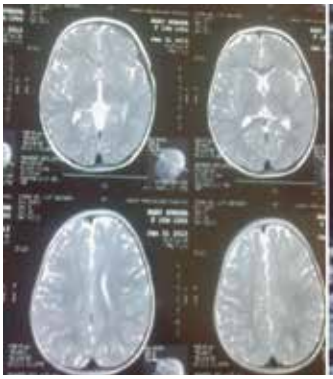

Fig 1. MRI brain showing normal findings

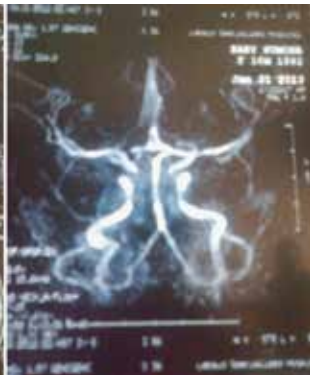

Fig 2. MRA brain showing normal findings

Discussion

AHC is a rare disorder that was first reported by Verret & Steele in 1971.[4] Since this disease occurs so infrequently and is variable in presentation, knowledge of the clinical characteristics, response to treatment, and prognosis are based on few small cohort studies.[5,6]

The onset of the disease occurs in first few months of life. The hemiplegic attacks usually last few minutes to several days and are associated with slowly progressive neurologic deficits over years.The syndrome begins with abnormal ocular movements

(nystagmus, esotropia, exotropia) or dystonia in a majority of patients by three months of age. Hemiplegic attacks occur by six months of age in more than half of the patients. Motor findings during an attack have been described as flaccid and areflexic paralysis. Attacks are frequently associated with triggers, most commonly environmental (temperature extremes, odors) but also water exposure, physical activities (exercise, swinging), lights (sunlight, fluorescent bulbs), or foods (chocolate, food dye).[5,6]

In this report, the onset was at 9 month in the first one and 3½ months in the second one. Both had flaccid areflexic hemiparesis lasting few hours to 3 days. In the case 2, there was history of precipitation of symptom with hot bath and temperature. None of the patients developed quadriparesis during follow-up. In AHC the paralysis is usually flaccid with absence of reflexes, but brisk reflexes and extensor plantars are also described. Virtually all children have episodes of quadriparesis. This is either as the hemiparesis shifting sides or it may start with bilateral involvement. During these episodes, the child is markedly hypotonic, unable to eat or talk and breathing may be affected. At the end of these generalized attacks the children commonly have regression of their motor and cognitive abilities.[5] In both cases the symptoms disappeared during sleep, which leads to the diagnosis in favor of AHC.

Regarding birth history, the first case was uneventful, but the 2nd case had perinatal asphyxia. Developmental milestone was normal in the first case, while the other had motor and speech delay prior to diagnosis. This child was a diagnosed case of cerebral palsy. Children with AHC may have developmental delay. One study reported that there was gross motor delay in 84% (132/157) patients at 0–2 years.[7]

Along with alternate hemiperesis, both the patients had involuntary movement in the form of dystonia during attack. In the second case dystonia persisted beyond attack in later stage. In one study, 88% (138/157) patients of AHC experienced tonic/dystonic attacks involving one limb or two or more limbs on ipsilateral or contralateral sides of the body and occurring alone or mixed with hemiplegic episodes.[7] Another case report from India revealed that there was nystagmus, sweating, vomiting and dysarthria in each episode. Later on the child became ataxic.[8]

Intermittent abnormal ocular movements (AOM), nystagmus or strabismus are another features of AHC. It may accompany or occur separately from dystonic episodes or hemiplegia.[9] One of the cases had squint but no AOM. Epilepsy may occur early in some patients with AHC.[10] Epileptic seizure can occur in 20–50% patients in AHC. They can be focal clonic, generalized tonic clonic or myoclonic.[5] One of the cases presented here had early onset epilepsy. Seizure was initially partial tonic, then atonic and subsequently tonic clonic. It was confirmed by EEG.

The exact cause of AHC is obscure, but it is likely a symptom complex with multiple causes. Neurophysiologic recordings during an attack have shown impaired brainstem circuits.[11] Patients with AHC may show elevated levels of brain lactate during episodes.[12] In contrast, FDG-PET during the interictal period showed low glucose metabolism in the frontal lobes and putamen with normal metabolism in the brainstem which could explain the progressive neurologic symptoms reported with AHC.[13] Microscopic postmortem evaluation of patients with AHC has shown abnormal vascular smooth muscle cells which could result in a functional vascular disorder causing transient small vessel dysfunction in the brain.[14] Another study of MRS of brain suggests that AHC is associated with an initial phase of relative focal cerebral hypoperfusion followed by prolonged hyperperfusion.[15]

The familial occurrence of AHC is reported.[16] AHC complicating migraine often has a strong family history of classic migraine in at least one first degree relative.[15] The attacks occurring in AHC and familial hemiplegic migraine (FHM) are clinically similar, raising the question of a channelopathy as the underlying dysfunction for both. FHM has been associated with several ion transport genes including SCN1A (sodium channel, neuronal type 1, alpha subunit), CACNA1A (calcium channel, voltage dependent, P/Q type, alpha-1A subunit), and ATP1A2 (ATPase, Na+/K+ transporting, alpha-2 polypeptide). There was no positive family history in our cases.

The diagnosis of AHC is clinical. Laboratory tests are not helpful. Structural neuroimaging may be normal or show cerebral atrophy. Ictal electroencephalogram during episodes of hemiplegia may be normal or show slowing.[5] We have investigated both the patients with neuroimaging (CT scan, MRI and MRA) which

showed normal findings. The patient with epilepsy had generalized epileptic discharge. In addition to that one patient had iron deficiency anemia. The diagnosis is usually delayed despite typical manifestations. The differential diagnoses are vascular disorders, aminoacidopathies and encephalo-myopathies with stroke like episodes.[17]

Current therapies for AHC tend to be inadequate and the literature on treatment mostly consists of case reports. Numerous drugs have been used to treat AHC. Flunarizine at a dose of 5–20 mg/day has been reported to decrease severity, duration and frequency of the attacks of hemiplegia in some patients. There have also been case reports of topiramate and aripiprazole resulting in a reduction in frequency, duration and severity of episodes.[18-20] We administered flunarizine in both cases. There was some improvement in both cases. Avoiding triggers, i.e. cold, emotional stress, fatigue, bathing in hot water, hot or cold weather can help but may not be practical. Management of attacks with early sleep induction using benzodiazepines with or without melatonin has been used to shorten attacks. Associated pain should be treated with simple analgesia.[1]

Conclusion

The early and accurate diagnosis of AHC is essential to establish drug therapy and improve the prognosis and the quality of life of patients and their families.

References

1. Neville BGR, Ninan M. The treatment and management of alternating hemiplegia of childhood. Dev Med Child Neurol 2007; 49: 777–780.
2. Bourgeois M, Aicardi J, Goutieres F. Alternating hemiplegia of childhood. J Pediatr 1993; 122: 673–679.
3. Jeffrey R. Alternating hemiplegia of childhood. Neurology 2010; 74(14): 57–59.
4. Verret S, Steele JC. Alternating hemiplegia in childhood: a report of eight patients with complicated migraine beginning in infancy. Pediatrics 1971; 47: 675–680.
5. Mikati MA, Kramer U, Zupanc ML. Alternating hemiplegia of childhood: clinical manifestations and long-term outcome. Pediatric Neurology 2000; 23: 134 –141.
6. Sweney MT, Silver K, Gerard-Blanluet M. Alternating hemiplegia of childhood: early characteristics and evolution of a neurodevelopmental syndrome. Pediatrics 2009; 123: 534–541.
7. Eleni P, Giuseppe G. Evidence of a non-progressive course of alternating hemiplegia of childhood: study of a large cohort of children and adults. Brain 2010; 133: 3598–3610.
8. Kalra V, Rathi S. Alternating hemiplegia of childhood. Indian Pediatrics 1996; 233: 33–35.
9. Karen P. Alternating hemiplegia of childhood. Journal of Pediatric Neurology 2010; 8: 35–36.
10. Aicardi J. Alternating hemiplegia of childhood. Int Pediatr 1987; 2: 115–119.
11. Rinalduzzi S, Valeriani M, Vigevano F. Brainstem dysfunction in alternating hemiplegia of childhood: a neurophysiological study. Cephalalgia 2006; 26: 511–519.
12. Rust RS, Thomas A, Zupanc ML. H volume localized in vivo magnetic resonance spectroscopy and single-photon emission computed tomography in alternating hemiplegia. Ann Neurol 1992; 32: 452.
13. Sasaki M, Sakuma H, Fukushima A, Yamada K, Ohnishi T, Matsuda H. Abnormal cerebral glucose metabolism in alternating hemiplegia of childhood. Brain Dev 2009; 31: 20–26.
14. Auvin S, Joriot-Chekaf S, Cuvellier JC, Pandit F, Cuisset JM, Ruchoux MM et al. Small vessel abnormalities in alternating hemiplegia of childhood. Neurology 2006; 66: 499–504.
15. Arnold D, Silver K, Andermann F. Evidence for mitochondrial dysfunction in patients with alternating hemiplegia of childhood. Ann Neurol 1993; 33: 604–607.
16. Bradshaw P, Parson M. Hemiplegic migraine, a clinical study. Quart J Med 1965; 34: 65–85.
17. Pavlkis SG, Phillips PC, DiMauro S. Mitochondrial myopathy, encephalopathy, lactic acidosis and strokelike episodes. A distinctive clinical syndrome. Ann Neurol 1984; 16: 481–488.
18. Haffejee S, Santosh P. Treatment of alternating hemiplegia of childhood with aripiprazole. Dev Med Child Neurol 2009; 51: 74–77.
19. Di Rosa G, Spano M, Pustorino G. Alternating hemiplegia of childhood successfully treated with topiramate: 18 months of follow-up. Neurology 2006; 66:146.
20. Silver K, Andermann F. Alternating hemiplegia of childhood: a study of 10 patients and results of flunarizine treatment. Neurology 1993; 43(1): 36–41.