Case Report

Multi-Disciplinary Therapeutic Approach of Cerebral Atrophy Ammonia: A Single Case Study

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ABSTRACT

Cerebral atrophy ammonia, a neuro developmental disorder, is a rare, progressive that has been reported only in the girl child. A case of an 8-year-old girl with Cerebral atrophy ammonia is presented here. The present study observed who have normal development till the age of 3 years. However, gradually over the next few months, she lost her acquired, purposeful hand skills; expressive and receptive language; and reciprocal social interaction; she gradually developed a broad-based gait and typical stereotyped hand movements. EEG and MRI were abnormal. Awareness of this disorder is required for early diagnosis and prompt treatment. The inclusion Criteria which consists of partial or complete loss of acquired purposeful hand skills. Gait abnormalities; impaired (dyspraxia) or absence of ability. This case report emphasizes the importance of being aware of rare yet significant disorders of interest to paediatric physiotherapist.

Keywords: Cerebral atrophy ammonia, methyl ECP pervasive developmental disorder, neurodevelopmental disorder

INTRODUCTION

Cerebral atrophy ammonia is a neurodevelopmental disorder that exclusively affects the girl child.[1] It is characterized by normal development till 6 months to 48 months of age followed by gradual loss of purposeful hand movements and development of characteristic, stereotypical hand movements; loss of previously acquired speech; psychomotor retardation; ataxia; truncal apraxia; deceleration of head circumference; and autistic symptoms.[1, 2, 3, 4]

A characteristic hand wringing or hand washing stereo type develop. Expressive and receptive language skills become severely impaired and are associated with marked mental retardation. A loss of social interaction skills is frequently observed during the preschool years, but social interest often increases later.[5,6] Originally, the condition was thought to be confined only to girls, but boys with this disorder are quite close to it had been described. [7] The estimated prevalence ranges from 1 in 10,000 to 1 in 22,000. Despite several reports from the all over the world very few cases have been reported from the Indian subcontinent.[8,9,10]

CASE REPORT

An 8-year-old female child presented to the OPD at NIMHANS Hospital, with a gradual loss of speech, social interaction and hand skills, stereo typed movements of the hand and body since last five years. Born of a non-consanguineous marriage, an uncomplicated pregnancy, full term normal delivery at hospital. Regular immunizations were carried out. At birth her weight and height were normal. Gross motor, fine motor, social & emotional and language milestone were normal during first three years of life.

History of presenting illness: At about the age of three years her development seemed to stagnate. Her

developmental milestones then became delayed gradually. By the age of 8 years, she could not walk, whereas she used to run previously. She could not speak any meaningful words, whereas she used to narrate small sentences earlier. The mother also reported her lack of attachment with family members, her inability to hold, pick up or grasp things in her hands.

She would keep both palms of her hands one over the other and would move or rub one hand over the other. Teeth grinding was also reported. The child walked with a broad-based gait. She was unable to indicate her need for daily activities such for toilet, passing stools, or for food. Marked cognitive and communicative delay was noted. Features suggestive of severe mental retardation were obvious. Family history suggestive of mild mental retardation in elder sister.

Examination: No eye contact. Characteristic stereotyped hand movements. General physical and systemic examination was not contributory. Gait ataxia and muscle wasting was noticed. Head circumference was 48 cm, less than 3 standard deviations from the mean for her age (ICMR, 1989) (As per the mother, her head circumference had decreased compared to that at birth). Dental check up revealed a high-arched palate, dental attrition, and dental caries.

Investigation: Hemoglobin, TLC, DLC, and ESR were normal. EEG: Generalized slow waves observed throughout the EEG recording, suggestive of inter-ictal period of generalized seizure disorder. The same abnormality was also observed during the photo stimulation. However, hyperventilation could not be performed (although there was no history of any seizure episode).

MRI: Diffuse cerebral atrophy with T2 hypointensity of the basal ganglia, thalami and midbrain and focal T2 hypointense left occipital lobe lesion.

Diagnosis: Cerebral atrophy ammonia as per ICD-10 criteria (F84.2).

Treatment: Pharmacotherapy in the form Clonazepam 1mg B.I.D. and carbamazepine 200mg B.I.D was prescribed. Physiotherapy, speech therapy and dental treatment were advised but the patient never returned for follow up.

DISCUSSION

In 1966 pediatrician Andreas Rett, an Austrian physician, noticed that several retarded girls made peculiar, continuous "hand washing" motions.[13] Two decades later, in 1983, a Swedish researcher named Bengt Hagberg published a follow-up study in Annals of Neurology, which led to world- wide recognition of Cerebral atrophy ammonia.[14] The condition named after Andreas Rett has since been diagnosed in thousands of individuals, almost all of them girls. But the cause of the disorder still is a mystery, and the effective treatment is exclusive.[15]

Children with Cerebral atrophy ammonia often exhibit autistic-like behaviours in the early stages.[16] Other symptoms may include walking on the toes, sleep problems, a wide-based gait, teeth grinding and difficulty chewing, slowed growth, seizures, cognitive disabilities, and breathing difficulties while awake such as hyperventilation, apnea (breath holding), and air swallowing.[17]

This is a progressive disorder, in which the patient becomes wheelchair-bound due to rigidity and dystonia, and develops scoliosis in the late stages leading to decreased longevity.[18]

Four stages of Cerebral atrophy ammonia have been defined to help characterize the disorder and improve its recognition and diagnosis.[19] These stages may be described as follows:

1. Stage I: Early onset (6–18 months of age) - affects early development first with stagnation.
2. Stage II: Regressive/rapid deterioration stage (1-4 years) - devastating cognitive and motor regression.
3. Stage III: Relative stabilization/plateau (2-10 years)- partial recovery.
4. Stage IV: Late motor impairment (after 10 years) - cognitive stability with motor impairment.

MRI study shows diffuse cerebral atrophy, which has been noted in few earlier case reports (Bibat 2001).[16] EEG abnormalities are also reported in almost all reported cases (Kumar et al., 2004).[10] Oral findings of girls with Cerebral atrophy ammonia have also been described in few cases reported earlier.

There is no cure for cerebral atrophy ammonia. In the present case, management could not be carried out in an effective and comprehensive manner, as the case was lost to follow-up after assessment.

Treatment is intended to ease the symptoms and to keep the patient mobile as long as possible. The treatment requires an integrated, multidisciplinary approach, including symptomatic and supportive medical management, physical, occupational, and speech therapy, and special academic, social, vocational, and supportive services (Kerr AM et al., 2003).[9]

Pharmacotherapy, in the form of bromocriptine, magnesium citrate, L-carnitine (may help improve language skills, muscle mass, alertness, energy and quality of life while decreasing constipation and daytime

Figure 1: Before Therapeutic Approach

Figure 2: After Therapeutic Approach

sleepiness), naltrexone (to stabilize breathing irregularities), levodopa (to alleviate muscle stiff- ness) etc., has been tried for symptom control without reasonable success.

Cerebral atrophy ammonia occurs almost exclusively in females, therefore it had been proposed that cerebral atrophy ammonia is caused by an X-linked dominant mutation with lethality in hemizygous males. This proposal has been confirmed with the discovery that Rett's disorder result from mutations in the X-linked methyl-CpG-binding protein 2 (MECP2) gene on chromosome Xq28.

The MECP2 gene contains instructions for the synthesis of a protein called methyl cytosine binding protein 2 (MeCP2), which is needed for brain development and acts as one of the many biochemical switches that can either increase gene expression tell other genes when to turn off and stop producing their own unique proteins.

Because the MECP2 gene does not function properly in individuals with Rett's syndrome, insufficient amounts or structurally abnormal forms of the protein are produced and can cause other genes to be abnormally expressed.

Male fetuses with the disorder rarely survive to term. Because the disease causing gene is located on the X chromosome, a female born with a MECP2 mutation on her X chromosome has another X chromosome with an ostensibly normal copy of the same gene, while a male with the mutation on his X chromosome has no other X chromosome, only a Y chromosome; thus, he has no normal gene.

Without a normal gene to provide normal proteins in addition to the abnormal proteins caused by a MECP2 mutation, the XY karyotype male fetus is unable to check the development of the disease; hence this explains the failure of many male fetuses with a MECP2 mutation to survive to term. Females with a MECP2 mutation, however, have a non-mutant chromosome that provides them enough normal protein to survive at least to birth.

Research shows that males with cerebral atrophy ammonia almost all have Klinefelter's syndrome as well (in which the male has an XXY karyotype). Thus, a non-mutant MECP2 gene is necessary for a Rett's affected embryo to survive in most cases, and the embryo, male or female, must have another X chromosome.

CONCLUSION

In conclusion, it is important for clinicians to be aware of this disorder because increased identification will help ingreater understanding of this disorder and proper guidance will help the patient and family, and reduce the burden of care on the parents.

If possible, genetic analysis or gene mapping should be carried out (especially pre-natal testing for families with an affected daughter who has an identified MECP2 mutation). Thus, it is suggested that all female children presenting with low intelligence and autistic symptoms should be suspected of having cerebral atrophy ammonia until proved otherwise.

CONFLICT OF INTEREST :

The authors declared no conflict of interest.

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