

A Case Report on Aicardi-Goutieres Syndrome 7

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ABSTRACT

Aicardi-Goutieres Syndrome (AGS) is a genetically heterogeneous neurodevelopmental disorder which most typically affects brain and skin. It is an inflammatory disorder resulting from mutation of the genes. Majority of the affected individuals experiences physical as well as intellectual problems. Here we discuss a case of Aicardi-Goutieres Syndrome 7. And in our case, this syndrome is due to the mutation of IFIH1 gene.

Key words: AicardiGoutieres Syndrome, IFIH, Gene mutation, Neurodevelopmental disorder, Inflammatory disorder.

INTRODUCTION

Aicardi-Goutieres Syndrome (AGS) is an early onset neurodevelopmental disorder.¹ It is an inflammatory disorder resulting from mutation in any of the seven genes like TREX1,² RNASEH2A, RNASEH2B, RNASEH2C,³ SAMHD1,⁴ ADAR1,⁵ and IFIH1.⁶ This condition generally suffer from progressive microcephaly associated with severe neurological symptoms, such as hypotonia (state of low muscle tone), dystonia (abnormal muscle tone), seizures, severe developmental delay and spastic quadriplegia (paralysis of all the four limbs).^{7,8}

Aicardi-Goutieres Syndrome can be of two types on the basis of onset: early and late onset form. Early onset is very severe and affects 20 percent of the infant babies. These infants are born with liver (elevated liver enzymes and enlargement of the liver and spleen) and neurological abnormalities. But babies with later-onset, begin their symptoms after first few weeks or months of normal development, which projects as muscle spasticity, decline in head growth, developmental and cognitive delays. The risk to siblings are only less than 1%.

Ophthalmologic examination, brain MRI findings and skeletal findings (fused vertebrae, fuse ribs) can be used as diagnostic tool. Fetal MRI and prenatal ultrasound

examination may identify some features of Aicardi syndrome. Musculoskeletal support, occupational, physical, speech and vision therapy should begin at diagnosis.⁹

CASE REPORT

This case was seen in Believers Church Medical College Hospital, Thiruvalla, a multi centred, tertiary care, teaching hospital in South India. A female child, aged 4 years with regression of all milestones from 2 years of age was brought to our hospital with complaints of severe spasticity⁸ on both lower limbs, up rolling of eyes and drooling. Till 1 year 2 months of age no issues, developmental milestones were normal. After that, child had recurrent fever, detected to have tuberculosis, given Anti Tuberculosis Treatment (ATT) for 6 months. Parents noticed that child had frequent falls while walking. She can't drink from a straw and had difficulty in getting up from sitting and lying down position. So evaluated in Paediatric department at 2 years of age and diagnosed with congenital myopathy. Creatine phosphokinase was 93.2 U/L (Normal range: 34 – 145 U/L) and lactate was 1.9 mmol/L (Normal range: < 1.2 mmol/L). Survival of Motor Neuron (SMN) gene mutation was negative. Nerve biopsy showed chronic mild axonal neuropathy.

DOI: 10.5530/ijopp.13.3.45

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But electroencephalography (EEG) and Transcranial magnetic stimulation (TMS) were normal. Neurology gene analysis was done and identified heterozygous mutation in IFIH1 gene. She was diagnosed as Aicardi-Goutieres Syndrome -7 and was discharged with syndopa (carbidopa-levodopa) and baclofen. Then it was stopped after 1 month. She was readmitted due to high intermittent fever, brassy cough and horsy breathing since 2 days. At admission, child was febrile with inspiratory strider. But the child was looking nontoxic. SPO₂ was 100% in room air. A clinical possibility of laryngotracheo bronchitis was made. As child had significant strider, she was managed with nebulisation epinephrine, bronchodilators and steroids. And her condition was improved with the given treatment. Now she was admitted with complaints of elevation of upper limb with bending of trunk and up rolling of eyes, lasting for 10 to 20 sec, both in awake and sleep. Events had increased in duration to 30 sec each but frequency decreased associated with difficulty in breathing, but no change in skin colour. She gets around 20 episodes per day. Lactate was 3.03mmol/L and erythrocyte sedimentation rate (ESR) was 2mm/hr (Normal range: 1 – 20 mm/hr). She was initiated on oral Clobazam (5 mg twice a day), but no improvement was noticed. So dose of oral Clobazam was hiked up (7.5 mg twice a day) and oral valproate (100 mg twice a day) was added. She was initiated on low glycemic index diet. Her seizure frequency improved. Parents were counselled about oral – motor exercises for drooling, posture adjustments while feeding and asked them to stimulate chewing mechanisms. Now she is on Tab. Frisium (Clobazam) 7.5 mg twice a day (1 mg/ kg/day) and Tab. Valparin 100mg twice a day (14 mg/kg/day).

DISCUSSION

This child had recurrent fever, seizure, spasticity and feeding difficulty. But she doesn't have any organomegaly, ptosis (the prolapse of a bodily organ, especially drooping of the eyelid or the breasts) or ophthalmoplegia (complete paralysis of extra ocular muscles which are responsible for the eye movements). In this syndrome, associated symptoms or diseases should be treated. And she had given Tab. Frisium (benzodiazepine) and Valparin (sodium valproate) for seizure. Physical therapies like oral – motor exercises were also advised. The levels of CSF neopterin and interferon alpha activity^{10,11} were increased in this syndrome. And this can be taken as a diagnostic criteria.

Mir Sumsam Ali Khurram *et al.*¹² also reported a case on Aicardi-Goutieres Syndrome. In his case report, it was

a female patient and had symptoms like seizure, mental retardation, loss of speech and bilateral abnormalities. Also she had spasticity in the upper and lower limbs. For this, she had given broad spectrum antibiotics and antiepileptic agents (phenytoin and levetiracetam).

CONCLUSION

There are no direct treatment options for Aicardi-Goutieres Syndrome. Instead, we treat the associated symptoms. Physical and occupational therapies can also improve the conditions. Aicardi-Goutieres Syndrome can cause endocrine (hypothyroidism) as well as vision problems (glaucoma). So periodic check-up is required.

ACKNOWLEDGEMENT

I would like to thank our Department of Pharmacy Practice for the valuable suggestions in bringing the case report to completion. I would also like to thank the patient, her parents and the hospital authority for their cooperation. I am deeply indebted to Dr. Bincy Baby, Clinical specialist, Department of Neurology, Believers Church Medical College Hospital, for her immense help and time to suggestions during this work.

CONFLICT OF INTEREST

The author declare that there is no conflicts of interest.

ABBREVIATIONS

AGS: Aicardi-Goutieres Syndrome; **MRI:** Magnetic Resonance Imaging; **ATT:** Anti-Tubercular Treatment; **EEG:** Electroencephalogram; **TMS:** Transcranial Magnetic Stimulation; **SPO₂:** Peripheral capillary oxygen saturation; **ESR:** Erythrocyte Sedimentation Rate; **CSF:** Cerebrospinal fluid.

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