Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 19s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

A Rare Case of PLA2G6 – Infantile Neuroaxonal Dystrophy Type 1

Dr. Renuka S Jadhav[1], Dr. Shiji Chalipat[2], Dr. V Poornima Lakshmi[3], Dr. Karthik D[*4], Dr.Vineeta pande[5], Dr Shailaja Mane[6]

[1]MD Paediatrics, Professor, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: jrsrenuka@gmail.com

[2]MD Paediatrics, Professor & Paediatric Neurologist, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: dr_shiji@yahoo.in

[3]MD Paediatrics, Fellow in Paediatric Neurology, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: poornimavonteru@gmail.com

[4*]MBBS, MD Resident in Paediatrics, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr.D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: drkd2512@gmail.com

[5]MD Paediatrics, Professor Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: drvineetapande@gmail.com

[6]MD Paediatrics, Professor & Head of Department, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: shailaja.mane@dpu.edu.in

***Corresponding Author:**

Dr. Karthik D,

MBBS, MD Resident in Paediatrics, Department of Paediatrics, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune-411018, India.

Email ID: drkd2512@gmail.com

Cite this paper as: Dr. Renuka S Jadhav, Dr. Shiji Chalipat, Dr. V Poornima Lakshmi, Dr. Karthik D, Dr.Vineeta pande, Dr Shailaja Mane, (2025) A Rare Case of PLA2G6 – Infantile Neuroaxonal Dystrophy Type 1. *Advances in Consumer Research*, 2 (3), 635-638.

ABSTRACT

Background: The term PLA2G2-associated neurodegeneration (PLAN) refers to a range of neurodegenerative illnesses in which neurons experience oxidative stress and neuroinflammation as a result of phospholipase A2 enzyme deficiencies and mutations of the PLA2G2 gene. INAD is caused by mutation of the phospholipase A2 group VI (PLA2G6)

gene, mapped to chromosome 22q13.1

Case summary: A 6-year-old female patient with progressive neuroregression was brought

to the OPD with chief complaints of developmental delay, with recurrent respiratory

infections. With spasticity.

Conclusion: For pediatrics patients who show with early rapid cognitive decline, motor regression, and axial hypotonia, INAD is a pathology/differential diagnosis that should be taken into consideration. The current findings on those mutations suggest that genetic counselling and early diagnosis could benefit from screening for PLA2G6 gene variants.Additionally, biopsy analysis could help prevent high-risk pregnancies.

Keywords: *Group VI Phospholipases A2, Neurodegenerative Diseases, Glycerophospholipids, Muscle Hypotonia, Infantile neuroaxonal dystrophy.*

1. INTRODUCTION

The term PLA2G2-associated neurodegeneration (PLAN) refers to a range of neurodegenerative illnesses in which neurons experience oxidative stress and neuroinflammation as a result of phospholipase A2 enzyme deficiencies and mutations of the PLA2G2 gene. [1] An essential lipase found in human body tissues and broadly distributed throughout organ tissues is the iPLA2β protein, which is encoded by the PLA2G6 gene. The substantia nigra, cortex, and hippocampus of the human brain exhibit significant levels of iPLA2β expression. These conditions are classified into four categories: autosomal recessive-early-onset parkinsonism (AREP), adult-onset dystonia-parkinsonism (DP), atypical

neuroaxonal dystrophy (ANAD), and infantile neuroaxonal dystrophy (INAD) Infantile neuroaxonal dystrophy (INAD), is a rare progressive neurodegenerative disorder known as formerly known as Seitelberger's disease (Online Mendelian of Inheritance in Man ID 256600), was first reported by Franz Seitelberger in 1952[2], who described two siblings who presented with psychomotor delay in infancy followed by progressive neuroregression, which resulted in severe disability and death in the first decade of life. [3]. They usually present with no significant symptoms at birth. Usually, symptoms appear from 6 months to 36 months. Numerous symptoms are linked to this progressive neurological condition, presenting as psychomotor regression, hypotonia, extrapyramidal symptoms, spastic tetraplegia, vision issues, cerebellar ataxia, cognitive decline, and dementia. [4] Seizures are not reported. Pathologic hallmarks are marked neuroaxonal dystrophy, severe cerebellar atrophy and degeneration of the lateral corticospinal tracts, also associated with axonal inflammation, iron accumulation in brain, spheroid body development in various tissues of nervous system. So PLA2G6 -infantile neuroaxonal dystrophy type 1 is a rare case.

Case Report

A 6-year-old female child, 2nd order born out of 3rd degree consanguineous marriage with uneventful birth history with a background of global developmental delay along with neuroregression noted since 12 months of age presented to us with recurrent respiratory infections. She has attained walking without support and able to speak bisyllable by 1 year of age, Mother noticed the progressive regression in motor milestones along with regression in other domains, there was loss of her pincer and palmar grasp, and inability to reach for objects. Gradually child lost the ability to head control and was bed ridden by 20 months of age. Currently she can respond to loud noises and bright light. Her paternal cousin is having history of developmental delay which was not evaluated. Her younger brother have normal growth and development. she progressively showed signs of psychomotor retardation. she has history of multiple admissions due to repeated aspirations, diarrhoea, fractures and for bed sore management. On examination she was showing significant failure to thrive with her weight and length less than 3rd centile, vitally stable. Her neurological examination showed microcephaly, horizontal nystagmus, esotropia squint, grade 2 spasticity with severe muscle wasting, power grade 2 in Upper Limb and grade 1 in Lower Limb along with brisk deep tendon reflexes, Babinski, clonus positive bilaterally, cerebellar signs not able to assess. On MRI brain at 1 year as part of her workup done outside showed inferior vermian hypoplasia, Cerebellar hypoplasia with white matter and centum semiovale T2 / FLAIR hyperintensities was observed. EMG study, showed few of MUAPs with long duration and few of them were of high amplitude and evidence of late recruitment, Possibility of neurogenic process. NCV examination suggestive of Abnormal study with low amplitude and low velocity CMAP and

SNAP. Her clinical Genetics NGS reports at 1 year identified homozygous variant c.2138A>Tp.N713I Ex15 603604 likely pathogenic variant detected, on gene PLA2G6 infantile neuroaxonal dystrophy- 1 (autosomal recessive) homozygous on exon 15 was noted. We started her on multidisciplinary approach along with neurorehabilitation . In view of feeding difficulties PEG insertion was advised.80

Discussion:

In our case with above clinical presentation at 1 year of life with supporting evidence of genetics and MRI changes led to diagnosis. Neuroaxonal dystrophies are a group of neurodegenerative disease with autosomal recessive pattern, onset during the first three years of life, INAD is a rare progressive neurodegenerative illness marked by pathologic axonal enlargement and spheroid bodies in the central nervous system. [5] The majority of INAD patients have a progressive condition that includes early visual problems, spastic tetraplegia, cerebellar ataxia, significant trunk hypotonia with subsequent bilateral pyramidal tract symptoms, and motor and mental decline. [6] With typical findings compared to general population, our case did not have complications at pregnancy, but patient directly presented to us at 12 months of age with neuroregression.

The PLA2G6 phospholipase (iPLA2-VI) activity was shown to be greatly lowered by the mutations linked to INAD, according to Engel et al. [9] Pla2G6 encodes iPLA2-VI, a calcium-independent phospholipase that plays an essential role in preserving the homeostasis of cell membranes by means of phospholipid remodeling, apoptosis control, and glycerophospholipid hydrolysis catalysis. [10] According to Kinghorn et al.,[11] defects in the mitochondrial membrane follow lipid peroxidation and mitochondrial malfunction, which are caused by a loss of normal PLA2G6 gene activity. Axons deteriorate as a result of poor maintenance and rupture of the inner mitochondrial and presynaptic membranes, according to a unique pathogenic mechanism discovered by Sumi-Akamaru et al. [12] and potentially leading to axonal dystrophy.

Diagnostic criteria for INAD were defined based on analysis of clinicopathological findings I n 50 patients defined

(i) onset before 3 years,

(ii) progressive course of diffuse central nervous system disorder with psychomotor deterioration and increasing neurological involvement comprising symmetrical pyramidal tract signs and marked hypotonia &

(iii) presence of axonal spheroids on biopsy of central or peripheral nervous system tissue. [6] MRI findings are variable depending on the disease stage at which imaging was performed, with our case MRI done at 1year showed minimal changes but there is no serial MRIs at different age to compare the disease progression.Typical findings described include cerebral atrophy, white matter changes, and iron deposits in the globus pallidus, substantia nigra, and dentate nucleus. Due to the presence of iron deposits, INAD can be classified as a subtype of neurodegeneration with brain iron accumulation diseases (NBIA). However, iron deposits are not specific to INAD. [20] In our case, follow up MRI could not be done to prove the typical features.Management of INAD remains largely supportive, with no cure available yet. Recent research reported the successful use of gene therapy in patient-derived neural progenitor cells, in flies and mice in slowing the progress of INAD. [22] However, human studies are underway and results are awaited. With the advancement of next generation sequencing, newer genes are likely tobe identified as a cause of INAD and can be targeted for gene therapy. For parents at risk of having an INAD affected child, it is important to provide counselling, with advance technology and diagnostic tools early detection is and genetic testing of couples with risk should be counselled before conception.

It is necessary to report rare disease like these, as it helps in diagnostic and therapeutic approach in future, for improving patient's outcome. Therefore, keeping INAD as one of the differentials in cases of developmental neuroregression will be important.

2. CONCLUSION:

For pediatric patients who show with early rapid cognitive decline, motor regression, and axial hypotonia, INAD is a pathology/differential diagnosis that should be taken into consideration. To better understand the relationship between gene abnormalities and the pathophysiology of INAD, more research is required. In order to validate the diagnosis of INAD, cranial MRI and screening for PLA2G6 gene mutations should be carried out and based on the clinical symptoms. The current findings on those mutations suggest that genetic counselling and early diagnosis could benefit from screening for PLA2G6 gene variants.Additionally, biopsy analysis could help prevent high-risk pregnancies.

REFERENCES

[1] Gebril O, Uebe S, Reuter M, Schumacher J, Jamra RA, Reis A. A new missense mutation in PLA2G6 gene among a family with infantile neuroaxonal dystrophy INAD. Egyptian Pediatric Association Gazette. 2016;64(4):171–6.

[2] Guo Y-P, Tang B-S, Guo J-F. PLA2G6-Associated Neurodegeneration (PLAN): Review of Clinical Phenotypes and Genotypes. Front Neurol. 2018;9:1100

[3] Li H, Zou Y, Bao X, Wang H, Wang J, Jin H, et al. Monozygotic twins with infantile neuroaxonal dystrophy: A case report and literature review. Exp Ther Med.2016;12(5):3387–9.

[4] Iodice A, Spagnoli C, Salerno GG, Frattini D, Bertani G, Bergonzini P. Infantile neuroaxonal dystrophy and PLA2G6-associated neurodegeneration: An update for the diagnosis. Brain Dev . 2017;39:93–100.

[5] Zhang P, Gao Z, Jiang Y, Wang J, Zhang F, Wang S, et al. Follow-up study of 25 Chinese children with PLA2G6-associated neurodegeneration. European journal of neurology. 2013;20(2):322–30.

[6] Frattini D, Nardocci N, Pascarella R, Panteghini C, Garavaglia B, Fusco C. Downbeat nystagmus as the presenting symptom of infantile neuroaxonal dystrophy: a case report. Brain & development. 2015;37(2):270–2.

[7] Carrilho I, Santos M, Guimarães A, Teixeira J, Chorão R, Martins M, Dias C, Gregory A, Westaway S, Nguyen T, et al. Infantile neuroaxonal dystrophy: What's most important for the diagnosis? Eur J Paediatr Neurol. 2008;12:491–500. doi:10.1016/j.ejpn.2008.01.005.

[8] Illingworth MA, Meyer E, Chong WK, Manzur AY, Carr LJ, Younis R, Hardy C, McDonald F, Childs AM, Stewart B, et al. PLA2G6-associated neurodegeneration (PLAN): Further expansion of the clinical, radiological and mutation spectrumassociated with infantile and atypical childhood-onset disease. Mol Genet Metab.

[9] 2014;112:183–189. doi: 10.1016/j.ymgme.2014.03.008.Engel LA, Jing Z, O'brien DE, Sun M, Kotzbaueret PT. Catalytic function of PLA2G6 is impaired by mutations associated with infantile neuroaxonal dystrophy but not dystonia-parkinsonism. PLoS One. 2010;5:e12897. doi:10.1371/journal.pone.0012897.

[10] Ma Z, Turk J. The molecular biology of the group VIA Ca2+-independent phospholipase A2. Prog Nucleic

Acid Res Mol Biol. 2001;67:1–33. doi:10.1016/S0079-6603(01)67023-5.

[11] Kinghorn KJ, Castillo-Quan JI, Bartolome F, Angelova PR, Li L, Pope S, Cocheme HM, Khan S, Asghari S, Bhatia KP, et al. Loss of PLA2G6 leads to elevated mitochondrial lipid peroxidation and mitochondrial dysfunction. Brain.2015;138:1801–1816. doi: 10.1093/brain/awv132.

[12] Sumi-Akamaru H, Beck G, Kato S, Mochizuki H. Neuroaxonal dystrophy in PLA2G6. Neuropathology. 2015;35:289–302. doi: 10.1111/neup.12202.

..