LATE ONSET DYSTONIA - A RARE PRESENTATION OF GM1 GANGLIOSIDOSIS

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INTRODUCTION

Late onset dystonia leading to gait and speech abnormalities is a not so uncommon presentation in the pediatric neurology clinic. Common and treatable differentials include Dopa responsive dystonia, Wilsons's disease, neuronal brain iron accumulation. Describing a rare condition to add to the list.

CASE PRESENTATION

A 12 year old boy, born of a non-consanguineous marriage, with normal birth and early development presented with difficulty in walking noticed at 3 years of age.

He initially developed dystonic posturing of the left leg leading to frequent falls. Dystonia gradually progressed to involve the upper limb causing difficulty in fine motor activities. He gradually developed speech disturbance. He had no cognitive impairment, seizures, myoclonus, or tremors

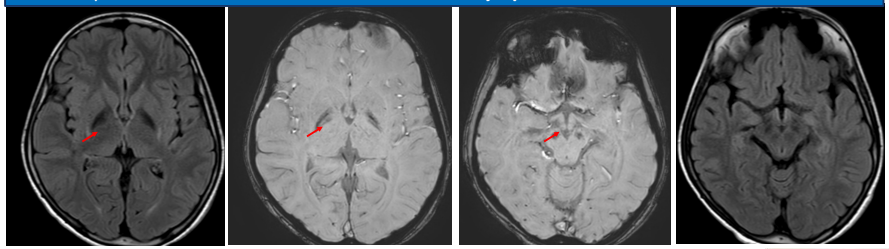
On examination, he had dysarthric speech with dystonia affecting mainly the appendicular and facial muscles. Other neurological examination including ophthalmological evaluation was normal.

His metabolic work up consisting of serum ceruloplasmin, vitamin B12, phenylalanine, prolactin, lactate were within normal limits. MRI brain at 10 years of age was reported normal. Trial of DOPA didn't show any improvement. Next generation sequencing was sent.

INVESTIGATION

Gene transcript	Location /Variant	Disease (omim)	Inheritance/Zygosity	Classification
NR4A2 (ENST00000409108.6)	Exon 7 c.1390C>T	Intellectual developmental disorder with language impairment and early onset DOPA responsive dystonia- parkinsonism (OMIM 619911)	Autosomal dominant heterozygous	Pathogenic
GLB1 (ENST00000307363.10)	Exon 13 c.1325G>A Intron 1 c.75+2dup	GM1 gangliosidosis Type III (OMIM 230650)	Autosomal recessive Likely compound heterozygous	uncertain significance

Parental testing was done for analysis of variant detected by NGS in the NR4A2 gene in the index patient . The **mother was found to be an asymptomatic carrier of the same variant.**



REPEAT MRI : Axial T2-WI (a) shows bilateral symmetrical atrophy and hyperintensities of posterior putamen. Axial SWI image (b) reveals '**wish bone**' pattern of hypointensities secondary to mineral deposition in the globus pallidi, forming the fork and substantia nigra, red nuclei, forming the stem

LEUKOCYTE ENZYME ACTIVITY

Test(units)	Disorder	Results	Biological reference interval (mean)	Status
Beta Galactosidase (nmol/hr/mg)	**GM1 Gangliosidosis**	**5.0**	**70-324 (148.1 +/-35.7)**	**low**

DISCUSSION

- The juvenile-onset form of GM1 gangliosidosis (type 3) is a clinically distinct type, with a variable age of onset presenting with progressive ataxia, dysarthria, intellectual disability, and spasticity. Survival is upto 4th decade.
- MRI may reveal global cerebral atrophy/volume loss, iron deposition in the basal ganglia in a wishbone pattern .
- There can be findings in the spine such as dysotosis, platyspondyly, vertebral beaking, hip dysplasia.
- Therapeutic strategies include substrate reduction therapy with Miglustat, Venglustat, enzyme replacement therapy with Beta Galactosidase, stem cell transplantation and gene therapy.

CONCLUSION

- Keeping an open mind and correlating clinically during each stage of diagnosis is important.
- Biochemical tests are still relevant in this age of genetics and that genetic reports to be interpreted with caution.

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