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Early Genetic Diagnosis Of Marinesco–Sjögren Syndrome In An Infant Without Cataract: Expanding The Phenotypic Spectrum

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Abstract-

Background: *Marinesco–Sjögren syndrome (MSS) is a rare autosomal recessive disorder, classically presenting with early-onset cataracts, cerebellar ataxia, and developmental delay.* ***Case Presentation:*** *we present a one-year-old male child born to third degree consanguineous parents with global developmental delay and hypotonia. Neuroimaging showed cerebellar hypoplasia. In view of clinical suspicion of MSS, even though the child hasn't developed cataract, whole-exome sequencing done which revealed homozygous frameshift mutation (c.302_303del) in exon 4 of the SIL1 gene. This case highlights that MSS may present before cataract onset, and early neuroimaging and genetic testing can clinch the diagnosis.* ***Conclusion:*** *MSS should be considered in infants with unexplained hypotonia and cerebellar hypoplasia, even in the absence of cataracts.*

Keywords: *Marinesco-sjogren syndrome, hypotonia in infant, SIL1 gene mutation, cataract in infant*

INTRODUCTION-

Marinesco–Sjögren syndrome (MSS) is a rare autosomal recessive multisystem disorder, most commonly caused by mutations in the *SIL1* gene. It is characterized by a classic triad of early-onset cataracts, cerebellar ataxia, and developmental delay, with additional features such as myopathy, hypotonia, and short stature. Among these, bilateral congenital or early childhood cataracts are often the most prominent and earliest presenting manifestation, frequently leading to diagnosis. Cataract onset typically occurs within the first decade of life and can result in significant visual impairment if untreated. Early recognition of ocular involvement is crucial for timely intervention and improved functional outcomes.

Case Report-

A 1-year-old male child born to third-degree consanguineous parents, presented with global developmental delay with uneventful birth history. There was no history of seizures, hearing loss, or visual complaints. Developmental assessment revealed a developmental quotient of 16, indicating severe global delay in gross motor, fine motor, and language domains, with age-appropriate social development.

On physical examination, child has plagiocephaly, low-set ears, and a prominent forehead. Anthropometry showed the child to be underweight for age. Child had generalized hypotonia with preserved deep tendon reflexes and intact cranial nerve function. Sensory and cerebellar functions appeared intact. Ophthalmologic evaluation was normal with no evidence of cataracts. MRI brain demonstrated cerebellar hypoplasia (Figure 1) with cerebellar cortical T2 hyperintensities (Figure 2).
Hypotonic cerebral palsy, congenital disorders of glycosylation, mitochondrial disorders, and muscular dystrophy were considered as differential diagnosis. Since our patient has significant hypotonia, developmental delay and imaging showing cerebellar hypoplasia, MSS was also considered but since child didn't develop cataract, our diagnosis was challenging. Hence genetic testing was done which revealed homozygous frameshift variant, c.302_303del (p.Glu101GlyfsTer6), in exon 4 of the SIL1 gene, confirming MSS.

DISCUSSION-

MSS is a rare neurodegenerative disorder caused by biallelic SIL1 mutations. It is characterized by developmental delay, cerebellar ataxia, myopathy, and early-onset bilateral cataracts. Skeletal anomalies such as kyphoscoliosis, short metatarsals, and delayed bone age may also occur [1,2].
While cataracts are considered a hallmark, they may develop later in childhood [3,4]. Our patient lacked cataracts at presentation, which made the diagnosis challenging. Cerebellar hypoplasia on MRI, especially when combined with hypotonia and developmental delay, should raise suspicion for MSS [4,5]. Genetic confirmation remains the gold standard.
From our literature search we found that MSS is rare with fewer than 200 cases reported worldwide and the youngest age group reported in india was a 4 months old child with cataract[6]. Our index patient is the only youngest child without cataract diagnosed as MSS in india. This article highlights the importance of genetic testing in atypical presentations.
Management is supportive, focusing on physiotherapy, speech therapy, nutritional support, regular ophthalmologic screening, and genetic counselling [7]. Early diagnosis enables timely intervention and early rehabilitation to improve the quality of life among those children.

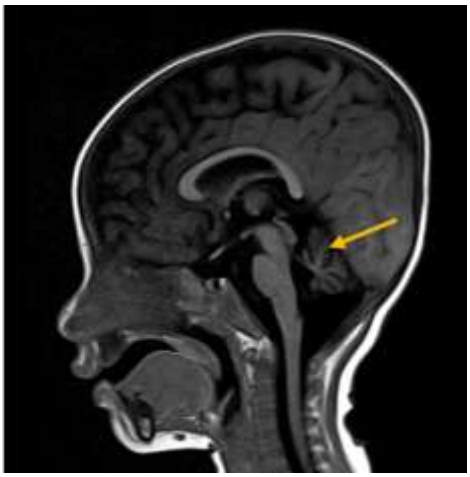

Figure 1- MRI Brain showing cerebellar hypoplasia

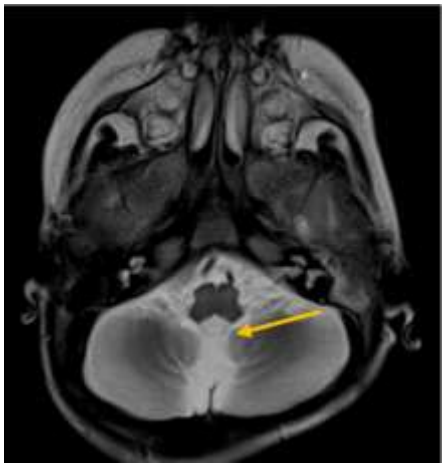

Figure 2- MRI brain showing cerebellar cortical T2 hyperintensities

CONCLUSION-

Our patient lacked the hallmark of early onset cataract, highlighting the need for early genetic testing in achieving a diagnosis, facilitating timely multidisciplinary interventions and genetic counselling. Hence MSS should be suspected in children with hypotonia, developmental delay, and cerebellar hypoplasia, even in the absence of cataracts.

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