

A Case Report on Spinal Muscular Atrophy

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Abstract: Case report on spinal muscular atrophy - Spinal Muscular Atrophy is characterised by degeneration of lower motor neurons in spinal cord, causing progressive paralysis of limbs and trunk, followed by muscle atrophy sparing extraocular muscles. SMA is one of most frequent Autosomal Recessive diseases, with a carrier frequency of 1 in 50 and is the most common genetic cause of childhood mortality.

Keywords: Spinal muscular atrophy, SMN gene, autosomal recessive mendelian inheritance, respiratory support, genetic analysis - chorionic villous sampling

1. Background

Spinal Muscular Atrophy is characterised by degeneration of lower motor neurons in spinal cord, causing progressive paralysis of limbs and trunk, followed by muscle atrophy. SMA is one of most frequent Autosomal Recessive diseases, with a carrier frequency of 1 in 50 and is the most common genetic cause of childhood mortality.

2. Case report

A 6 months old male child 2nd born to non consanguineous marriage brought by parents with complaints of rapid breathing for past 1 month. Child was normal upto 5 months

of life. History of 2 hospital admissions in past 1 month for similar complaints. history of NICU admission for delayed cry. Neck holding not yet attained. On examination – tone decreased in all limbs, absent reflexes, B/L pupils mid dilated reacting to light. hepatomegaly – present.

3. Investigations

Complete hemogram – normal, s. sodium – 138m.mol/l, s. potassium – 3.6m.mol/l, s.chloride – 98m.mol/l. s.creatinine – 0.9mg/dl. CPK – normal fundus – normal study, Gene analysis – showed homozygous deletion of exon 7 and 8 in SMN 1 gene.



RESULTS*

PATHOGENIC VARIANT CAUSATIVE OF THE SUSPECTED PHENOTYPE WAS IDENTIFIED

Sl. No.	Gene Exons*	Deletions /Duplications	MLPA probe ratio (Dosage quotient)	Copy number	Disease (OMIM)	Inheritance	Classification
1.	SMN1 (Exons 7 & 8)	Homozygous deletion	0.00	0	Spinal muscular atrophy	Autosomal recessive	Pathogenic
2.	SMN2 (Exons 7 & 8)	-	1.00	2			

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

CLINICAL CORRELATION AND VARIANT INTERPRETATION

Homozygous deletion of exons 7 and 8 in the SMN1 gene, was detected within the detection limits of MLPA, in this subject (Fig. 1). No deletions or duplications were detected in the exons 7 and 8 of the SMN2 gene. The subject has an SMN1:SMN2 gene copy number ratio of 0.2. Functional absence of SMN1 gene due to homozygous deletions is reported to be pathogenic in 95% of SMA cases (1). Hence, this deletion is pathogenic and has to be carefully correlated with clinical symptoms.

4. Treatment

On mechanical ventilator with chest physiotherapy and oral feeds.



5. Discussion

Spinal muscular atrophy is a degenerative disease of motor neurons that begins in fetal life and continues to be progressive in infancy and childhood. SMA is most common cause of infant mortality incidence of sma is 1 in 6000 to 10000 newborns. SMA is caused by homozygous deletion in survival motor neuron 1 (SMN1) gene on chromosome 5q13.

SMA is classified into severe infantile form also known as WERDNIG – HOFFMANN DISEASE or SMA type 1, a late infantile and more slowly progressive form – SMA type 2, a more chronic or juvenile form – KUGELBERG – WELANDER DISEASE or SMA type 3, an adult onset form – SMA type 4.

The cause of SMA is autosomal recessive mendelian trait. It appears to be a pathologic continuation of a process of programmed cell death (apoptosis) that is normal in embryonic life.

Differential diagnosis of SMA – Spinal cord disorders, other motor neuron disorders, Neuropathies, Neuromuscular junction disorders, Myopathies.

Treatment – multimodality approach – Respiratory support, Nutritional, Orthopedic physiotherapy, Psychological.

Hypotonic child with sparing of extraocular muscles and sphincters suspect SMA. Genetic analysis is the definitive diagnostic test. Muscle biopsy can be done in selective cases with equivocal or negative gene analysis.

6. Conclusion

For future pregnancies genetic analysis of chorionic villous sampling to be done for diagnosis of SMA.