Original Research Paper

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Pediatrics

A CASE REPORT ON SPINAL MUSCULAR ATROPHY TYPE 1 ASSOCIATED WITH EXTENSIVE LOWER LIMB HYPOTONIA

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ABSTRACT Spinal muscular atrophy (SMA) is a genetic motor neuron disease characterized by progressive degeneration of motor neurons. Here in, a 4.5 Months male child, born to healthy nonconsanguineous parents, has been brought with the chief complaints of weakness of both lower limbs since birthThere was no family history of neurological disease. On clinical examination, CVS function was normal. Fasciculations were seen in tongue. Respiratory muscles were mild affected. A diagnosis of SMA1 (deletion of SMN-I exons 7 and 8) was made on the basis of clinical presentation. No medical treatment was able to delay the progression, while In 2016, U.S. Food and Drug Administration approved nusinersen, treatment was improved muscle strength and movement in spinal muscular atrophy pediatrics and adults. Supporting therapy includes orthopedic care and mild physiotherapy.

KEYWORDS : Fasciculation, SMA1 gene, weakness of lower limbs. Nusinersen

INTRODUCTION

Spinal muscular atrophy (SMA) is an autosomal, recessive degenerative disease of motor neurons. It usually begins in fetal life associated with weakness and the loss of voluntary muscles, continues to be progressive in infancy and childhood. SMA causes weakness and the loss of voluntary muscles [(1)]. More than 95% of the patients with SMA have a homozygous disorder in the *SMN1* gene on chromosome 5q, caused either by mutation or deletion, leads to a loss of function of the SMN protein, which was involving maintaining muscle integrity [(2)]. The incidence of SMA is 10–15 in 100,000 live births, affecting all ethnic groups; it is the second most common neuromuscular disease, following Duchenne muscular dystrophy. The incidence of heterozygosity in autosomal recessive SMA is 1 in 50 [(3,4,5)].

CASE REPORT

4.5 months old male children was admitted to Kurnool medical government hospital with weakness of both lower limbs since birth. He was a child of nonconsanguineous parents. There was no history of early death or neurological disease in either parents family. He looked alert, showed social smiling, poor gross motor function, could not control head, posture was severely hypotonic. On examination, greater hypotonia of lower limbs, compared to upper limbs, gross motor delay, low voice of cry, normal sucking, no CNS, CVS risk, respiration had been mild distressed. Fasciculations were present lower limbs. A power of Grade 1- 2 was present in the upper limbs. Grade 0-1 power was present in the lower limbs. Deep tendon reflexes were absent. Tongue fasciculation was observed. Molecular genetic diagnosis for the analysis of genetic diagnosis revealed that deletion of the exon 7 and 8 of SMN-T (telomeric copy of survival motor neuron), which confirmed the diagnosis.

DISCUSSION

SMA is one of the most common genetic neuromuscular diseases, following Duchenne muscular dystrophy. SMA is classified into four types according to onset of symptoms, Very severe SMA Type 0: manifests before birth and it is characterized by a reduction in fetal movements in the final months of pregnancy. SMA Type 1: severe infantile form (Werdnig–Hoffmann disease), manifests within the 1st few weeks or months of life when abnormally low muscle tone is observed in the infant (the floppy baby syndrome). SMA Type 2: late infantile and more slowly progressive form. SMA Type 3: more chronic or juvenile form (Kugelberg–Welander disease). It is autosomal recessive inherited and is caused by the loss of the telomeric copy of the survival motor neuron gene (SMN1) on human chromosome 5q132 (Lefebvre S 1995). Expression of the SMN gene is prevalent in many kinds of neurons, but motor neurons are exclusively affected in SMA. These motor neuron defects cause the pathologic change of SMA1 [(6)].

Although the child may appear normal during infancy, there is a slow but progressive weakness of limbs. There is no medical treatment available to this condition. Respiratory system requires utmost attention in SMA, as once weakened it never recovers fully. Weakened pulmonary muscles in SMA Type I/II patients can make breathing more difficult and pose a risk of hypoxia, especially during sleep when the muscles are more relaxed [(6)].

Genetic counseling should be offered to all families of patients with SMA. The role of prenatal diagnosis, particularly in pregnant carriers or those with juvenile or adult-onset forms, should also be addressed. Preimplantation genetic diagnosis can be used to detect SMA-affected fetus, especially when undergoing *in-vitro* fertilization. Prenatal testing toward SMA is possible through chorionic villus sampling, cell-free fetal DNA analysis, and other methods. Those at risk of being carriers of *SMN1* deletion, and thus at risk of having offspring affected by SMA, can undergo carrier analysis using blood or saliva sample. Similarly current Patient genetic information was revealed thate mutations of SMA I gene. Currents US FDA recommended Nusinersen [(7)] is the first approved drug used for treatment of this disorder [(8,9,10)] directly to the central nervous system (CNS) using intrathecal injection. We conclude that genetic mutation in the retained SMN1 caused SMA in the patient, and suggest that this mutation is a critical factor in determining disease severity.

Conflicts of interest

There are no conflicts of interest.

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COMPLEX, ESHWAR
NAGAR(G)ANDHI BA

Name	: RIZWAN			Collected	: 12/2/2019 1:30:00PM
Lab No.	: 249083443	Age: 8 Months	Gender: Male	Received	
	:			Reported	
	:			Report Status	: 13/2/2019 12:31:16PM
					: 19/2/2019 4:05:20PM
A/c Status	P	Ref By : GOVT.HOSPITAL			: Final

Test Name	Results	Units	Bio. Ref. Interval
SPINAL MUSCULAR ATROPHY (SMA), MUTATION DETECTION @ (MLPA)	Detected		

Note: Deletion detected in SMN1 (Exons 7 and 8). Clinical correlation recommended.

Note

- PCR is a highly sensitive technique, however inherent PCR inhibitors in the specimen may result in amplification failures
- Results must be interpreted in context with clinical findings, family history and other relevant laboratory data
- Genetic counseling is recommended

Comment

Spinal Muscular Atrophy (SMA) is a group of autosomal recessive neuromuscular disorders characterized by degeneration of anterior horn cells of the spinal cord, leading to symmetrical muscle weakness & atrophy. With a prevalence of 1 in 10,000 live births and a carrier frequency of approximately 1 in 50, proximal SMA represents the second most common fatal autosomal recessive disorder after Cystic fibrosis. There are two highly similar genes playing a pivotal role in SMA, SMN1 and SMN2. These genes can be distinguished by two single nucleotide differences one in exon 7 and one in exon 8. SMN2 gene is much less efficient in making functional SMN protein, therefore SMN1 gene is the determinant factor in developing SMA. Individuals lacking a functioning copy of SMN1 gene is always a patient, whereas SMA carriers carrying a single copy of SMN1 gene are symptom-free.

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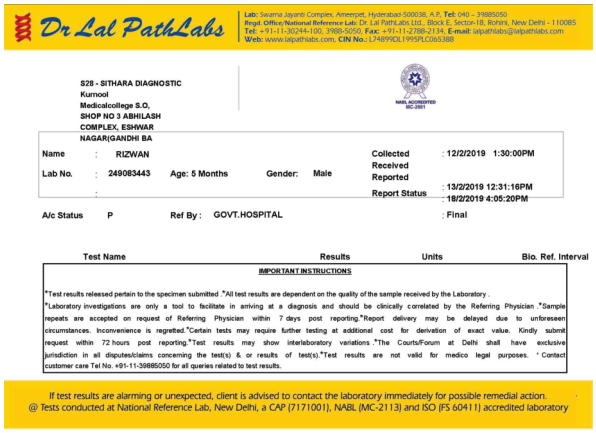
End of report

* Not in NABL scope Page 1 of 2



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Test Name	Results	Units	Bio. Ref. Interval

IMPORTANT INSTRUCTIONS

*Test results released pertain to the specimen submitted .*All test results are dependent on the quality of the sample received by the Laboratory .
*Laboratory investigations are only a tool to facilitate in arriving at a diagnosis and should be clinically correlated by the Referring Physician .*Sample repeats are accepted on request of Referring Physician within 7 days post reporting.*Report delivery may be delayed due to unforeseen circumstances. Inconvenience is regretted.*Certain tests may require further testing at additional cost for derivation of exact value. Kindly submit request within 72 hours post reporting.*Test results may show interlaboratory variations .*The Courts/Forum at Delhi shall have exclusive jurisdiction in all disputes/claims concerning the test(s) & or results of test(s).*Test results are not valid for medico legal purposes. * Contact customer care Tel No. +91-11-39885050 for all queries related to test results.

If test results are alarming or unexpected, client is advised to contact the laboratory immediately for possible remedial action.
@ Tests conducted at National Reference Lab, New Delhi, a CAP (7171001), NABL (MC-2113) and ISO (FS 60411) accredited laboratory

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