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CASE REPORT

Very severe spinal muscular atrophy (Type 0)

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ABSTRACT

This case report describes a rare phenotype of very severe spinal muscular atrophy (SMA) in a newborn who presented with reduced fetal movements in utero and significant respiratory distress at birth. The patient was homozygously deleted for exon 7 and exon 8 of the survival motor neuron gene 1. Very severe SMA should be considered in the differential diagnosis of respiratory distress at birth, and more research should be dedicated to investigate the genetic determinants of its widely variable phenotypes.

Key words: Exon, neurodegenerative, newborn, severe, spinal muscular atrophy

INTRODUCTION

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease characterized by progressive symmetrical muscle weakness resulting from the degeneration and loss of anterior horn cells in the spinal cord and brain stem nuclei. It is the most common genetic cause of infant mortality, affecting approximately 1 in 10,000 live births.[1]

The disease is conventionally classified into four phenotypes [Table 1].[2]

In 1999, MacLeod *et al*. have described five cases of very severe SMA Type 1, all of whom presented with reduced fetal movements in utero, severe weakness at birth, and short survival time.[3]

CASE REPORT

This male newborn was the second child of unrelated parents. He was born by spontaneous vaginal delivery at 38 + 0 weeks of gestation weighing 2620 g.

Antenatally, the mother, noticed reduced fetal movements in the last 2 weeks of gestation, and there was polyhydramnios on antenatal scans. She is a nonsmoker and denies any alcohol or drugs consumption.

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Around delivery, a mixture of nitrous oxide and oxygen (Entonox®) was used for pain relief during labor. The baby was born cyanotic, floppy with no respiratory effort and no chest wall movement. After two cycles of assisted breaths, the patient remained bradycardic with heart rate <20/min and therefore, chest compressions were initiated. The patient was intubated with size - 3.5 tube which resulted in an improvement in his oxygenation and circulatory response.

On day 9 of age, examination by neurologist revealed a generalized hypotonia with absent gag and suck reflexes. Contractures of the shoulders, elbows, hips, and knees were noted. Deep tendon reflexes and jaw jerk were absent.

A chest X-ray showed a right upper lobe consolidation, likely to be due to aspiration. Baby was covered with broad spectrum antibiotics: Benzylpenicillin (50 mg/kg twice daily) and gentamicin (5 mg/kg every 36 h) then vancomycin (15 mg/kg every 8 h) and ceftazidime (25 mg/kg twice daily). Cranial ultrasound showed the normal appearance of brain and ventricles with no signs of hemorrhage. A metabolic screen of amino acids and acylcarnitine was unremarkable.

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Table 1: Phenotypes of spinal muscular atrophy

	Age of onset	Maximum of function achieved	Prognosis	Proposed sub-classification	SMN copy number
Type 1 (severe)	0-6 months	Never sits	If untreated, life expectancy <2 years	1A: No head control, onset in neonatal period 1B: No head control, onset after neonatal period 1C: Head control achieved, onset after neonatal period	One or two copies of SMN2 in 80% of patients
Type 2 (intermediate)	7-18 months	Sits but never stands	Survival into adulthood	Decimal classification according to functional level, from 2.1 to 2.9	Three copies of SMN2 in >80% of patients
Type 3 (mild)	>18 months	Stands and walks	Survival into adulthood	3A: Onset of weakness before 3 years 3B: Onset of weakness after 3 years	Three or four copies of SMN2 in 96% of patients
Type 4 (adult)	10-30 years	Stands and walks	Survival into adulthood		Four or more copies of SMN2

SMN: Survival motor neuron

In genetic studies, myotonic dystrophy Type 1 was negative but the baby was homozygously deleted for exon 7 and exon 8 of survival motor neuron gene 1 (SMN1).

The diagnosis was fully explained to parents and on day 12 of life, the baby was discharged to the local hospice for compassionate extubation after which he passed away.

DISCUSSION

SMA is caused by homozygous deletions or mutations in the SMN1 gene on chromosome 5 q13.[4] SMN1 exon 7 is homozygously absent in approximately 94% of patients with clinically typical SMA.[5] There is a marked correlation between SMN-encoded protein levels and disease severity in SMA.[6] In all SMA Type 0 cases reported by MacLeod and her team, centromeric SMN gene was present but in reduced copy number compared with a control group of children with the less severe Type 1 SMA.[3]

Although in this case, SMA has been confirmed, polyhydramnios, to some extent, might have contributed to the clinical features and presentation. Cessation of fetal movements associated with polyhydramnios has been reported in the medical literature.[7] A review showed that, in polyhydramnios, there is a 2–5-fold increase in the risk of perinatal mortality.[8]

Patients with SMA and their families or carers should be routinely offered genetic counseling. Being an autosomal recessive disease indicates that there is a 25% chance to have an affected child if both parents were found to be carriers. In an American study, Caucasians have the highest carrier's frequency and detection rate whereas African Americans had the lowest.[9]

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Conflicts of interest

There are no conflicts of interest.

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