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Case Report

A rare case of X-linked centronuclear myopathy in a neonate

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ABSTRACT

We present the case of a late preterm male neonate who was limp at birth requiring extensive resuscitation in delivery room, requiring mechanical ventilation requiring higher settings and progressively worsening respiratory failure. Investigative panel reports later showed that the baby had a X-Linked myotubular myopathy (XLMTM)-centronuclear myopathy (CNM), which was the diagnosis responsible for the baby's clinical presentation. Although CNMs do not have a specific treatment, early diagnosis of milder variants and understanding their pathophysiology helps in further facilitating diagnostic approach for the future.

Keywords: Centronuclear myopathy, Myotubular myopathy, Whole exome sequencing

INTRODUCTION

Centronuclear myopathy (CNM) is a neuromuscular disorder having an incidence of 2 per 100,000 among males.[1] It is due to mutation in myotubularin (MTM1) gene and centrally placed nuclei in muscle fibers.[2,3] CNM presents with severe phenotypic changes in male at birth with profound weakness, severe hypotonia and respiratory failure. Signs of antenatal onset are frequent and comprise reduced fetal movements and polyhydramnios.[4] Few case reports show CNM present as intrauterine deaths, abortions and adults with mild variety due to variable expressivity. CNM is similar to spinal muscular atrophy and congenital myotonic dystrophy in clinical presentation. We report a baby boy born with MTM1 gene mutation.

CASE REPORT

A preterm, 34-week, male baby, with birth weight of 1880g was born to a 31-year-old primigravida mother who was diagnosed as gestational diabetes mellitus, by non-consanguineous marriage. Baby was delivered through caesarean section on 23 January 2024 at 5.57 pm due to premature rupture of membranes and was limp at birth, requiring positive pressure ventilation, intubation and chest compression in labour room. Antenatally, mother had history of polyhydramnios and decreased fetal movements perception in 2nd trimester but no history of sibling deaths. On examination, baby had spontaneous eye opening, long facies, hypotonic posture, paradoxical breathing, scaphoid abdomen and Bilateral undescended testes and slender limbs. Tone decreased on all limbs, power <3/5 in hip knee and elbow joints. Tongue fasciculations and contractures were absent.

Baby was continued on mechanical ventilation due to poor respiratory efforts, IV fluids and feeds initiated. Baby progressively required increasing ventilator settings due to poor clinical response.

Investigations revealed serum creatine phosphokinase of 222 U/l, ammonia of 85 µmol/l, Lactate levels, tandem mass spectrometry (TMS) and urine gas chromatography

mass spectrometry (GCMS) were normal. Abdominal ultrasound showed bilateral renal pelvicalectasia. Cranial Ultrasound revealed no significant abnormality. Gene analysis revealed MTM1 gene mutation. Baby remained ventilated in hospital with multiple extubation failures and died on day 9 of life.

Table 1: Blood investigations of the baby.

Parameters	Value
Hb	14 g/dl
TC	3730 cells/mm^3
DC	N 81, L 11 E1
Platelet	46000 cells/mm^3
ESR	14 mm/hr
PCV	42.3
Urea	43.7 mg/dl
Creatinine	0.56 mg/dl
Calcium	7.7 mg/dl
Na	136 mEq/l
K	4.2 mEq/l
Cl	99 mEq/l
SBR	5.48 mg/dl

DISCUSSION

Myotubular myopathy refers to the X-linked form of the condition (XLMTM), which is the severe, catastrophic presentation; whereas the term CNM is normally used to indicate the autosomal variety. The autosomal CNM may be dominant in more than 90% of documented cases or rarely may present as a recessive trait, in less than 10%. The autosomal recessive CNM is less severe in clinical manifestations. The first symptoms may appear in utero presenting as polyhydramnios and reduced perception of fetal movements. Affected subjects are predominantly boys presenting at birth with hypotonia and respiratory insufficiency or failure. CNM afflicted cases may present with multiple arthrogryposis associated with spinal and rib cage deformities. Due to early onset dysphagia and poor suck-swallow co-ordination, nasogastric tube is often needed for feeding. Reduced eye movements and eyelid ptosis are also noted in myotublar myopathies. Babies are often macrosomic and may have other associated surgical pathologies such as pyloric stenosis, inguinal hernias and cryptorchidism.[4,5] XLMTM and CNM have short life expectancy and majority die during the first year of life due to respiratory insufficiency or aspiration pneumonia.[6,7] However, there are no reports of cardiomyopathy, cardiac conduction defects or arrhythmias amongst XLMTM and CNM.[8,9]

While a definitive diagnosis of XLMTM is normally performed based on characteristic findings in a muscle biopsy, our baby was diagnosed with XLMTM by genetic analysis done by Whole exome sequencing without performing a muscle biopsy, suggesting that genetic testing can be performed as a confirmative method of diagnostic testing before performing an invasive procedure such as a muscle biopsy.[10,11] With the positive results from genetic analysis, a muscle biopsy can be treated as unnecessary for the diagnosis, especially considering it is invasive procedure. Furthermore, genetic testing can provide useful guidance to parents considering prenatal genetic testing for their future pregnancy outcomes.[12]

CONCLUSION

We have described a neonate with XLMTM, which was confirmed by the genetic testing of MTM1 gene. Although a muscle biopsy remains an essential diagnostic tool for neuromuscular diseases, advanced molecular genetic testing can provide a correct diagnosis while avoiding invasive procedures. Further research studies on genotype-phenotype correlations and the function of myotubularin will provide new insights into this disorder.

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