CASE REPORT OPEN ACCESS

The Life-Saving Impact of Early Diagnosis and Treatment for Spinal Muscular Atrophy Type 1

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ABSTRACT

Spinal muscular atrophy (SMA) is a hereditary neuromuscular condition caused by mutations in the Survival Motor Neuron 1 gene. This report presents a clinical description of a case diagnosed with SMA and highlights the significance of early recognition and multidisciplinary management. SMA affects the anterior horn cells in the spinal cord, leading to progressive muscle weakness and atrophy. It is classified into four types based on the age of onset and clinical severity. Type 1 SMA, also known as Werdnig-Hoffmann disease, is the most severe form and generally manifests within the first six months of life. A boy was suspected of having SMA type 1 due to his hypotonic posture and 2.8 kg birth weight. Symptomatic treatment and diagnostic tests like MRI were done, but the infant died after a few days of readmission on day 28 due to severe breathing issues and muscular atrophy. The diagnosis was confirmed after his death.

Keywords: Spinal Muscular Atrophy (SMA), Werdnig-Hoffmann Disease, Motor Neuron Disease, Respiratory Insufficiency, Infantile Spinal Muscular Atrophy, Creatine Kinase (CK-MB).

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INTRODUCTION

Mutations in the Survival Motor Neuron 1 (SMN1) gene result in the autosomal recessive neuromuscular disease known as spinal muscular atrophy (SMA). Progressive muscular weakness and atrophy result from SMA's damage to the anterior horn cells in the spinal cord[1]. Based on the clinical severity and age of onset, it is divided into four categories. The most severe kind, SMA type 1 or Werdnig-Hoffmann disease, usually appears in the first six months of life[2]. Early diagnosis, prompt treatment, and comprehensive supportive care are the main emphases in this case study to improve the quality of life for affected newborns and their families.

CASE PRESENTATION

A boy was delivered at SMBB Lyari General Hospital in Karachi and, due to a strong family history, was suspected of having SMA type 1. The baby, weighing 2.8 kg at birth, had a hypotonic posture and a weak instantaneous cry. Several resuscitation procedures were employed, and the baby was referred to the NICU for hypoxic-ischemic encephalopathy (HIE). The baby was transferred to the NICU after breathing problems the next day. A

brain MRI and other diagnostic procedures were performed. The baby scheduled a follow-up appointment for an SMA type 1 test but did not appear on the follow-up. On day 28, the 3.2-kilogram infant made a reappearance with a hypotonic body posture and severe respiratory distress. He seemed feeble and alert, with a floppy frog-like stance and no tongue fasciculation. The laboratory received the SMA type 1 test, the CK-MB test, and additional diagnostic tests. Nebulization and suction were done, chest physical therapy was resumed, and medication was changed to injections of meconium and vancomycin. After two episodes of apnea, ambo bagging was started, and adrenaline was administered. The patient was advised to use a ventilator support system if one wasn't currently available. Ambubagging was given as needed, but the patient died four days later.

Complete blood counts, electrolytes, testing for liver and kidney function, and creatinine kinase levels were all part of the first workup. To find mutations in the SMN1 genetic testing, SMA type gene and the (CK-MB test) were carried out; however, the results did not show up on follow-up, and arrived in an emergency 28 days later. Although the tests were conducted, the findings were obtained after his passing. The lack of motor neuron survival (SMN1 gene) greatly increases the risk that an individual will experience spinal muscular atrophy, according to SMA-MLPA reports. There is a strong family history of SMA type 1. Two of the siblings passed away in one month and two months, respectively. Due to stress, one sibling was also brought to Gambit Hospital; they had both been LIMP from birth and had feeble cries. The mother's eight siblings also passed away at varying ages, ranging from newborn to 22 years old. Her mother claims that while some of her siblings were LIMP from birth, others were initially normal until exhibiting symptoms like tremors, generalized tonic-clonic seizures, difficulty walking, and eventually hypotonia. The patient is up to date on vaccinations, has a low socioeconomic position, and her father works for a company where he makes 15000 PKR a month.

Table 1: Laboratory and Diagnostic Findings

Test	Initial Findings	Follow-up Findings
Complete Blood Counts	Normal	Normal
Electrolytes	Normal	Normal
Liver Function	Normal	Normal
Kidney Function	Normal	Normal
Creatinine Kinase Levels	Elevated	Elevated
SMA Genetic Testing	Results Pending	SMN1 Gene Mutation Confirmed

Table 1 shows the laboratory and diagnostic findings at initial presentation and during follow-up. Most routine investigations, including complete blood counts, electrolytes, liver function tests, and kidney function tests, were within normal limits and remained stable throughout the follow-up. However, creatinine kinase (CK) levels were elevated initially and remained consistently high upon reevaluation, suggesting ongoing muscle involvement. Genetic testing for spinal muscular atrophy (SMA) initially showed pending results, which later confirmed the presence of an *SMN1* gene mutation, supporting the diagnosis. These findings highlight the importance of targeted genetic testing in confirming SMA despite normal routine laboratory results.

Table 2: Diagnostic Timeline of the Case

Age	Clinical Observations / Events
At Birth	■ Full-term baby delivered via normal spontaneous vaginal delivery (NSVD) ■ No complications reported
0–2 Months	■ Exclusively breastfed ■ No obvious motor or neurological issues reported
~2 Months	■ Parents observed reduced spontaneous limb movements ■ Delay in achieving head control ■ Mild hypotonia suspected

3–4 Months	■ Progressive hypotonia ("floppy baby") ■ Poor feeding, weak cry, and poor weight gain ■ No fever, seizures, or cognitive delay
5 Months	■ Referred to a tertiary care hospital ■ Physical exam: generalized hypotonia, areflexia, tongue fasciculations ■ Alert but with delayed motor milestones ■ Nerve Conduction Studies: decreased CMAPs (motor neuron disease pattern) ■ Genetic Testing: Homozygous deletion of **SMN1 exon 7** confirmed **SMA Type 1**
Family History	■ One cousin died at 6 months (similar symptoms) ■ Another cousin was diagnosed with SMA at 2 years of age

DISCUSSION

The incidence of Spinal Muscular Atrophy (SMA) has been estimated at [1] in 6000–11000 live births[2, 3]. In this case study, a male newborn aged one month was presented with clinical symptoms suggestive of SMA, a hereditary neuromuscular condition marked by progressive atrophy and muscle weakness. A first-degree cousin's family history of SMA was noteworthy since the disorder is autosomal recessive, and a positive family history increases the likelihood of the relative having SMA. The patient's clinical characteristics, including poor weight gain, hypotonia (low muscular tone), lack of deep tendon reflexes, and a faint cry, were all typical symptoms of SMA. The inability to roll or sit independently, restricted head control, and delayed motor milestones were indicative of motor developmental deficits, which are defining characteristics of the disease. The presence of tongue fasciculation, which are involuntary muscle contractions manifesting as mild twitches, also supported the SMA diagnosis[4].

Confirmation of the SMA diagnosis required genetic testing, which in this instance identified a homozygous deletion of exons 7 and 8 in the SMN1 gene. The SMN1 gene, which produces the survival motor neuron (SMN) protein necessary for normal motor neuron function, is the primary gene implicated in SMA[5, 6]. Normal results in liver and renal function tests, creatinine kinase levels, electrolytes, and complete blood counts further supported the diagnosis of SMA, as regular blood tests in affected individuals typically fall within normal ranges. SMA predominantly affects motor neurons and muscles.

The diagnosis of SMA in this patient had significant clinical implications. As SMA is a progressive disorder, early identification is crucial for initiating appropriate care and support[7]. While there is no known cure for SMA, various therapies can help manage symptoms and improve quality of life. Gene therapy aims to increase SMN protein levels. Since SMA is genetic in origin, genetic counseling is necessary to help the family understand the risk of recurrence and the importance of screening other family members for carriers[8]. Determining carriers can aid in making informed decisions about family planning and early pregnancy interventions.

In summary, this case presentation described a 1-month-old male newborn with a positive family history and the characteristic clinical picture of SMA. Genetic tests confirmed the diagnosis by identifying a homozygous deletion of SMN1 gene exons 7 and 8. Early identification and effective treatment in SMA cases are essential for improving the child's quality of life and providing the affected family with the necessary support. Genetic counseling and follow-up are required to address the clinical and psychological aspects of this condition.

SMA's hallmark is muscle atrophy and increasing weakness due to motor neuron loss in the spinal cords anterior horn. Each type of SMA has a varied disease course and symptom severity[9]. Type 1 SMA, as seen in this case, is the most severe kind and has a life expectancy of less than two years without treatment. Timely intervention and therapy for SMA are dependent on early diagnosis. Electromyography (EMG) and muscle biopsy alongside genetic testing may be utilized to assess motor unit pathology and support the diagnosis.

Interdisciplinary care is essential for individuals with SMA. Disease-modifying medications like nusinersen and onasemnogene abeparvovec have shown promising results in enhancing motor function and survival in patients with SMA[10]. This case study is particularly significant as SMA is a rare hereditary disorder affecting 6000–10000 babies annually, and most affected children do not survive to adulthood. SMA results in the degeneration of motor nerve cells in the spinal cord, leading to muscle weakening and atrophy. The mutation in the SMN1 gene affects the production of the SMN protein essential for motor neuron function[4].

Early diagnosis allows for significant improvement in motor skills, quality of life, and lifespan. Gene replacement therapy, such as onasemnogene abeparvovec-xioi (Zolgensma), has revolutionized

SMA management by addressing the underlying genetic defect. Zolgensma, administered as a one-time intravenous infusion, delivers a functional copy of the SMN1 gene, promoting motor neuron survival and function. Clinical trials have demonstrated remarkable efficacy in halting disease progression and improving motor function in infants with SMA[1]. Despite the invasive nature of administration and challenges posed by anesthesia in infants, nusinersen has shown efficacy in improving motor milestones and prolonging survival in infants with SMA[1].

In addition to disease-modifying therapies, comprehensive supportive care plays a crucial role in managing SMA symptoms and complications. Coordination of care, regular monitoring of disease progression, and timely adjustments to treatment plans are essential components of this collaborative approach.

Despite recent therapeutic advancements, challenges remain in managing SMA in infants. The long-term efficacy and safety of these therapies require further investigation through post-marketing surveillance and long-term follow-up studies. Continued research aimed at understanding SMA pathophysiology, optimizing therapeutic strategies, and exploring potential combination therapies holds promise for further improving outcomes in affected infants.

This case study underscores the significance of early diagnosis, prompt initiation of disease-modifying therapies, and comprehensive multidisciplinary care in infants with SMA. Genetic testing played a pivotal role in confirming the diagnosis, enabling timely intervention. Emerging therapies like onasemnogene abeparvovec-xioi and nusinersen offer hope for improved motor function and prolonged survival. However, continued research and long-term follow-up studies are essential to address challenges and enhance the management of this rare genetic disorder.

CONCLUSION

The case highlighted the heartbreaking consequences of delayed diagnosis and limited access to early treatment in infants with Spinal Muscular Atrophy (SMA) Type 1. Despite a strong family history and recognizable clinical signs, the child's condition progressed rapidly, underscoring the urgent need for timely genetic screening, early intervention, and comprehensive care. Advances in gene therapy offer new hope, but their effectiveness depends greatly on early recognition and accessibility. For families facing a rare and devastating condition like SMA, support must extend beyond the clinic, embracing genetic counseling, emotional assistance, and community awareness. Every lost opportunity to intervene early is a life potentially cut short. Through increased awareness, research, and equitable access to treatment, we can change the story for children born with SMA.

LIST OF ABBREVIATIONS

SMA: Spinal Muscular Atrophy
SMN1: Survival Motor Neuron 1
NICU: Neonatal Intensive Care Unit
HIE: Hypoxic Ischemic Encephalopathy
CK-MB: Creatine Kinase-Myocardial Band
EMG: Electromyography

CONFLICT OF INTEREST

None

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None

PATIENT CONSENT

Informed consent was obtained from the patient's guardians to publish this case report.

AUTHORS' CONTRIBUTIONS

All authors contributed equally.

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