



Neonatal Spinal Muscular Atrophy: A Case Report

Pestana Magali Andrea*, Maria Lucia Martinez, Juan Manuel, Joaquin Pedre, Guadalupe Albornoz and Pedraza Ana Maria

Department of Neonatology, Suizo Argentina Clinic and Maternity - University of Buenos Aires, Argentina

***Corresponding Author:** Pestana Magali Andrea, Department of Neonatology, Suizo Argentina Clinic and Maternity - University of Buenos Aires, Argentina.

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Abstract

Spinal muscular atrophy type 0 is a genetic condition and is the severest phenotype expression of the five types of SMA. Moreover, it affects patients from birth and is rapidly fatal within days to months. We describe a case of a patient who was born with axial hypotony, abolished of osteotendinous reflexes and Moro's reflex, and lingual fasciculations but eye opening and movements were present and how we imagined that we were dealing with spinal muscular atrophy type 0 and how we promptly diagnosed this uncommon pathology. In this report we want to highlight the importance of knowing the most relevant characteristics of the disease and being capable of suspecting this condition during pregnancy and after birth. In addition, as physicians we should give proper palliative care and genetic counseling to the family.

Keywords: Neonatal; Hypotonia; Spinal Muscular Atrophy

Abbreviations

SMA: Spinal Muscular Atrophy; SMN: Survival Motor Neuron; SMN1: Survival Motor Neuron 1; SMN2: Survival Motor Neuron 2; MRI: Magnetic Resonance Imaging; FDA: Food and Drug Administration; ANMAT: Drug, Food and Medical Technology National Administration (Argentina); NICU: Neonatal Intensive Care Unit; CGH array: Comparative Genomic Hybridization

Introduction

SMA is an autosomal recessive disease caused by the homozygous absence of the SMN1 gene. Its incidence varies between 1:6.000 and 1:10.000 live newborns. The lack of SMN protein coded by the SMN1 gene causes the degeneration of the motor neurons of the anterior horn of the spinal cord, thus leading to muscular atrophy [1]. This situation compromises not only voluntary movements, but also the thoracic musculature and the muscles involved in swallowing.

The disease presents in different clinical forms, and it was initially classified into four types (I to IV) according to the age at symptoms onset and the highest motor milestone developed by patients. (Table 1). The most severe type of classic SMA is type I [2]. More recently, a more severe expression of the disease was described, named type 0. It was defined by the onset of symptoms in the fetus and diagnosis at birth.² It is also called Neonatal Spinal Muscular Atrophy. However, SMA type 0 is a rare expression of a rare disease, we believe that the case we are presenting will add to the bibliography on the matter.

Case Presentation

A boy weighing 2334 gr was born via c-section delivery and his mother was a 37-year-old healthy and primigravida woman. During the pregnancy nuchal translucency sonogram showed an abnormal result and as a consequence a chorionic villus biopsy was performed with normal karyotype result (46 XY). The c-section de-

SMA type	Age of onset	Highest motor milestone achieved	Life expectancy
SMA 0	Prenatal	Requires ventilatory support	< 1 month
SMA I	0 – 6 months	Never sits	< 2 years
SMA II	6 – 18 months	Sits, never walks independently	> 2 years
SMA III	IIIa: 18 months – 3 years IIIb: > 3 years	Walks independently, may lose this ability during adulthood	Adulthood
SMA IV	Adulthood	Walks independently	Adulthood

Table 1: SMA types and their characteristics. Adapted from Matesanz., *et al.* [3].

livery was done at 35 week due to a non-reactive fetal monitoring and the mother's story about feeling low fetal movements from 28 weeks to birth.

The patient Apgar was 2/5/7 and did not present any kind of breath effort and as a result of it the newborn was intubated in the delivery room. Also, during physical examination, it was observed in the patient: axial hypotony, abolished of osteotendinous reflexes and Moro's reflex, and lingual fasciculations but eye opening and movements were present.

At NICU, the neonate remained in mechanical ventilation during the whole hospital stay. In addition, an echocardiography revealed a 7 mm atrial communication which needed treatment with diuretics. A considerable number of other studies were run as X-ray - images, brain magnetic resonance imaging, brain sonogram, and a polysomnogram which did not find any anomaly.

Finally, it was possible to confirm SMA diagnosis through an array CGH. After all, knowing the diagnosis and the severity of the disease and with curative treatment available; medical therapy was suspended and the patient died at the age of 44 days surrounded by his parents.

Materials and Methods

Digital medical records were used to access information of the patient, and it included Xray – images, magnetic resonance imaging and the registration of any point of view or thoughts of the different colleagues, from a variety of fields like neurophysiology and genetics, which evaluated the patient.

Informed consent

In addition, an informed consent form was provided to the parents of the patient and was signed in conformity by them.

Results and Discussion

SMA type 0 is a rare autosomal recessive disease “caused by mutations in the survival motor neuron 1 (SMN1) gene located on chromosome 5q12.2-q13.3.1” [17] and the prenatal form of SMA is characterized by “severe, extensive weakness with dysphagia, facial diplegia, respiratory failure, variable degree of arthrogryposis, and early neonatal death.” [17].

The mutation affects SMN1 which fails in produce SMN protein and as a consequence produces the degeneration of neurons located in the anterior horn of the spinal cord. An homologous gene to SMN1, called SMN2, partially compensates for the lack of SMN protein, and a higher amount of copies of the SMN2 gene is associated with less severe phenotypes of the disease. SMA type 0 correlates to genotype 0SMN1/1SMN2. It is very infrequent, and it shows the highest severity [1].

The largest series of SMA type 0 patients was reported by Grotto., *et al.* (n = 16), [2] In this article, the authors described clinical manifestations of SMA type 0 and the most remarkable were that fetal movements were decreased, the size of nuchal translucency was enlarged, also presented muscular hypotonia and muscular atrophy, the suction reflex was abolished, lingual fasciculations, and the need of mechanical ventilation support. All those clinical characteristics were found in our patient presented in this report. Furthermore, there are several other case reports or very small case series [4-26] that add to the scarce evidence on the topic.

Currently, there are three approved treatments for the rest of the type of SMA which one is known as Nusinersen. This drug has been allowed to be used in Argentina since 2019 and in the USA was approved by the FDA in 2016. Moreover, another drug for the treatment of this illness is Onasemnogene Apeparovovec which is approved for patients with a biallelic mutation of SMN1. Also, it was approved by FDA and ANMAT for the pediatric population.

The limitation of this case report is there is no existing curative treatment for SMA type 0, and the efforts are focused in clinical management with an ominous result. Furthermore, we have only found an article in the literature which was published by Matezans, *et al.* in 2020 and reported only one patient who suffered from SMA type 0 and they decided to treat it with Nusinersen and Onasemnogen Abeparvovec together. Although the patient showed some motor skill improvements the progression of SMA was inevitable.

Conclusion

Overall, to our knowledge, at the moment of this publication, there is no specific and proven treatment for SMA type 0 and it is necessary to continue performing well conducted studies to assess a possible treatment. In the meantime, the early diagnosis after-birth or even the intra uterus suspicion, could help the physician to provide proper palliative care and genetic consulting to the family.

Conflict of Interest

The authors Pestana M, Martinez ML, Olejarzick JM, Albornos G and Pedraza A.M don't have any conflict of interest. Pedro J d declares being scientific assessor and associate at Biogen Argentina. However, PJ did not have any access to personal and sensitive information of the patient.

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