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Werdnig-Hoffmann Disease in A Female Child: A Rare Case Report

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Abstract
Spinal muscular atrophies (SMAs) are rare degenerative diseases that affect motor neuron. It is inherited as autosomal recessive disorder and mainly affect male baby but female may be affected. Disease can occurs all age groups but more severe form of the disease generally involved paediatric age group. Most severe infantile form also known as type 1 SMA or Werdnig- Hoffmann disease usually presented before the age of 6 months with generalisedhypotonia with recurrent respiratory tract infection. Definite diagnosis is by genetic study and treatment is generally supportive and prognosis is poor. Here we present such rare disease in a female child.

Keywords: *spinal muscular atrophy, hypotonia, Werdnig – Hoffmann disease.*

Introduction

The spinal muscular atrophies (SMAs) comprise a group of autosomal-recessive disorders character-rized by progressive weakness of the limbs. In the early 1980s, Werdnig and Hoffman described a disorder of progressive muscular weakness begin-ing in infancy that resulted in early death, though the age of death was variable. In pathologic terms, the disease was characterized by loss of anterior horn cells. The central role of lower motor neuron degeneration was confirmed in subsequent pathologic studies demonstrating a loss of anterior horn cells in the spinal cord and cranial nerve nuclei [1]. Since then several types of spinal muscular atrophies have been described based on age when accompanying clinical features appear. The most common types are acute infantile (SMA type I or Werdnig-Hoffman disease), chronic infantile (SMA type II), chronic juvenile (SMA type III or Kugelberg-Welander disease) and adult

onset (SMA type IV) forms. SMA type0, a severe fatal form that is usually fatal in the perinatal period. The genetic defects associated with SMA types I-III are localized on chromosome 5q11.2-13.3 [2,3,4,5]. In 1995, the spinal muscular atrophy disease causing gene, termed the survival motor neuron *(*SMN*)*, was discovered[6]. Each individual has 2 SMN genes, SMN1and SMN2. More than 95% of patients with spinal muscular atrophy have a homozygous disruption in the SMN1 gene on chromosome 5q, caused by mutation, deletion, or rearrangement. However, all patients with spinal muscular atrophy retain at least 1 copy of SMN2, which generates only 10% of the amount of full-length SMN protein versus SMN1. This genomic organization provides a therapeutic pathway to promote SMN2, existing in all patients, to function like the missing SMN1 gene[7]. Many classification systems have been proposed and include variants based on inheritance, clinical and genetic criteria. Among these are the Emery [8], Pearn [9] and International SMA Consortium (ISMAC) system [10]. The ISMAC system is most widely accepted and is used in this review.

The ISMAC classification system is based on the age of onset [11]. According to the ISMAC system, the age of onset for spinal muscular atrophies is as follows:

SMA type I (acute infantile or Werdnig Hoffman): Onset is from birth to 6 months.

SMA type II (chronic infantile): Onset is between 6 and 18 months.

SMA type III (chronic juvenile): Onset is after 18 months.

SMA type IV (adult onset): Onset is in adulthood (mean onset, mid 30s).

The acute infantile-onset SMA (type I) affects approximately 1 per 10,000 live births; the chronic forms (types II and III) affect 1 per 24,000 births. SMA types I and III each account for about one fourth of cases, whereas SMA type II is the largest group and accounts for one half of all cases [11]. The incidence of spinal muscular atrophy is about 1 in 10,000 live births with a carrier frequency of approximately 1 in 50 [12,13]. Male individuals are most frequently affected, especially with the early-onset forms of spinal muscular atrophy, i.e., types I and II [14].

SMA type I - Acute infantile or Werdnig-Hoffman disease

Patients present before 6 months of age with 95% of patients having signs and symptoms by 3 months. They have severe, progressive muscle weakness and flaccid or reduced muscle tone (hypotonia). Bulbar dysfunction includes poor sucking ability, reduced swallowing, and respiratory failure. Patients have no involvement of the extraocular muscles, and facial weakness is often minimal or absent. They have no evidence of cerebral involvement, and infants appear alert. Reports of impaired fetal movements are observed in 30% of cases, and 60% of infants with SMA type I are floppy babies at birth. Prolonged cyanosis may be noted at delivery. In some instances, the disease can cause fulminant weakness in the first few days of life. Such severe weakness and early bulbar dysfunction are associated with short life expectancy with a mean survival of 5.9 months. In 95% of cases, infants die from complications of the disease by 18 months [15,16,17,18]

Case Presentation

A 8 month old female child admitted in our paediatric ward with complaints of fever, cough and respiratory difficulty for 3 days. There was similar episodes in past. There was no history of perinatal asphyxia or any other significant post-natal events. Child was on exclusively breast feeding for 6 months and vaccination was given asper age. On examination child was conscious, afebrile, heart rate 116/ min, regular, respiratory rate 58/ min, regular, spo2 96% in room air. On head to toe examination no facial dysmorphism, congenital anomaly, cyanosis or clubbing. Onsystemic examination chest indrawing was there and bilateral crackles on chest auscultation. On CNS examination gross hypotonia both upper and lower limbs (fig1, 2, 3), power diminishedin

both lower limbs comparison to upper limb (fig 4). All deep tendon reflexes were absent. Cardiovascular and other systemic examination was normal. On investigation complete blood count was normal except leucocytosis. Liver function, renal function, urine test was also normal. Serum creatinine phosphokinase was within normal limit, 98.7 IU/L, CSF study and CT scan was also normal. On genetic study there was deletion of exon 7&8 of SMN 1 gene.

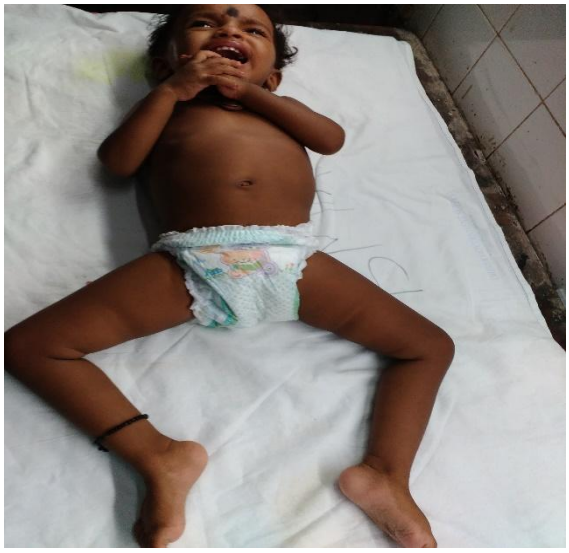

Fig 1

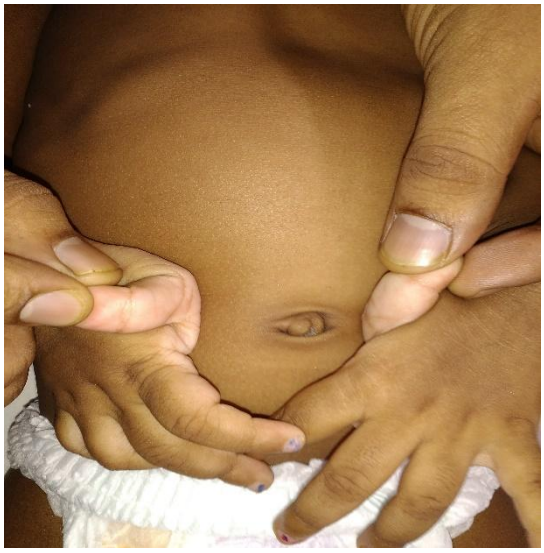

Fig 2

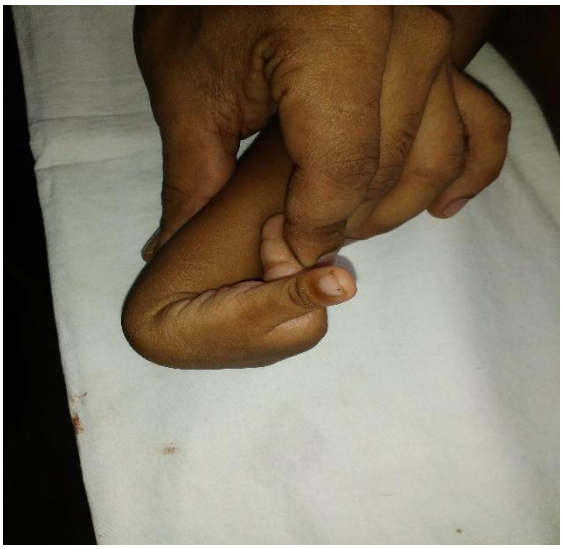

Fig 3

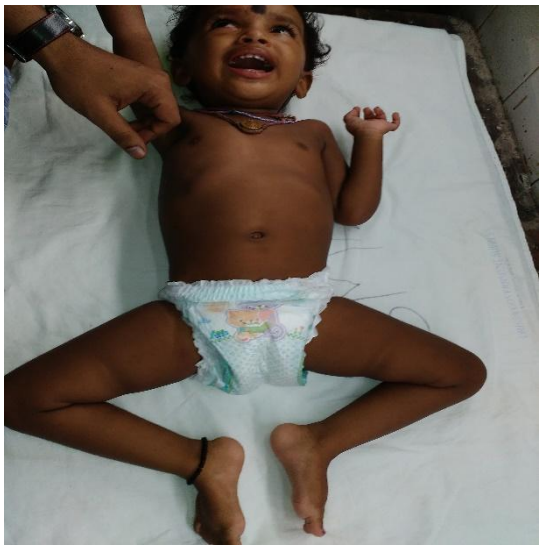

Fig 4

Discussion

SMA is one of the most common genetic neuromuscular diseases. Itis caused by the loss of the telomeric copy of the survival motor neuron gene (SMN1) on human chromosome 5q11.2-13.3 [19]. 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[20]. Symmetric proximal muscle weakness begins during the fetal period and progresses through infancy and childhood [21]. Diagnosis is generally on the basis of history, clinical examination and confirmed by genetic study. This child having history of developmental delay, not able to sit, stand and walk since birth

and no significant post-natal history. Management is mainly supportive, no specific therapy. Physiotherapy and orthopaedics care is the main stay of therapy. Whatever therapy is given prognosis is always poor and child generally survive up to the age of 18 months to 2 yr.

Conclusion

Though SMA a rare disease, it can be an important differential diagnosis of a floppyinfant. Any floppy infant with recurrent respiratory tract infection with are flexiathe possibility of SMA should be considered. Though the common cause of floppy infant being Down syndrome, hypothyroidism, hypotonic cerebral palsy butdetailed history and clinical examination along with genetic study can clinch the diagnosis of SMA.

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