Spinal Muscular Atrophy: Non-Curative Disease

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A one-month-old baby girl with spinal muscular atrophy type 1 with generalized muscle weakness is presented. She was fully investigated and diagnosed with spinal muscular atrophy type 1. She was managed conservatively and with supportive treatment. She died at the age of 13 months.

Spinal Muscular Atrophy (SMA) is a non-curative disease with a wide degree of clinical and genetic heterogeneity that we must take into consideration because of the serious prognosis. It targets the muscles which result in weakness and atrophy.

Several therapeutic approaches have been proposed and investigated. They are focused on increasing the availability of Survival of Motor Neuron (SMN) protein which has been found effective when tried in animal modelling studies.

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Spinal muscular atrophies (SMA) are a group of autosomal recessive neurodegenerative disorders. The patient has 2 copies of the gene affected. It is known as progressive weakness of the lower motor neuron, characterized by degeneration of the spinal cord motor neurons and atrophy of the skeletal muscles[1,2].

Spinal muscular atrophy is due to mutation in a SMN gene encoding a novel protein (SMN 1) which plays a role in RNA metabolism and also has an important role in interacting with actin-binding proteins and mediators of programmed cell death[3]. This defect is found in 5q11-2 q13-3 genes[3].

The incidence is 1 in 6000 to 1 in 10000 live birth and is considered as the second most fatal autosomal recessive disorder after cystic fibrosis[4].

The aim of this report is to present a case of spinal muscular atrophy and highlight the nature of clinical progress of such genetic disease.

THE CASE

A forty-day-old baby girl presented by the parents who were concerned about the position of her arms. She held her arms similar to a bilateral "waiters-tip" position with her arms internally rotated. She was born at 37 weeks of gestation by normal vaginal delivery with a birth weight of 3.065 kilograms and without perinatal complications; Apgar score was 8, 9 and 10 at 1, 5 and 10 minutes respectively. Fetal movements were normal and she was delivered vaginally with vertex presentation. The patient was the first child to non-consanguineous parents. Her family history was negative for neuromuscular disorders. Since the age of one month, her motor activity had decreased. The patient had hypotonic posture, but looked alert. She had symmetrical reduced tone and power of the upper and lower extremities. There was also a bell-shaped chest deformity, see figures 1 and 2. Deep tendon reflexes were absent and muscle bulk was normal. No contractures were noted nor any deformities; however, she had some paradoxical breathing. There was no tongue fasciculation. Genetic study was performed and SMA type 1 was confirmed by detecting the homozygous deletion of axons 7 and 8 of the SMN gene. Nerve conduction study revealed severe motor axonal neuropathy in the upper and lower limbs.

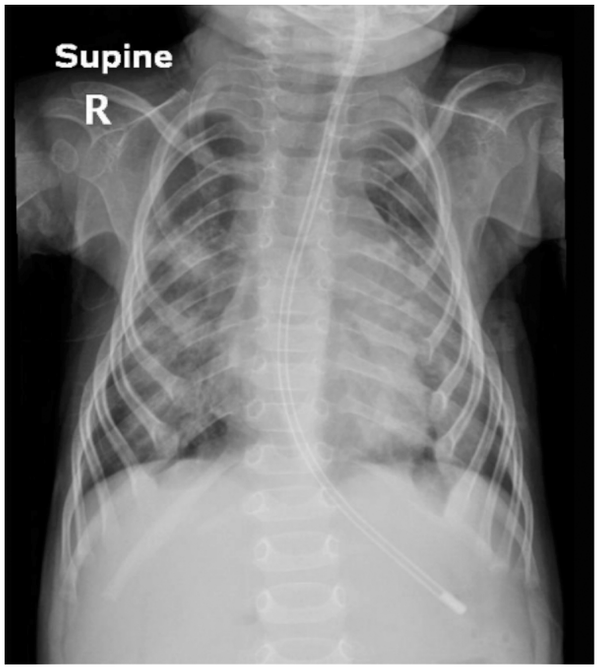

Figure 1: Abnormal Shape of Chest Ribs

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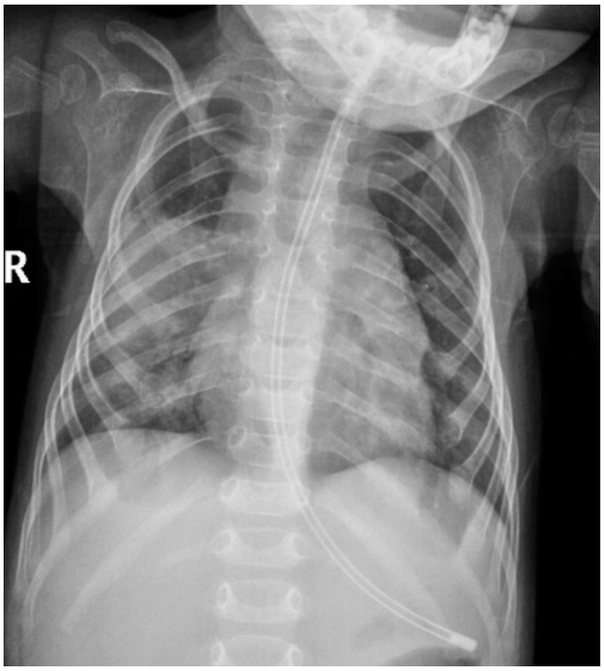

Figure 2: White Patch on the Right-Lung Indicating Aspiration Pneumonia

Serum ammonia was low (64 umol/l) and lactate was high (4.8 mmol/l). Serum very-long-chain fatty acid was within normal ratio. It included behenic acid, lignoceric acid, cerotic acid, phytanic acid and Pristanic acid. Genetic study was performed on the parents and found that both of them are carriers of the SMN gene.

At the age of six months, the patient was admitted due to aspiration pneumonia and one month later, she underwent a gastrostomy. At the age of eight months, she was readmitted due to the same problem.

She had another admission at the age of nine months where she had several episodes of desaturation and required mechanical ventilation; however, the family refused. She was placed on oxygen via a nasal cannula at home. Her respiration was progressively distressed, and her sucking power weakened. All her admissions were due to respiratory distress and frequent aspiration.

The family understood the prognosis of the disease, and they requested not to cause any more pain for her, only support her acute issue, which meant no CPR and no intubation to be performed.

At the age of one year, she presented with respiratory distress, fever, and inability to maintain saturation despite being on oxygen. She was clinically deteriorating with infrequent gasping, minimal air entry bilaterally and crepitation. Artificial ventilation via Ambu bag was performed on her seven times. Her saturation would pick up, but rapidly desaturate, and bradycardia would occur within 2 minutes. Antibiotics were given, and IV fluid was administered. Despite all the support, there was no improvement in the pulse, respiratory function, and the pupils were fixed and dilated. The patient died at the age of 13 months.

DISCUSSION

Spinal muscular atrophy was first reported by Werdnig and Hoffmann in the 1890s[4]. It is classified clinically into four categories based on motor function and age of onset.

SMA type 1: Also known as Werdnig-Hoffmann, is the most severe and common phenotype. It is characterized by floppy limbs and trunk, feeble movement of the arms and legs, impaired breathing, difficulty in swallowing and weak sucking reflex. This type is evident at birth or within the first few months of life. Most infants of this type would die due to respiratory failure and before reaching the first year of life, similar to what happened to the case we have presented[5].

SMA type 2: Also known as intermediate form or chronic SMA appears between 6 and 18 months and is characterized by the inability to crawl or walk. It affects the lower limbs more than the upper limbs. These infants could sit without support if placed in position. They are at increased risk for respiratory infections. They could survive up to childhood, but with severe motor disabilities[5]. Most cases were reported as having scoliosis, and it occurs as the muscle supporting the spine becomes weaker[6].

SMA type 3: Known as Kugerberg-Welander disease (mild form). It could begin early or as late as adolescence. They could stand and walk, have difficulty getting up from sitting position. They are also at increased risk of respiratory infections[5].

SMA type 4: This type occurs during adulthood; it is rare and does not affect life expectancy. Symptoms vary and could include muscle weakness, difficulty in walking and muscle tremors[6].

All types demonstrate common features, which are progressive muscle weakness with normal cognitive abilities, which frequently manifest in infancy and childhood[7].

The severity of the weakness of the muscles correlates with the amount of full length of SMN protein produced[8].

To diagnose this disease, a blood test is available to detect whether there is deletion or mutation of the SMN 1 gene[5]. Another diagnostic method is electromyography (EMG), for detecting nerve conduction velocities and muscle biopsy[5].

There is no cure for SMA. The treatment is only conservative, managing the symptoms and preventing complications, managing the breathing by non-invasive methods including negative pressure ventilation, bi-level positive airways pressure support and chest physiotherapy. Tracheostomy is occasionally needed[5, 9].

Failure to thrive is due to weak sucking reflex which could be managed by a nasogastric tube or placement of a gastrostomy tube[5,9].

Weak limbs could be managed with physical therapy and exercise, which help to improve the mobility of the patient[5,9].

Orthopedic complications could be managed medically and surgically, such as scoliosis, mainly in type 1 and 2 could be managed by body jacket to prevent severe scoliosis[5,9].

Spinal muscular atrophies, particularly type 1, have a poor prognosis. Most patients die within the first 2 years of life[9].

Genetic counseling is important for couples with a child with SMA. They have 25% risk of producing an affected child, 50% risk of producing an asymptomatic carrier and 25% risk of producing an unaffected child that is not a carrier[8].

Researches are continuing to find a treatment and cure for SMA by identifying four possible treatment targets: Correction or replacement of the affected gene, modulation of the low-function SMN 2 gene, neuroprotection of the affected motor neurons and muscle protection[10].

CONCLUSION

Spinal muscular atrophy type 1 was managed conservatively with respiratory and feeding support. SMA is a fatal genetic disorder, once diagnosed, it has poor prognosis as it is a non-curative disease.

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