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Case Report

Spinal muscular atrophy with severe scoliosis: a case report

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Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease that causes general weakness, muscle atrophy, and poor muscle movement. This condition is due to a homozygous disruption of the survival motor neuron 1 (SMN-1) survival gene due to deletion, conversion, or mutation.[1] **[Paediatr Indones. 2023;63:314-24; DOI: https://doi.org/10.14238/pi63.2.2023.314-24].**

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Spinal muscular atrophy is a rare in pediatric neurology. The prevalence of SMA is 1-2 per 100,000 people, with an incidence of 1 in 10,000 live births. There are four types of SMA. Type 1, also called Werdnig-Hoffmann disease, has the most severe symptoms with onset of paralysis occurring at <6 months of age. Children with type 1 SMA have very low life expectancy, with 95% mortality in those < 1 year of age.[2] Type II SMA, or the intermediate type, has milder symptoms than type I. The initial symptoms of motor weakness begin after 6 to 18 months of age, resulting in growth and development disorders in the form of motor delays. The life expectancy of type II SMA is better compared to Type I, as these children reach adulthood with a due to better preservation of abilities.2 Among the SMA types, 60% are type 1.[3] Type III SMA, also known as Kegelberg-Welander disease, has the lightest severity. Symptoms do not begin until 18 months of age. In rare cases, new symptoms begin to appear in adulthood, so some experts call this group type IV.[2]

All types of SMA are caused by defects in the survival motor neuron (SMN) gene on the long arm of chromosome 5 (5q13). A small proportion of SMA cases are not caused by gene deletion, but by intragenic mutation of SMNI. SMA is inherited in an autosomal recessive manner. [4]

The clinical symptoms of SMA are characterized by hypotension, paresis, areflexia and fasciculation, while sensory and cognitive functions are within normal limits. Paralysis is caused by damage of motor neurons in the anterior horn of the spinal cord. Creatine phosphokinase (CPK) levels are usually within normal limits, but it can be used to distinguish paralysis due to myopathic disorders, which are characterized by elevated CPK levels. Genetic testing (SMN gene analysis) is currently considered to be the gold standard of SMA diagnosis.[5]

Management of SMA patients is currently focused on supportive, palliative, and preventive therapy. The key is multidisciplinary management, which is important to improve, maintain, and support muscle strength and function, as well as to prevent and manage possible complications that arise since there is no clinically proven curative therapy.[4]

The case

A 16-year-old girl was brought to the Pediatric Neurology Division Dr. Sardjito Hospital by her

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parents with the chief complaint of being unable to walk. The patient wass monitored for 16 months. The initial complaint appeared in the form of a child limping since the age of 1 year (weaker right leg). This child was healthy and active until 1 year of age. She underwent a normal delivery assisted by midwife, with birth weight of 3,000 grams. She was regularly taken to health centers for routine immunizations according to government programs. The impression of development at that time was normal according to her age (1-year-old). Following her 1st birthday, her parents noticed that her leg strength was weak, as she walk with a limp. She had no history of seizures or falls. At the age of 4 years, the child still walked with a weak, dragging left leg. She visited a private hospital in Yogyakarta, where she was advised to have a biopsy, but the parents refused due to the cost. The child received medication, but did not know what it was. She underwent physiotherapy for 2 years, but there was no improvement, so her parents discontinued the physiotherapy sessions.

At the age of 11 years, (5 years before hospital admission) the child could not walk, so she used a wheelchair. There were no urinary complaints. She complained of infrequent bowel movements once every 5 days. The patient was assisted in daily activities. One month before admission, the child could only crawl and use a wheelchair. She underwent laboratory examinations at a private hospital in Yogyakarta remarkable for: serum glutamic oxaloacetic transaminase of 27.5 U/L; creatinine kinase (CK) of 232.3 U/L; electroneuromyography (ENMG) consistent with polyneuropathy. The CT scan of the leg revealed diffuse signs of atrophy throughout the lower extremity muscles. She was then referred to the Pediatric Policlinic at Dr. Sardjito Hospital, Yogyakarta, and was hospitalized for further evaluation.

The patient was the third of three children. Her first brother was unable to walk and died at 17 because of a spinal disorder. Her father worked as a construction laborer and her mother was a homemaker. Family tree of the patient is shown in **Figure 1**. Her parents received education about the child's disease and prognosis of SMA. Neither the patient nor her parents had a chromosome analysis for SMA. The patient started walking at 1 year of age, spoke fluently in sentences at the age of 2 years, and at her current age of 16 years had no learning difficulties. At the time of this publication, the girl was in grade 2 of senior high school.

Physical examination , fully aware and sentient, and vital signs within normal limits. However, the girl had poor nutritional status. Laboratory results showed CK levels of 232.3 U/L (normal range 46-171 U/L). Anatomical pathology images from biopsies of the right and left calf muscles showed dystrophin positive fibers on part of the muscle bundle membrane. Hence, the morphology and immunohistochemistry results supported the diagnosis of Becker muscular dystrophy (manifesting carrier) (**Figure 2**).

The patient underwent genetic testing for deletion analysis of the SMN1 gene exon 7 and exon 8 using a PCR-RFLP technique. As described in **Figure 3**, there was a deletion in the SMN1 exon 7 gene, while the SMN1 exon 8 gene did not have the deletion.

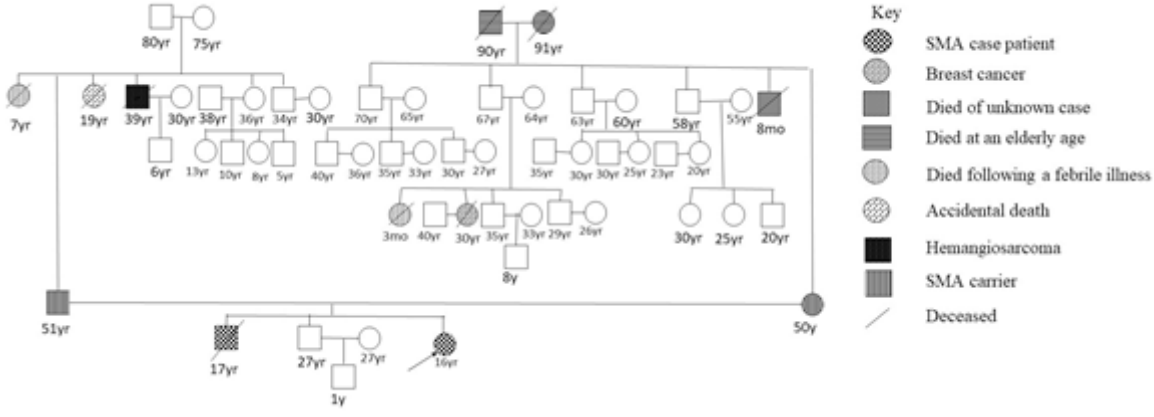


Figure 1. Family tree of patient

At the start of monitoring, the patient assisted when we helped her change position from prone to sitting. Since February 2019, the patient routinely consumed valproic acid 15 mg/kgBW/day and salbutamol 1mg/kgBW/day. Routine physiotherapy was done at home and the hospital. The patient also used a lumbosacral orthotic girdle (LSO) since the start of monitoring. At the end of monitoring, the muscle strength of her upper and lower limbs was the same as at the beginning of the monitoring. However, the angle of scoliosis curvature (Cobb angle) increased from 600 to 820 (**Figure 4**).

At the end of the observation, the child was still taking valproic acid and salbutamol, using a LSO girdle, and undergoing physiotherapy to limit disease progression. Due to time constraints at school, physiotherapy was done at home and sometimes at the hospital.

Spirometry examinations were done five times, including a force vital capacity (FVC) test to assess lung function. Pulmonary function test at the beginning of observation showed mild restrictive results with FVC 2.51 (FEV1/FVC=83%). Interventions in the form of chest physiotherapy and general physiotherapy were carried out. The FVC at the end of monitoring was 2.11 (97%) (**Table 1**). A FEV1 / FVC ratio of more than 85% indicates normal lung function. The child underwent spirometry evaluations every 3 months in the Pediatric Respirology Clinic. During monitoring, the child never had a serious respiratory infection. Respiratory infection symptoms were never reported during follow-up. The girl's echocardiography results were normal both at the beginning and at the end of the monitoring.

Growth assessment was done by measuring body weight and height every 3 months at home or at clinic visits. At the time of initial monitoring, the patient was in a malnourished condition, with height (based on knee height) according to age being normal. To overcome the problem of malnutrition, we provided information on variations in types of food and the amount of food consumed. Finally, at the end of the monitoring, the patient was still malnourished (**Table 2**), but BMI based on age had improved, with more frequent meals and adequate food intake. Energy and protein needs were met according to the *Recommended Dietary Allowance* (RDA).[6] Fluid requirements were met based on *Holliday Fresh* according to body weight.[7]

When the child was in grade 2 at senior high school in Yogyakarta, she had good cognitive abilities, could follow school lessons, and ranked 2nd academically in her class. During the observation, she maintained 2nd or 3rd rank in her class. By the end of the observation, the child had graduated from

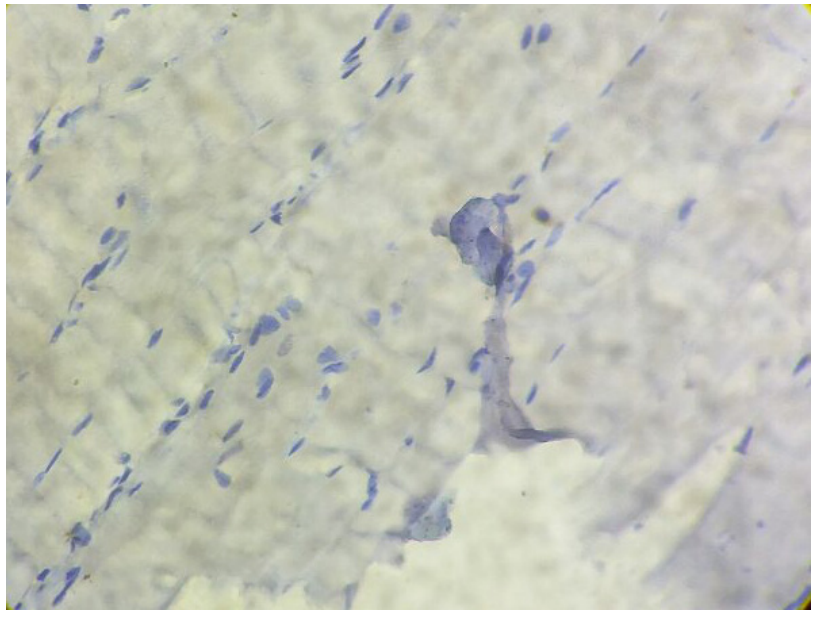


Figure 2. Examination of muscle biopsy with hematoxyilin eosin. Dystrophin: obtained positive streak on a portion of the muscle fiber membrane (possibly a Becker muscular dystrophy manifesting carrier)

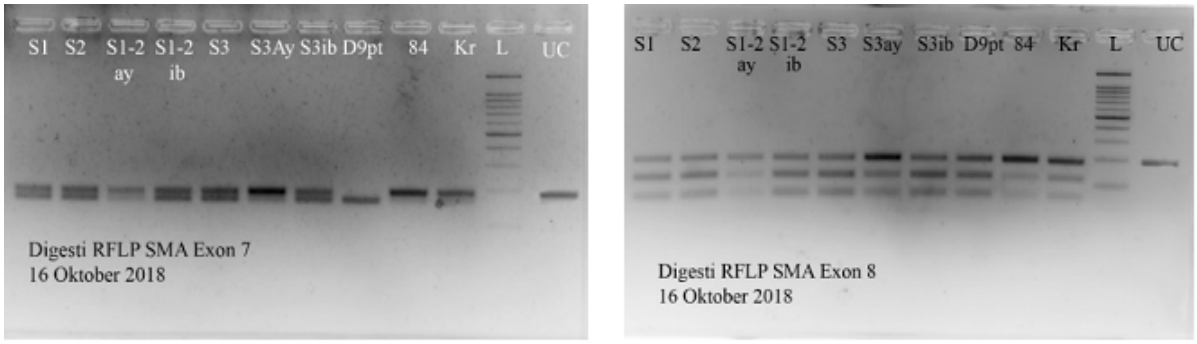
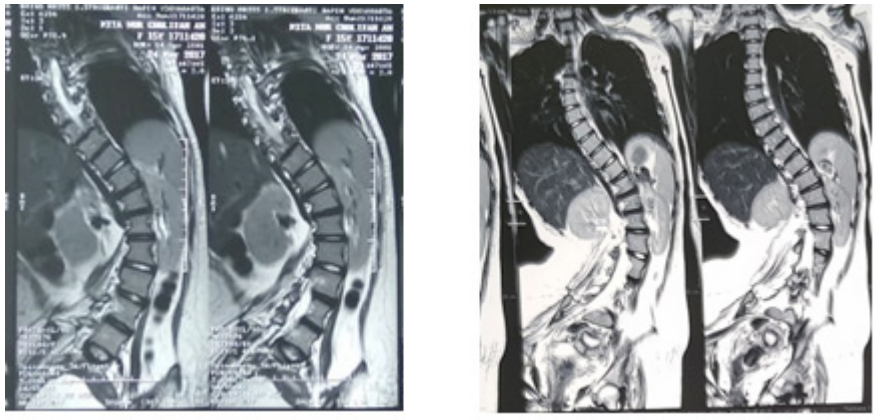


Figure 3. Deletion analysis of SMN1 exons 7 and 8 gene by PCR-RFLP (lane D9pt was our patient)



March 2017
60° Cobb angle

May 2019
60° Cobb angle

Figure 4. Thoracolumbal MRI before and after observation

Table 1. Spirometry results

Parameter	May 2018	August 2018	November 2018	February 2019	May 2019
FVC	2.51	2.58	1.53	1.63	2.11
FEV1/FVC	83%	98%	100%	100%	97%
Conclusion	Mild restriction	Normal	Normal	Normal	Normal

Table 2. Nutritional status

Observation	Basic data	Months observation				
		3rd	6th	9th	12th	15th
Month	Feb 2018	May 2018	August 2018	Nov 2018	Feb 2019	May 2019
Weight, kg	33	33	34	35	36	38
Knee height, cm	43	43	43	44	44	44
Height, cm	144	144	144	146	146	146
BMI	15.9	15.9	16.3	16.4	16.8	16.8
Body height//age	-3<Z<-2	-3<Z<-2	-3<Z<-2	-3<Z<-2	-2<Z<-1	-2<Z<-1

high school ranked 2nd in her class and ranked 5th in her school.

Behavioral development evaluations using the *Strength and Difficulties Questionnaire* (SDQ) were done at the beginning and end of the monitoring period. The patient completed the SDQ by herself. An SDQ score of 20-40 indicates a behavioral abnormality. Clinically significant problems in this area are unlikely if the SDQ score 0-13.[8] At the beginning, her SDQ total difficulty score was 22. Her SDQ at the end of follow-up showed improvement with a total difficulty score of 19, and she showed borderline improvement in the emotional aspect of the problem.

We used the PedsQL form to assess four aspects of quality of life, namely, to physical function, emotional function, social function, and children's school function, from both the parents' and child's points of view. The patient and her parents filled the PedsQL at the beginning and end of the monitoring period. A total PedsQL score ≥70 indicates good quality of life, and a score <70 indicates poor quality of life. The child's major impediment was her physical function, which was a complication of the disease. The patient's PedsQL score did not change much over the period, from 45.6 at the start to 50.6 at the end of the monitoring.

Some intervention plans so that the angle of scoliosis does not worsen such as compliance in using the LSO corset. The corset felt tight and uncomfortable. With the help of parents, medical personnel, family members, and teachers, the child's growth and development can be monitored for 16 months.

Discussion

A 16-year-old female patient with a diagnosis of SMA and severe scoliosis was monitored for 18 months. SMA is the most common genetic disease of the spinal neuromotor system. It can occur at any time from before birth to adulthood, with varying degrees of severity and impact. It is the leading genetic cause of infant death. Even though the genetic defect causing SMA was discovered nearly 20 years ago, no treatment is available yet. However, effectively designed supportive care can significantly reduce the burden of disease and improve quality of life. Despite major advances in our understanding of the biological consequences of survival motor neuron (SMN) reduction, the pathogenic mechanism of SMA with low levels of SMN protein leading to selective loss of motor neurons remains undefined. Preclinical developments have resulted in several SMN recovery therapies that have shown dramatic success in animal models of the disease, and several studies are being tested in early phase clinical trials.[9]

Scoliosis is a major musculoskeletal problem in SMA type 2 and 3 patients (the patients is SMA type 2). If untreated, scoliosis causes chest deformities that complicate breathing. Therefore, anticipatory observation is very important. The rate of scoliosis progression is faster in non-ambulatory patients at or before puberty. This suggests that maintaining the ability to stand and/or walk can delay the severity of scoliosis. Physiotherapy and other interventions can help maintain ambulatory care.[5] Our patient's scoliosis condition was evaluated before the monitoring period. Chest X-rays and thoracolumbar MRI revealed a curvature (Cobb angle) of 600.

Orthopedists recommend the use of a scoliosis corset (thoracolumbar sacral or the so-called thoracolumbal sacral orthosis / TLSO). The corset should be used 16-23 hours per day. A meta-analysis showed that wearing the corset 23 hours per day was significantly more successful in preventing progression of the curvature than was 8 or 16 hours per day of use.[10] Other studies showed that the more hours the corset is worn per day, the better the results. The rest periods are for bathing, swimming, physical education, and sports, and should average two to four hours per day to ensure the wearing of the corset for 20 to 22 hours per day.[8] During monitoring, our patient did not routinely wear the corset for 16-23 hours a day as it felt uncomfortable and tight when worn for long time periods. Chest X-rays performed 18 months after wearing the corset showed a 22-degree increase in curvature, from 600 to 820.

Pulmonary complications are a major source of morbidity and mortality in SMA. Respiratory problems include weakness in the cough reflex and hypoventilation. Pulmonary complications are related to disease severity, requiring close monitoring and more frequent interventions. All children with type 1 SMA and about one-third of those with type 2 develop respiratory distress or respiratory failure during childhood. The expiratory respiratory muscles are

often deteriorated, leading to difficulty with secretions and respiratory failure.[5]

The patient is SMA type II, which is characterized by onset between 7 and 18 months of age, patients achieve the ability to sit unsupported and some of them are able to acquire standing position, but they do not acquire the ability to walk dependenly. Deep tendon reflexes are absent and fine tremors of upper extremities are common. Joint contractures and kyphoscoliosis are very common and occur in the first years of life in the more severe type II patients.[11] Patients received minimal proactive intervention in addition to antibiotics for pulmonary infections. SMA patients are prone to recurrent respiratory tract infections that may progress to atelectasis and lung collapse. Teenagers may experience nocturnal hypoventilation and impaired chest and lung wall growth.[9]

The patient's nutritional status is good nutrition. The CDC 2000 charts are used for anthropometric measurements in teens.[12] The height of teens with scoliosis is calculated based on knee height. Knee height is rarely used to estimate stature in children, although its measurement might have benefit because not influenced by some musculoskeletal disorder in spinal region.[13]

During monitoring, the PedsQL score did not change significantly, from 45.6 at the beginning of monitoring to 50.6 at the end of monitoring. Various instruments can be used to assess children's quality of life, one of which is the pediatric quality of life (PedsQL) inventoryTM questionnaire.[14] This instrument consists of 4 assessment functions, namely, psychological, emotional, social, and school functions. This questionnaire is quite easy to complete and has been widely used throughout the world for both healthy and ill children. The questionnaire consists of both child and parents' reports. The PedsQL can reveal which problems require interventions in order to minimize psychosocial impacts.

In conclusion, a 16-year-old girl with a diagnosis of spinal muscular atrophy (SMA) and severe scoliosis underwent an 18-month follow-up. At the end of the monitoring period, she had no decrease in motor function, no respiratory problems, and no digestive disorders. However, her scoliosis worsened, due to less than optimal use of a corset and the progression of the SMA.

Further multidisciplinary monitoring and management were still needed considering that weakness in SMA is progressive with many complications, including scoliosis as in our patient. This condition puts the patient at risk of experiencing respiratory, gastrointestinal, nutritional and psychological problems in the future. Support from the medical staff, family, and the goverment is needed to optimize quality of life for SMA patients.

Conflict of interest

None declared.

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