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CASE REPORT

Spinal fusion as a viable treatment option for scoliosis management in Pompe disease: a postoperative 3-year follow-up

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Abstract
Purpose This study presents 3-year postoperative outcomes of posterior spinal correction and fusion of a patient diagnosed with late-onset Pompe disease (PD) for his progressive scoliosis.
Methods The patient was diagnosed for PD during his infancy. Enzyme replacement therapy (ERT) was initiated at the age of 13. First office visit for his spinal deformity was at the age of 15, and 40°, 34°, 6° spinal curvatures were seen in T6–L3, T1–6, and L3–S, respectively. Reduced pulmonary function, limited gait function and atrophied limb were documented. Initial brace treatment could not control curve progression; therefore, posterior spinal correction and fusion were performed at the age of 17.
Results Immediate preoperative curves of 55°, 42° and 23° were corrected to 18°, 26° and 7° in T6–L2, T1–T6 and L2–S, respectively. Spinal fusion was performed from T3 to L4. The patient exhibited an excessively low pulmonary function preoperatively with a VC, FVC, and %VC of 1.45 L, 1.36 L, and 35 %, respectively. This has been managed with only moderate reductions despite reduced pulmonary function from PD throughout the operative period and at 3 years. At the final follow-up, VC, FVC and %VC were 1.33 L, 1.12 L and 28.5 %, respectively.
Conclusion Posterior spinal correction and fusion adequately controlled spinal curvatures for 3 years after surgery. Additionally, pulmonary function was managed throughout the follow-up period. Despite ERT, skeletal muscle and pulmonary function can still be severely affected by PD. Spinal correction and fusion is a useful method for the management of spinal curvature and pulmonary function in patients with PD.

Keywords Scoliosis · Pompe disease · Posterior fusion · Pulmonary function · GSD type II · Neuromuscular

Introduction

Alpha Glucosidase deficiency syndrome, commonly known as Pompe disease (PD), is caused by a mutation in the glucosidase, alpha; acid (GAA) gene. It is a genetic autosomal recessive disorder resulting in the deficiency or dysfunctional lysosomal Alpha-Glucosidase enzyme. A deficiency of this enzyme leads to an accretion of internal glycogen in the lysosomes of muscular tissue, and further induces autophagic build-up within the cell [1]. The onset of the PD is anytime after the birth and once triggered, it was considered fatal until the usage of enzyme replacement therapy (ERT) in recent years [2]. The estimated prevalence of PD in the world is between 1 in 33,000 and 1 in 300,000 [3].

In recent years, the role of abnormal activation of autophagic pathways has been brought to attention in patients with PD, which damages normal tissue structure and replaces healthy muscle fibres with autophagic debris [4, 5]. Clinically, severe muscle weakness and atrophy [6], and increased prevalence of spinal deformity were reported in patients with PD. For example, Roberts et al. [3] found spinal deformities in 33 % of patients with PD. Spinal deformities in patients with PD are especially problematic since their cardiopulmonary systems are already compromised by their weakened muscles. The aforementioned

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study by Roberts et al. [3] have also compared the pulmonary function of scoliotic and non-scoliotic patients with PD and have found significantly reduced pulmonary function in the scoliosis group [3].

Pompe disease is considered a neuromuscular disorder and shares many common grounds with other diseases that cause neuromuscular scoliosis. Neuromuscular scoliosis is known to continue its progression beyond the age of maturity and has known implications in the loss of sitting and standing posture as well as implications to pulmonary and cardiac function [3]. Mild spinal deformities are commonly treated by bracing [7], and more severe scoliosis cases require surgical interventions [7]. However, operative treatments are not always possible to some severe cases. For example, a study by Haaker et al. [8] which reports on surgical intervention done on patients with PD for the treatment of scoliosis and other orthopedic morbidities, reported that milder forms of scoliosis were found in milder forms of PD and vice versa. The study describes four patients who were indicated for surgical intervention to treat scoliosis, yet out of which, only half of them were able to receive the treatment due to their poor pulmonary function, respiratory disorder and neurological issues [8]. Out of the two that received surgical treatment, only one was available for regular follow-up, whereas the data for the other patient were available 7 months post operation. Posterior fusion via a screw and wire construct was employed in both of the patients and major curve were corrected from 60 to 23 at L1–L5 in the patient which follow-up was not possible, and 90–35 at T6–L5 in the patient whose 2 year follow-up was possible. At 2-year follow-up, scoliosis was managed with a major curve of 37°. In our study, we were able to follow outcomes of patients with PD for 3 years after the spine surgery. The purpose of this study is to present 3-year postoperative outcomes of posterior spinal correction and fusion of a patient diagnosed with late-onset PD for his progressive scoliosis.

Clinical overview

A boy was born at 38 weeks into pregnancy, with a bodyweight of 3124 g. His first unassisted gait was at 1 year and 4 months, and his motor development delay was recognized at the age of 1. Through muscle biopsy and blood tests, the patient was diagnosed as PD at age of 1. There was no family history of PD. The patient received his first ERT at age 13 and continued the therapy biweekly until present. The late initiation of the ERT was due to the unavailability of Alglucosidase Alpha in Japan until 2006. The patient did not exhibit any signs of infusion-associated reaction.

He first visited our institution for his spinal deformity at age of 15. On physical examination, the patient showed scoliosis along with classical signs of PD such as winged scapula, drastically atrophied limb and torso, muscle weakness, and breathing difficulties. No neurological and cardiological abnormalities were observed. Blood tests demonstrated elevated levels of creatine kinase (CK), a biomarker for PD. At the first visit, his major curve scoliosis was 40° (MC, T6–L3), 34° in the upper curve (UC, T1–6), and 6° at the lower curve (LC, L3–S) (Fig. 1).

The patient started a brace treatment program; however, a steady progress of scoliosis was seen for 2 years and 6 months until surgery was planned. The patient reported persistent low back pain and hip pain from sitting. In addition, the patient exhibited a reduced ability to keep sitting posture for an extended duration of time, where he

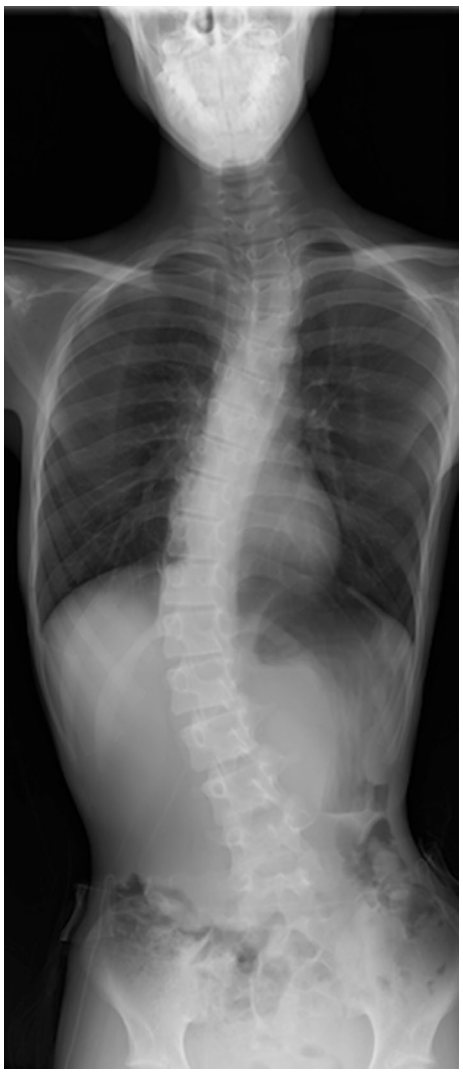

Fig. 1 First visit coronal and X-P radiographs. Coronal and sagittal X-P radiographs obtained at the time of first visit. Main *curve* scoliosis was 40° (T6–L3), 34° in the *upper curve* (T1–6), and 6° at the *lower curve* (L3-S). Sagittal image was not available

will start to decompensate to the side of scoliotic concavity. The patient also complained of pain at the apical area of the thoracic curve and the lower side of the opposing lumbar, which are both symptoms that are representative of fatigue pain that arises from the muscle of the apical area from scoliosis. At the same visit, breathing difficulty was noted and the patient started a nighttime biphasic positive airway pressure (BIPAP) regime. Blood gas was not available, albeit it was not measured due to the lack of cyanosis and dyspnea during rest, and breathing difficulties were assumed as a result of the reduced vital capacity as result of a restrictive lung condition.

Although the patient was able to walk unassisted for short distances he has shown difficulty in keeping balance during gait and frequently fell down due to his progressive muscular atrophy. Therefore, his primary means for the transfer was using a wheelchair. At the age of 17 years and 8 months, patient was 158.5 cm in height and 31 kg in weight; his scoliosis had progressed to 55° in the MC (T6–L2), 42° in the UC (T1–T6) and 23° in the LC (L2–S). Due to the inability to keep constant sitting posture, pain in low back and apical area during sitting, and progressive nature of neuromuscular scoliosis, surgical treatment was suggested (Fig. 2) to him and his family. Upon the agreement for the surgical intervention, total of 8 units of blood were preoperatively drawn in preparation for auto transfusion.

Posterior spinal fusion and correction was performed from T2 to L4 using pedicle screws segmentally with local bone graft and allograft. Spinal curvatures were corrected in the MC, UC and LC angles to 18°, 26°, and 7°, respectively (Fig. 3). The total surgical time was 5 h and 43 min, with an estimated blood loss (EBL) of 5732 mL with cell saver employed. Patient required 10 units of blood transfusion in addition to auto blood transfusion and PC transfusions of 20 units. Dural tear and an excessive EBL were two intraoperative complications recognized during this surgery. Induction of general anesthesia was uneventful.

The patient received biweekly ERT and one ERT infusion during the stay in our institution. The patient was on

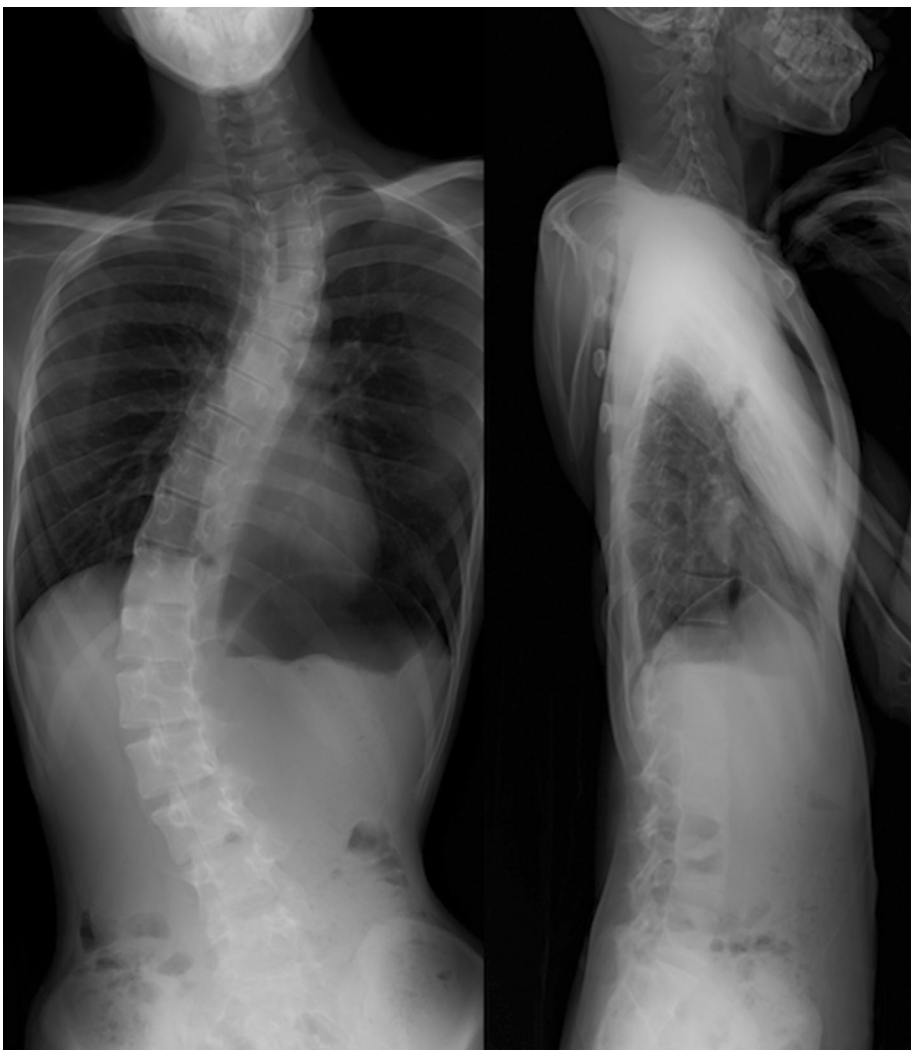

Fig. 2 Preoperative coronal and sagittal X-P radiographs. Coronal and sagittal X-P radiographs obtained preoperatively. Main *curve* scoliosis was 55° (T6–L2), 42° in the *upper curve* (T1–T6) and 22° at the *lower curve* (L2–S)

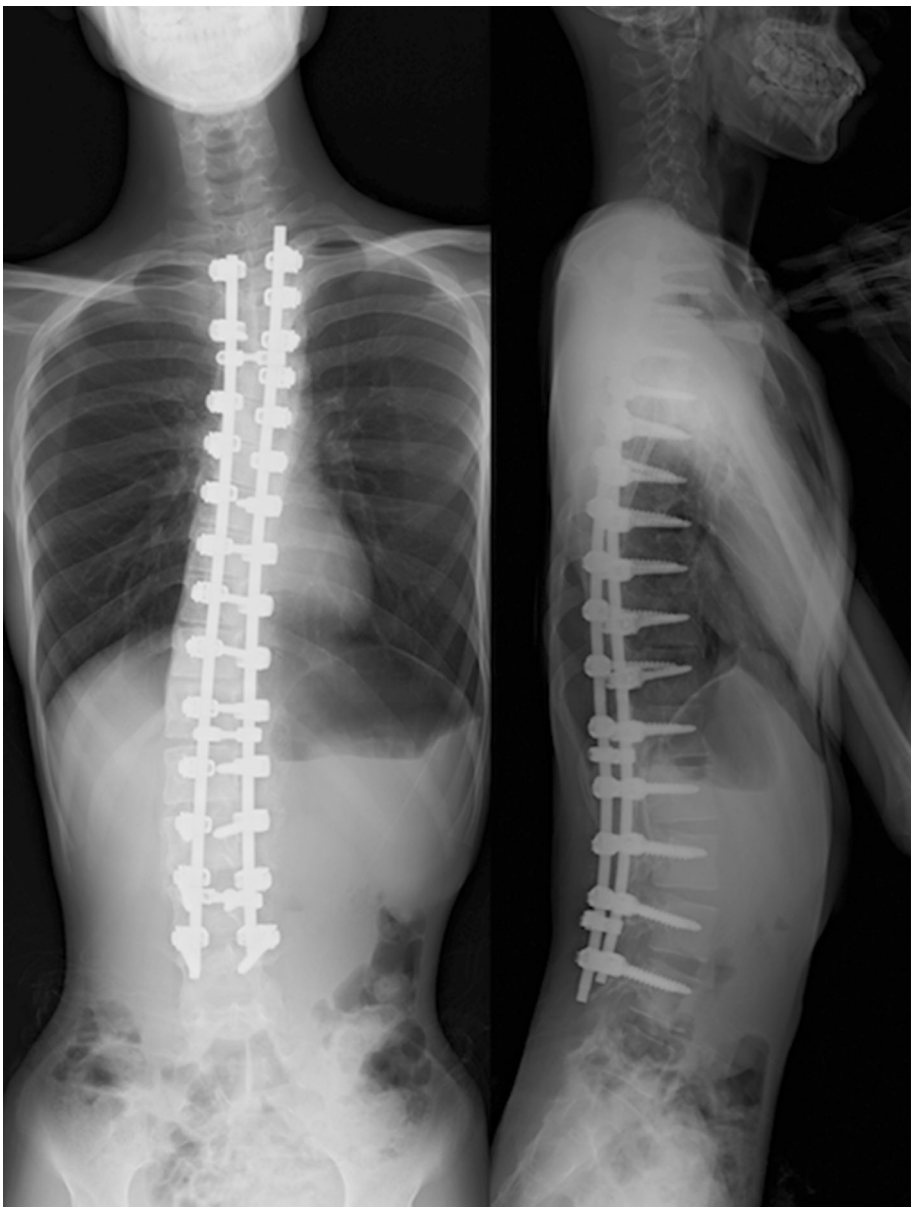

Fig. 3 Postoperative coronal and sagittal X-P radiographs. Coronal and sagittal X-P radiographs obtained postoperatively. Main *curve* scoliosis was 22° (T6–L2), 27° in the *upper curve* (T1–T6) and 6° at the *lower curve* (L2–S)

BIPAP throughout the day most of the stay; however, the patient's breathing became stabilized, and only required BIPAP during the night at the end. Patient was able to regain his ambulation at the time of discharge. The patient exhibited biomarker of PD; elevated CK, alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) [9].

Postoperatively, the patient did not have any complications from the scoliosis surgery and his curve corrections maintained throughout the follow-up (Fig. 4). At the follow-up visit, the use of wheelchair for 3–4 h a day was reported due to increasing muscle weakness in lower extremities. There was no low back pain reported for 2 years after the surgery. The patient is able to keep sitting posture for extended duration of time without decompensation and no longer feel pain in the apical area that existed preoperatively. At the 3-year postoperative visit, progressively worsening in muscle strength was observed with 2/5 in knee extension and flexion, 2/5 ankle dorsiflexion, 3/5 in ankle plantar flexion, 3/5 in biceps and triceps flexion. The nighttime usage of BIPAP remained to be the case and sleep disturbance was reported. Pulmonary function test (PFT) data obtained at 1-year postoperative visit have shown reduced values than those obtained at the 3-months postoperative follow-up, and pulmonary physical exercise was conducted, and was taught to the patient.

Despite the correction of the spinal deformity, PD symptoms progressed with slow rate and increased weakness in the extremities. It is important to note that despite a large fusion area, the patient had shown growth in height to

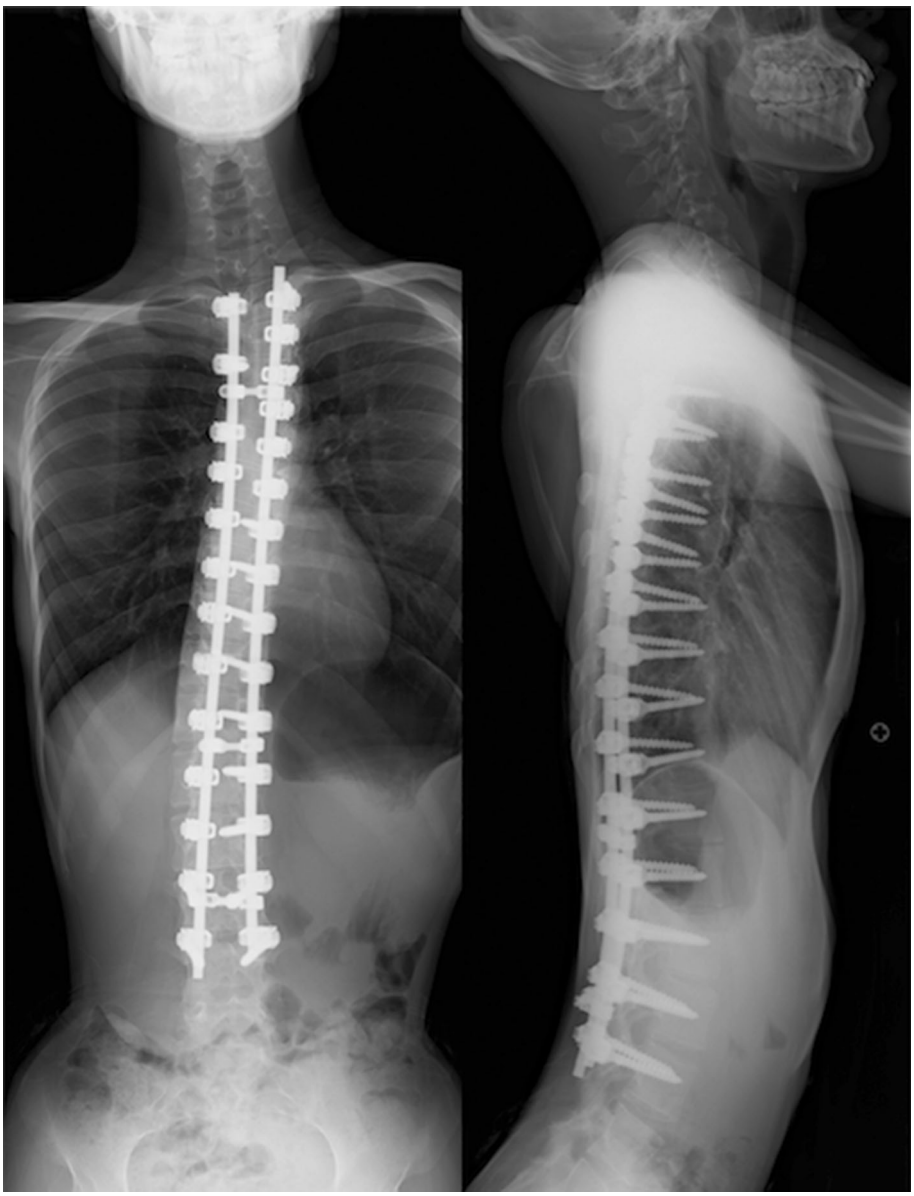

Fig. 4 Postoperative 3 year coronal and sagittal X-P radiographs. Coronal and sagittal X-P radiographs obtained postoperatively. Main *curve* scoliosis was 20° (T6–L2), 26° in the *upper curve* (T1–T6) and 7° at the *lower curve* (L2–S)

184 cm, nevertheless, with a low body weight of 33 kg due to PD.

The patient's preoperative PFT values consisted of a VC of 1.45 L, forced vital capacity (FVC) of 1.36 L, and percent vital capacity (%VC) of 35 %. At the 3 months' postoperative follow-up, VC, FVC, and %VC were 1.31 L, 1.20 L and 32.3 %, respectively. At postoperative 1-year visit, VC, FVC, and %VC were 0.82 L, 0.80 L, and 18.1 %. At the final visit, PFT results at postoperative 3 years for VC, FVC, and %VC were 1.33 L, 1.12 L, and 28.5 %, respectively. Full pulmonary function test (PFT) data from the preoperative through the postoperative follow-up period are tabulated in Table 1.

The patient's qualitative clinical outcome was measured using the SRS-30 questionnaire collected at preoperative and postoperative over 3-year follow-up. Preoperative mean scores for each domain: function/activity, pain, self image/appearance, mental health, were 3.6, 4.4, 2.5, 4.4, respectively. Mean scores for the aforementioned four domains, followed by the satisfaction with management domain at the patient's postoperative 4-year follow-up were 3.5, 2.0, 2.9, 3.2, and 2.3, respectively.

Discussion

Pompe disease is a rare neuromuscular disorder that results in progressive muscular atrophy that may manifest throughout the body in terms of cardiac, skeletal, pulmonary systems. Once a fatal disorder, PD can now be

Table 1 Pulmonary function test data collected throughout the clinical course of the patient from preoperative to postoperative 3-year follow-up

	Preop.	PO 3 months	PO 1 year	PO 2 years	PO 3 years
VC (L)	1.45	1.31	0.82	1.28	1.33
TV (L)	0.35	0.27	0.37	0.36	0.30
FVC (L)	1.36	1.20	0.80	1.24	1.12
FEV1.0 (L)	1.18	1.20	0.78	1.24	1.10
FEV1/FVC	86.8 %	100 %	97.5 %	100 %	98.2 %
%VC	35.0 %	32.3 %	18.1 %	27.6 %	28.5 %

Predicted VC for the Preop %VC values has been corrected for height using the equation by Kono et al. in order to account for height difference from scoliosis [10]

managed through ERT. Despite the availability of a treatment; however, patients do suffer from other complications that persist, such as scoliosis and progressive muscular atrophy. Previous accounts of surgical treatment of scoliosis in patients with PD are rare since ERT only became available in recent years.

A large discrepancy is seen in the changes in height and weight when comparing preoperative values with immediately at postoperative, and postoperative 3-year values, and this may be attributed to the progressive muscular atrophy that is occurring due to PD. Around the time when operation was conducted, and even at the time of discharge, patient was able to walk unassisted, albeit unbalanced and frequently trips over. Yet at 2 and 3-year follow-up, patient was unable to keep a standing posture for less than a minute, and requires constant use of wheelchair for locomotion. The same can be said for pulmonary function as well, where pulmonary function parameters [VC, %VC, tidal volume (TV), FVC, forced expiratory volume in 1.0 Second (FEV1.0)] all have not recovered to or beyond preop values even past postoperative 3 years.

The efficacy of the conducted surgery should be considered based upon several factors. First and foremost is the potential of further progression of scoliosis to a point that may start to affect the pulmonary function of the patient as well as their activities of daily living (ADL). Neuromuscular scoliosis, unlike many forms of idiopathic scoliosis, commonly continues to progress beyond the age of maturity. This patient had shown a progressive course of scoliosis curvature beyond 50° in the 2 years prior to operation, and therefore was indicated for surgery to avoid any further progression of scoliosis. Also, in patients with skeletal muscle disease who have a weak pulmonary function to begin with, any further physical changes such as scoliosis that may affect the dynamics of the thoracic cavity can have detrimental effect on the breathing mechanism of the patient.

Secondly, the patient had shown an inability to keep adequate sitting posture for extended duration of time, with obvious decompensation to the side of scoliotic concavity. Through this surgery, both of these symptoms have been treated by providing a stable trunk that allows for postural stability despite easily fatigued muscle and progressive atrophy. Furthermore, it can be said that since the patient did not have the ability to use the full range of motion (ROM) in the patient's limbs even at the preoperative time, the limitation imposed via the fusion surgery did not have a detrimental effect on the patient's ADL. Finally, it is important to recognize that the condition of this patient is similar to other neuromuscular types of scoliosis and short apical fusion is not an option as the pathology affects the whole spine. As with other neuromuscular scoliosis, muscle balance is deteriorated, and trunk control is impeded. If only thoracic spine was fused, then the correction to sitting posture cannot be achieved. To repeat, the strategy of this surgery is not only to alleviate the worsening pulmonary function, but to maintain a spinal balance to allow sitting position without support.

Additionally, when considering the preoperative and postoperative SRS-30 scores, a noticeable reduction in the pain domain and a modest increase in the self image/appearance domain were recognized at the patient's postoperative 3-year follow-up. On the other hand, the patient did exhibit a slight decrease in the function/activity domain and a minor decrease in the mental health domain. Taking both of these into account, it may be interpreted that the surgery was successful in reducing the pain felt by the patient along with an improvement of their self-image, albeit the increasingly disabling symptoms of PD further limits the ADL along with potential negative psychological effects arising from of living with disabilities. Psychological management along with further ADL support are issues that must be addressed when considering the treatment of patients with PD and other chronic neuromuscular conditions.

This study is one of the first few studies to report on the surgical outcome of a patient with late-onset PD for scoliosis treatment with detailed pulmonary and scoliotic curvature measurements in its prognosis over a 3-year period. Surgical outcome at the time of operation was good, despite the large amount of blood lost during surgery, and patient did show modest recovery in pulmonary functions

that are close to but not beyond preoperative values. The excessive blood loss recorded during operation may be a result of tissue weakness in various tissue structures with abnormal autophagy seen in PD contributing to its manifestation, albeit no experimental validation is available that correlates tissue structure in patients with PD and blood loss during surgery [4, 5].

This surgery allowed the patient to keep a stable sitting posture and trunk support as well as preventing further progression in scoliosis. The patient did show decreased reflex and further skeletal muscle atrophy in their limbs, which are most likely attributed to PD, and is a shortcoming of the current ERT regime. As seen in this patient, while ERT have decreased the mortality risk in PD, with the patients living longer than pre-ERT accounts, we are now seeing complications previously discussed only sparsely in literature, and in essence, have been given a chance to treat symptoms of PD that were beyond the primary objective of PD treatment.

Conclusion

Surgical intervention for the treatment of scoliosis in Pompe Disease remains to be a challenging field with varying degree of muscular atrophy and pulmonary function. This study exhibited a well-maintained clinical outcome in terms of scoliosis and pulmonary function at postoperative 3 years with the achievement of adequate sitting posture and reduction of pain although limitations of ADL gradually aggravated due to muscle atrophy in a patient with PD. Treatment options will require careful consideration of pulmonary and cardiac function, ADL of the patient, and potential course of natural history if scoliosis is not corrected granted a neuromuscular condition.

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Compliance with ethical standards

Conflict of interest The author(s) of this publication serves as a consultant for Medtronic and Depuy Synthes. The author(s) also receives Grant/Research Support from Japan Spinal Deformity Institute. However, all aforementioned relationships are not related to the production of this paper.

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