

How to Prevent Small Stature in Rett Syndrome—Associated Collapsing Spine Syndrome

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Severe scoliosis in Rett syndrome is an important orthopedic, neurologic, and pediatric problem. The curve in Rett syndrome is of a neurologic type, has its highest incidence during early childhood, and shows rapid progression. In this study, the authors report the results of a 4-year follow-up of a 10-year-old Rett syndrome female patient with early onset and severe rapid progressive thoracolumbar scoliosis. The first signs of spinal deformity were documented at age 3 years. During adolescence, the patient developed a 115-degree thoracolumbar scoliosis with reduced respiratory volume due to a collapsing spine syndrome. To stop this life-threatening progression of the curve, the patient was treated by a 2-stage surgical procedure. The combination of an anterior release, halo traction, and posterior instrumented fusion from Th3 to L5 using a computer-assisted

technique was performed. An excellent reduction of the deformity was achieved (postoperative 24-degree Cobb angle). After 4 years, the authors found a radiologically solid spinal fusion and no progression of the deformity. Operative treatment regimes and etiology of severe spinal deformities in Rett syndrome were discussed. The high perioperative risks in Rett syndrome patients who underwent spinal surgery may be reduced by an early cooperation between orthopedic and pediatric specialists. When considering recent data from literature, it can be concluded that an early correction of spine deformities in Rett syndrome patients may prevent a life-threatening collapsing spine syndrome.

Keywords: Rett syndrome; scoliosis; spine; kyphosis

Rett syndrome (RS) is a rare progressive neurological disease that affects nearly exclusively female patients and has a prevalence of 1:10 000 to 15 000 births each year. The syndrome was described first by Rett in 1966.¹ In 2001, Schwartzman et al² reported an RS male patient with associated Klinefelter syndrome (XXY). Most cases appear sporadic, some also familial (x-chromosomal hereditary path). The responsible gene (methyl-CpG-binding protein 2 [MECP-2]) for this disorder was identified in 1998; mutations of this form were found in approximately 80% of the patients with RS.^{2,3} In particular, the MECP-2 mutation affects the growth and differentiation of lymphocytes negatively, but not genetic expression in the blood or

cells of the central nervous system. Rett syndrome is characterized by a neurologic developmental disorder that first shows a stagnation of the development, typically at the age of 7 to 18 months, followed by regression.⁴ The clinical manifestations contain autistic, demential, apractic, and atactic symptoms as well as sleeping and breathing malfunctions, stereotyped movements of the hand, slowed-down head movements, and the loss of already learned verbal abilities. In addition, foot and hip deformities as well as scoliosis can be found. Also, an initial hypertonic muscle can often be detected, which can lead to hyperreflexia and spasticity.^{5,6}

Life-threatening spine deformities are frequently observed in patients with RS. These deformities are based on neuromuscular imbalance and marked by long thoracolumbar curves.⁷⁻⁹ This type of scoliosis appears normally around the eighth year and shows a rapid progression in the second decade of life. Upon recognition of these symptoms, early diagnosis and therapy of the deformity, including continuous clinical and radiological follow-up, is essential in RS patients. The indication for surgical corrections of idiopathic scoliosis usually begins at a Cobb angle of more than 40 degrees.¹⁰ Further indications for operative treatment are rapid progression of the spinal deformity, discomfort, or functional loss. The purpose of

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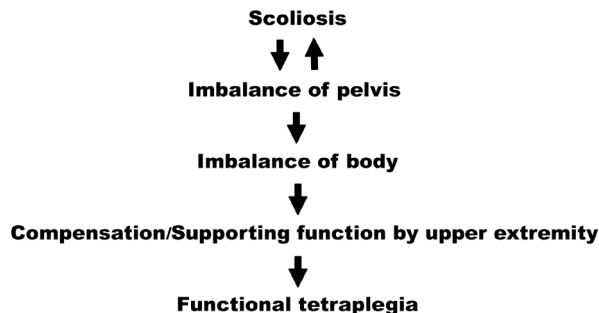


Figure 1. Synopsis of the development of a functional tetraparesis.

a surgical treatment is to prevent further progression, correct the deformity, and improve trunk balance in seated and standing positions.

Another important factor when considering surgical treatment in RS-associated scoliosis is the possibility of further spinal growth in adolescent patients. In the past, the Luque procedure was developed to correct deformities without the need for bracing.^{11,12} Some authors have, however, described high complication rates during management of infantile scoliosis with this procedure.¹³⁻¹⁵ In recent years, several new techniques for spinal management of deformities in the growing spine were developed to enable further growing of the spine. One technique, which enables further growth of the spine after instrumentation, is described in this case.

In this case report, we present an 11-year-old female RS patient with a severe spine deformity diagnosed at 3 years of age, which showed rapid progression. The pre- and postsurgical clinical and radiological examinations are analyzed. Furthermore, etiopathogenetical and differential diagnostic questions regarding the type of scoliosis are discussed.

Case

In a female RS patient, a spine deformity was diagnosed at 3 years of age. The deformity was treated conservatively (physiotherapy, orthosis) and followed up clinically and radiologically. From the seventh year of age, the curve showed a rapid progression with a right convex thoracolumbar scoliosis. Within 2 years, the Cobb angle of a King type II curve changed from 35 to 70 degrees, corresponding to a rotation degree of II-III of Nash and Moe. At an age of 9 years, rapid progression in scoliosis manifested itself in a so-called collapsing spine syndrome, which was characterized by complete decompensation of body axis and imbalance. The upper extremities were forced to assume gradually more and more compensatory supporting functions. In the end, we found a functional tetraparesis in this patient (Figure 1). At that time, x-rays

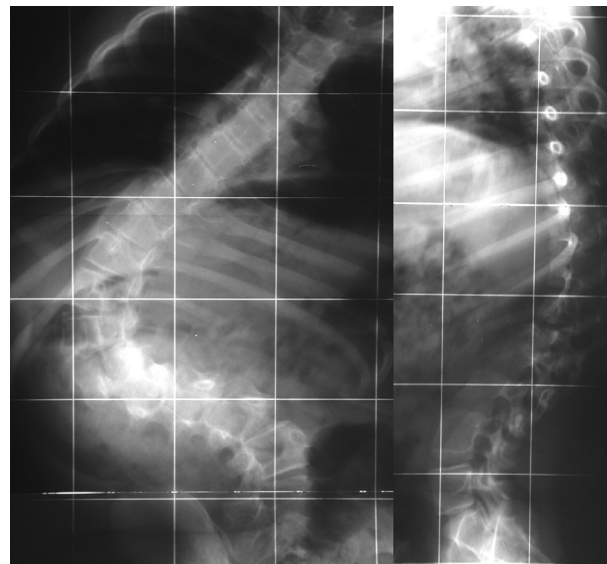


Figure 2. The anterior-posterior and lateral preoperative x-rays show a right convex thoracolumbar scoliosis and Cobb angle of 115 degrees (Th8-L3) with a left convex lumbar Cobb angle of 52 degrees. In the lateral view, a hyperkyphosis of 48 degrees appears between Th4 and Th12.

of the spine in anterior-posterior and lateral x-ray planes showed an S-shaped, lumbar left convex and thoracolumbar right convex spine corresponding to a severe 3-dimensional deformity.

The thoracolumbar Cobb angle was 115 degrees and lumbar 52 degrees with a rotation degree of II-III of Nash and Moe (Figure 2). In addition, we found a thoracic kyphosis of 48 degrees between Th4 and Th12. In bilateral bending x-rays, the left convex lumbar angle could be compensated to a great extent, and the right convex thoracolumbar angle was reduced to 54 degrees. To exclude other pathologies, a magnetic resonance imaging scan of the thoracic and lumbar spine was performed.¹⁶ We found no aberration or other pathologies of the spinal cord. At this time, the patient was immobilized in a wheelchair supported by an orthosis and was not able to stand alone. The clinical investigation showed a distinctive thoracic right convex and lumbar left convex scoliosis with consecutive pelvic imbalance. In addition, a complicated deformity of the foot was found (tip foot with a pronation component).

To prevent life-threatening complications, a 2-stage surgical procedure was performed. First, an anterior release from Th10 to L3 via a thoracophrenico-lumbotomy approach over the 10th right rib was performed. In addition, halo traction with 10% of the body weight was carried out subsequently to support the correction of the deformity. Two weeks later, a posterior instrumented correction of the curve and fusion from Th3 to L5 followed. To allow for further spinal growth, we used the Small Stature USS II

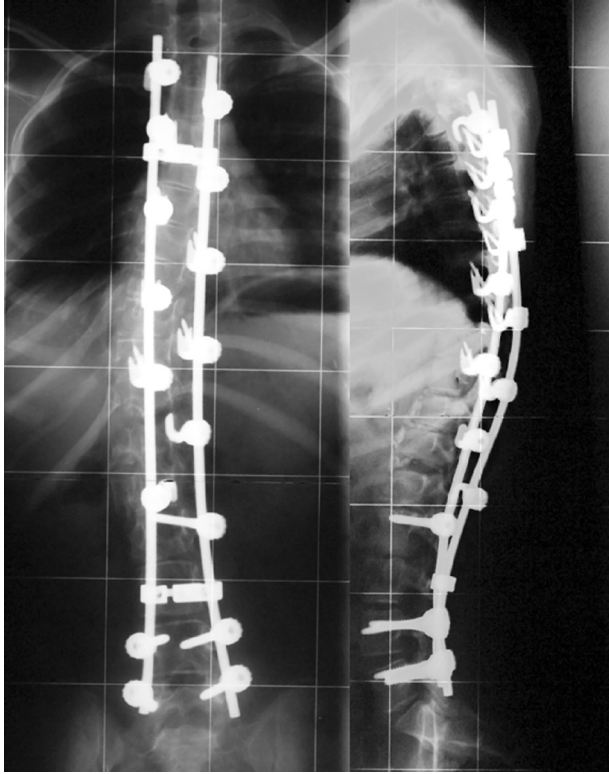


Figure 3. The anterior-posterior and lateral postoperative x-rays at the time of reexamination 4 years after surgery showed a significant reduced right convex thoracolumbar scoliosis to a 24-degree Cobb angle (Th8-L3). In the lateral view, kyphosis angles were 32 degrees between Th4 and Th12.

System (Synthes, West Chester, Pa), as has been described by Wild et al.¹⁷ Pedicle screws were applied in the computer navigation technique (Medivision, Oberdorf, Switzerland) to minimize intraoperative risks.

In addition, demineralized bone matrix (Grafton Putty, Osteotech, Eatontown, NJ) and autologous bone graft were transplanted into the fusion area to support local bone regeneration. Postoperatively, we found a scoliotic curve between Th8 and L3 of a 24-degree Cobb angle (Figure 3).

The hyperkyphosis was reduced to an angle of 32 degrees between Th4 and Th12. During the last surgical intervention, the foot deformity was also corrected. The postsurgical course with intensive physiotherapy and mobilization in a brace was uneventful, so she was discharged as an outclinic patient 20 days after surgery. The clinical follow-up at the time of the last examination (4 years after surgery) showed a standing and walking patient without any pain. The radiologic investigation of the spine showed a very good alignment in the anterior-posterior and lateral x-ray planes. The computed tomography scan of the spine with sagittal reconstruction after 18 months showed a fusion in all segments with correct implant position.

Discussion

In addition to other factors, neuromuscular imbalance is the major pathogenetic cause for a rapid progression in scoliosis and cannot significantly be affected by nonoperative treatment concepts. In addition to failures in the development of the vertebra or spinal canal, systemic neurologic diseases play a subordinated role in comparison to the high number of idiopathic scoliosis. Indeed, the incidence of scoliosis with neuromuscular dysbalance varies from 30% to 40% up to 100%.^{7,9,18-20} In comparison to idiopathic scoliosis, the spine deformity in RS appears usually in early school age. Some authors described a mean age of onset between 7 and 11 years.^{7,9,19} In a retrospective study of 78 RS patients, Lidstrom et al²¹ showed that a pathologic spinal development can appear already before the fifth year of age. Budden et al²² described patients with distinctive scoliosis who were corrected surgically at an age between 9 and 13 years. Holm and King¹⁸ reported 32 RS patients with a scoliosis manifestation between the ages of 5 and 18 years. These studies correspond to other authors who report a rapid progression of scoliosis at the age between 8 and 13 years.^{9,19,21,22}

In contrast to these reports, we present an RS patient with an early onset of scoliosis at an age of 3 years. Despite conservative treatment, including physiotherapy and a corset, a rapid progression was observed to occur. There was a parental apprehension toward surgery; therefore, it was not possible to perform an operative correction until the patient had reached an age of 10 years. At this time, the right convex thoracolumbar angle of 115 degrees, the left convex lumbar angle of 52 degrees, and the hyperkyphosis of 48 degrees were corrected. The right convex thoracolumbar scoliosis was reduced from a 115-degree to a 24-degree Cobb angle. The kyphosis angle was reduced to 32 degrees. After a 4-year follow-up, no loss of correction appeared on radiographs.

The indication for surgical treatment was already stated at a Cobb angle of 60 degrees on account of the rapid progression of the scoliosis and the collapsing spine syndrome to improve the long-term survival chance and quality of life of the patient.²³ The accompanying diseases in Rett syndrome, such as dystrophia, hyperreflexia, or spasticity of muscles, are a further risk of complications, which require intensive physiotherapeutic, pediatric, neurologic, and orthopedic collaboration.

The type of scoliosis and spinal deformity in RS shows characteristics of neuromuscular scoliosis with a rapid progression and an early onset in comparison to idiopathic scoliosis. Because of the rapid progression of the spine deformity, we recommend an early surgical treatment in RS patients. Other authors could likewise achieve a substantial reduction of scoliosis in patients with RS by a successful surgical treatment. This can prevent a progression of the curve and improve the seat and walking ability.^{7,19}

Furthermore, the use of new techniques for the surgical treatment of severe spine deformities in the growing spine allows for an excellent adaptation of spinal growth. This reduces the complication rates, such as implant failure, pseudarthrosis, loss of correction, and modest spinal growth with small stature.¹⁷

In view of the disease-related polymorbidity of patients with RS, we recommend an early operative treatment of the spine deformity with a growth-adapted instrumentation. In addition, an interdisciplinary treatment concept, including orthopedic surgeons, pediatricians, and neurosurgeons, may help to reduce the risk of potentially irreversible damage to these patients and guarantees a successful pre- and postoperative treatment of the deformities in these young patients.

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