Spinal Deformity in Sotos Syndrome: First Results of Growth-friendly Spine Surgery

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Background: Sotos syndrome (SS), or cerebral gigantism, describes children with macrocephaly, craniofacial abnormalities, general overgrowth, ligamentous laxity, developmental delay, and neurological disabilities. Fewer than 500 cases have been reported since Sotos and colleagues described the condition in 1964 and no literature exists on the management of spinal deformity in children under 10 years old. The aims of this study were: (1) to characterize the presentation of spinal deformities in patients with SS; and (2) to provide preliminary results of growth-friendly instrumentation (GFI) in these children.

Methods: Thirteen children (9 boys) with SS and minimum of 2-year follow-up were identified from 2 multicenter early-onset scoliosis (EOS) databases (1997-2017). Mean age at index surgery and follow-up duration were 5.0 years (range, 1.8 to 10 y) and 7.2 years (range, 2.1 to 14.9 y), respectively. Patients underwent GFI for a mean of 5.7 years (range, 2 to 10.2 y), with an average of 9 lengthenings (range, 2 to 18). Definitive spinal fusion was performed in 4 patients (31%). Major curve magnitude, T1-T12 and T1-S1 lengths, thoracic kyphosis, and lumbar lordosis were evaluated preindex, postindex, latest GFI, and postfusion, when possible.

Results: Five thoracolumbar (38%), 4 double major (31%), 2 main thoracic (15%), and 2 double thoracic curves (15%) were seen that spanned a mean of 6.8 levels (5 to 9). Major curves improved 36% (range, 5% to 71%), from a mean of 71 degrees (range, 48 to 90 degrees) to 46 degrees (range, 20 to 73 degrees) postindex surgery ($P < 0.001$). Major curves remained stable at a mean of 52 degrees (range, 20 to 87 degrees) at latest GFI ($P = 0.36$). True T1-T12 and T1-S1 growth velocities during GFI were 0.5 mm/mo (range, 0.4 to 0.8 mm/mo) and 0.8 mm/mo (range, 0.1 to 2.1 mm/mo), respectively. Twenty-six complications occurred in 9 patients (69%) averaging 2 complications per patient (range, 0 to 7).

Conclusions: This is the first study to evaluate the outcomes of GFI in children with SS and EOS. Compared with published data for outcomes of GFI in EOS, children with SS may have less major curve correction. Growth-friendly surgery remains an effective treatment method for EOS in patients with SS.

Levels of Evidence: Level IV—retrospective case-series.

Key Words: Sotos syndrome, Sotos, early-onset scoliosis, growth-friendly spine surgery, growth-friendly instrumentation, spinal fusion, outcomes, adverse events, complications

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See the Appendix for the members of the Children's Spine Study Group, and the Growing Spine Study Group.

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Sotos syndrome (SS), or cerebral gigantism, describes children with macrocephaly, developmental delay, distinctive craniofacial abnormalities, general overgrowth, ligamentous laxity, hypotonia, and neurological disabilities.[1] The prevalence is estimated between 1/10,000 to 1/50,000 and fewer than 500 cases have been reported since Sotos and colleagues described 5 cases at the Massachusetts General Hospital in 1964.[1–3] Gene analysis has identified abnormalities in the nuclear receptor SET domain-containing protein 1 (*NSD1*) gene on chromosome 5q35 which is present in 90% of SS patients.[3] *NSD1* alterations cause global excessive overgrowth during the first 5 years of life and children are often above the 97th percentile in size.[4] Numerous musculoskeletal pathologies such as advanced bone age, laxity, pes planovalgus, genu valgum/varum, hip dislocations, and spinal deformity are encountered.[4–8]

Literature on spinal deformities in children with SS is extremely rare and limited to small case-reports with mixed findings.[6,9–12] The incidence of scoliosis is reported between 7% and 63% with various curve severities and treatment methods.[3,4,7,9] Rapidly progressive (kypho)scoliosis develops early, often before 5 years, and has been found in infants as young as 10 months.[6,10,11,13] However, spinal deformity can also develop later in adolescence.[12]

Tatton-Brown et al[3] evaluated the largest series of SS and identified scoliosis of variable severity in one third of the 266 patients (33%). However, the authors did not include the exact number of patients with spinal deformity or details regarding management. Corrado et al[6] reported severe scoliosis or kyphosis in 8 of 42 patients (19%) with SS. Spinal fusion was required in 7 of the 8 children (88%) at a mean of 11.2 years of age. Others describe low incidences of mild scoliosis only requiring observation.[7] In a series by Cole and Hughes,[7] only 3 of 41 patients (7%) developed kyphoscoliosis and none were treated.

Most agree that scoliosis develops early in life and close follow-up is required in SS patients.[6,10,11] However, poor results with bracing are reported and excessive overgrowth raises additional concerns following spinal fusion.[6,10,12,13] The advent of growth-friendly instrumentation (GFI) such as VEPTR (vertical expandable prosthetic titanium rib), TGR (traditional growing rods), and MCGR (magnetically controlled growing rods) has provided an alternative to spinal fusion in young children with early-onset scoliosis (EOS).

To the authors' knowledge, only 1 child with SS treated with GFI has been described in the literature and no data currently exists on the outcomes of GFI.[6] The goals of this case-series were: (1) to describe the presentation of spinal deformity in patients with SS and EOS; and (2) to report the long-term outcomes and complications of GFI in these patients.

METHODS

Study Design

Institutional Review Board approval (IRB-P00032030) was gained. Two multicenter EOS databases (Pediatric Spine Study Group, previously the Growing Spine Foundation and Children's Spine Foundation) were retrospectively queried for patients who received GFI for the treatment of progressive spinal deformity (1997-2017). Children 10 years old and below diagnosed with SS and EOS and with a minimum of 2-year follow-up after GFI were included. Growth-friendly constructs were determined by surgeon preference.

Radiographic Parameters

Radiographs were evaluated for major curve magnitude, T1-T12 length, T1-S1 length, thoracic kyphosis, and lumbar lordosis at 4 time points, when applicable: (1) baseline; (2) postindex surgery; (3) final GFI before definitive fusion or latest follow-up; (4) postdefinitive fusion. Outcomes of GFI were measured through changes in major curve magnitude, T1-T12 length, and T1-S1 length. Thoracic height (T1-T12 length) and true spinal height (T1-S1 length) growth velocities (represented in mm/mo) were calculated: [(last GFI length−postindex length)/ months GFI]. This represented the true spinal growth resulting from GFI.[14]

Statistical Analysis

Demographic, surgical, complication, and GFI data were summarized using SPSSv.23 (IBM Corp, Armonk, NY). Continuous characteristics were summarized by mean and SD or median and interquartile range (25th to 75th percentile), as appropriate, and frequency and percent for categorical characteristics. Characteristics were compared using the paired Student t test or Wilcoxon sum-rank test, as indicated. Tests were 2-sided and $P < 0.05$ was considered significant.

RESULTS

Demographics

Thirteen patients (9 males) with a mean of 3.7 ± 2.30 years old (range, 0.4 to 7.5 y) at presentation diagnosed with SS and EOS were identified (Table 1). Mean BMI was 19 ± 7.6 kg/m^2 (range, 14 to 39 kg/m^2). The child with a BMI of 39 was a 1.8-year-old boy (height 80 cm, weight 25 kg). A total of 44 comorbidities were recorded for a mean of 4 ± 2.8 comorbidities (range, 1 to 10) per child, with developmental delay (n = 8, 62%) and pulmonary disorders (n = 6, 46%) most commonly seen (Table 2). Associated nonspine neurological and musculoskeletal disorders were found in 5 patients (38%) each. Prior nonoperative treatment was attempted in 7 patients (54%) (Table 3).

Curve Characteristics

There were 4 double major (31%), 3 left thoracolumbar (23%), 2 right thoracolumbar (15%), 2 double thoracic (15%), and 2 left thoracic curves (15%) that spanned a mean of 7 ± 1.0 vertebral levels (range, 5 to 9) (Tables 1 and 2, Figs. 1–4B). Mean major curve magnitudes at time of index surgery were 71 ± 13.0 degrees (range, 48 to 90 degrees). Minor curves were a mean of 51 ± 9.3 degrees (range, 38 to 64 degrees) with 5 ± 1.3 involved levels (range, 4 to 8). Initial kyphosis and lordosis were 65 ± 16.1 degrees (range, 42 to 90 degrees) and -45 ± 10.9 degrees (range, −60 to −28 degrees), respectively (Table 4).

GFI Outcomes

Patients were a mean of 5 ± 2.4 years old (range, 1.8 to 10 y) at GFI index surgery (Table 1). All procedures were performed through a posterior approach. Eight patients were treated with TGR (62%), 2 received MCGR (15%), and 2 VEPTR (15%) were inserted (Table 3). One patient (8%) with severe progressive kyphoscoliosis and rotational deformity was treated with immediate posterior spinal fusion at 4.8 years of age and was excluded from the GFI analysis.

Mean GFI duration was 5.7 ± 2.84 years (range, 2 to 10.2 y) with an average of 9 ± 4.0 lengthening procedures (range, 2 to 18). Major curve magnitudes improved from a mean of 71 ± 13.0 degrees (range, 48 to 90 degrees) to

TABLE 1. Cohort Summary (n = 13)

Patient Demographics	Frequency (%)	Range
Age at presentation (mean ± SD; y)	3.7 ± 2.30	0.4-7.5
Sex (male)	9 (69)	
Height (mean ± SD; mm)	111 ± 20.2	80-140
Weight (mean ± SD; kg)	24 ± 6.9	13-37
Body mass index (mean ± SD; kg/m^2)	19.1 ± 7.61	14.3-39.1
Comorbidities (mean ± SD)	4 ± 2.8	1-10
Prior treatment with bracing or casting	7 (54)	
Age at index surgery (mean ± SD; y)	5.0 ± 2.40	1.8-10
Construct type		
TGR	8 (62)	
MCGR	2 (15)	
VEPTR	2 (15)	
PSF	1 (8)	
GFI treatment duration (n = 12; mean ± SD; y)	5.7 ± 2.84	2-10.2
No. GFI interventions (mean ± SD)	9 ± 4.0	2-18
Follow-up duration (mean ± SD; y)	7.2 ± 3.66	2.1-14.9
Major curve characteristics*	Mean ± SD	Range
Levels spanned	6.8 ± 1.05	5-9
Curve magnitude at presentation	71 ± 13.0	48-90
Curve magnitude postindex surgery	46 ± 17.0	20-73
Absolute change	25 ± 15.6	4-50
%Correction†	36% ± 20.4%	5%-71%
Curve magnitude at final/latest GFI or predefinitive fusion	52 ± 19.4	20-87
Curve magnitude postfusion (n = 4)	36 ± 15.2	23-61
Index surgery details (n = 8)	Mean ± SD	IQR
Anesthesia duration (min)	342 ± 234	239-467
Surgical duration (min)	234 ± 116	160-301
Estimated blood loss (mL)	122 ± 58	75-150
ICU (d)	1.1 ± 2.42	0-1
Length of stay	5.6 ± 3.1	3-14
Thoracic length‡	Mean ± SD	Range
T1-T12 growth velocity (mm/mo)	0.5 ± 0.15	0.4-0.8
T1-S1 growth velocity (mm/mo)	0.8 ± 0.51	0.1-2.1
Complications	Mean ± SD	Range
Complications per patient	2 ± 2.0	0-7
Revisions per patient	1.8 ± 1.3	0-4

*Represented in (degrees) unless otherwise specified.

†%Major curve correction: [(preindex curve magnitude−postindex curve magnitude)/(preindex curve magnitude)]×100%.

‡Thoracic length growth velocity calculated as (final GFI−preindex)/months GFI), represented as mm/mo GFI.

GFI indicates growth-friendly instrumentation; ICU, intensive care unit; MCGR, magnetically controlled growing rods; n, number of patients with complete data available; PSF, posterior spinal fusion; TGR, traditional growing rods; VEPTR, vertical expandable prosthetic titanium rib.

46 ± 17.0 degrees (range, 20 to 73 degrees), or 36% ± 20.4% (range, 5% to 71%) correction, postindex ($P < 0.001$) (Table 1). A nonsignificant progression to 52 ± 19.4 degrees (range, 20 to 87 degrees) was seen at final GFI ($P = 0.36$).

Postindex T1-T12 length increased from 186 ± 33.5 mm (range, 138 to 230 mm) to 210 ± 49.3 mm (range, 134 to 270 mm) before final GFI/predefinitive fusion or latest follow-up ($P = 0.01$) and corresponded to a mean true T1-T12 growth of 0.5 ± 0.15 mm/mo (range, 0.4 to 0.8 mm/mo) (Table 4). Similarly, postindex T1-S1 length increased from 300 ± 49.0 mm (range, 227 to 390 mm) to 348 ± 67.0 mm (range, 219 to 424 mm) at final/latest GFI ($P = 0.001$), representing true spinal growth of 0.8 ± 0.51 mm/mo (range, 0.1 to 2.1 mm/mo).

Thoracic kyphosis improved from 65 ± 16.1 degrees (range, 42 to 90 degrees) at presentation to 48 ± 10.9 degrees (range, 33 to 63 degrees) postindex surgery but was not significant ($P = 0.054$) (Table 4). An increase to 65 ± 23.5 degrees (range, 33 to 100 degrees) before latest or final GFI/predefinitive fusion ($P = 0.033$) was seen. Mean lordosis did not change significantly postindex ($P = 0.079$), from −45 ± 10.9 degrees (range, −60 to −28 degrees) to −39 ± 5.5 degrees (range, −45 to −27 degrees), but increased to −53 ± 13.9 degrees (range, −75 to −25 degrees) at latest GFI ($P = 0.029$) (Table 4).

Definitive Spinal Fusion

Four patients (31%) underwent spinal fusion at a mean age of 11.9 ± 4.14 years (range, 4.8 to 15.1 y). The 3 patients were treated with GFI for a mean of 7.5 ± 2.10 years (range, 5.1 to 10.2 y). Mean levels fused was 12 ± 4.5 (range, 4 to 15). All procedures were performed posteriorly without pelvic fixation (T2-L5, T2-L5, T3-L4, and T5-T9). Surgical details include (mean, range): anesthesia duration [673 min (range, 640 to 713 min)], surgical duration [456 min (range, 297 to 534 min)], estimated blood loss [732 mL (range, 160 to 2000 mL)], ICU days [0.5 d (range, 0 to 2 d)], and length of stay [5.8 d (range, 2 to 11 d)].

Adverse Events

Complication details are found in Table 3. Twenty-six complications and 24 revisions occurred for an average of 2 complications (range, 0 to 7) and 1.8 revisions (range, 0 to 4) per patient. Of the 26 total complications, rod fractures (n = 9) and infections (n = 6) were the most common. Six patients (46%) experienced a rod fracture: 3 patients (23%) developed 1 rod fracture and 3 patients (23%) fractured a rod on 2 separate occasions (Table 3). Three patients (23%) developed 6 infections. Persistent paravertebral/parascapular pain was reported in 2 children (15%). Other adverse events included (1 case each): unplanned conversion to spinal fusion, rod corrosion, failure to lengthen rods, seroma, pseudarthrosis, L4/L5 disc degeneration, pneumonia, draining noninfectious sinus tract, and progressive kyphoscoliosis.

DISCUSSION

This is the first study to evaluate the outcomes of growth-friendly surgery for the treatment of EOS in patients with SS since it was discovered in 1964.[1] Our data suggest that GFI is an effective method to prevent curve progression, support thoracic growth, increase total spinal height, and avoid spinal fusion in skeletally immature children. Although less curve correction may be seen in SS patients, the overall results and complications of GFI are comparable to other syndromic EOS etiologies.

Spinal deformity in SS is variable with respect to incidence, age at presentation, associated comorbidities, curve characterization, severity, and management. It is difficult to determine the true incidence of scoliosis due to the wide range

TABLE 2. Patient Demographics and Curve Characteristics at Index Surgery

Patient	Age (y)	Sex	Comorbidities	Curve Type	UEV/LEV	Levels	Major Curve (deg.)
1	10.0	M	Developmental delay, musculoskeletal	Double thoracic	T6-T12	6	78
2	4.0	M	Cardiac, developmental delay	Double major	T10-L4	6	89
3	6.7	M	GI, pulmonary, renal	Right thoracolumbar	T5-L2	9	52
4	5.3	F	Developmental delay, nonspine neurological, musculoskeletal, pulmonary, renal	Double major	T10-L4	6	70
5	6.3	M	Developmental delay, renal	Left thoracolumbar	T5-L1	8	66
6	7.3	F	Nonspine neurological	Double major	T4-T12	8	70
7	3.0	M	Cardiac, pulmonary	Double thoracic	T1-T8	7	59
8	7.5	M	Developmental delay, musculoskeletal, nonspine neurological (2×), psychiatric (2×), GI, pulmonary	Left thoracic	T3-T8	5	48
9	4.8	M	Developmental delay, renal, non-spine neurologic	Left thoracic	T6-T12	6	89*
10	1.8	M	Pulmonary	Left thoracolumbar	T7-L2	7	78
11	2.9	M	Developmental delay, GI (2×), musculoskeletal	Right thoracolumbar	T4-T10	6	75
12	2.5	F	Renal	Double major	T5-T12	7	41†
13	2.3	F	Developmental delay, pulmonary (2×), nonspine neurological (3×), GI (2×), cardiac, musculoskeletal	Left thoracolumbar	T8-L3	7	90

The change in major curve postindex was not analyzed in this patient.
*This patient received immediate posterior spinal fusion and was not used in the analysis for GFI.
†In-traction PA spine radiograph demonstrated a major curve of 41 degrees without the possibility of obtaining previous radiographs.
F indicates female; GI, gastrointestinal; M, male; UEV/LEV, upper end vertebrae/lower end vertebrae.

TABLE 3. Surgical Details and Complications

Patient	Previous Treatment	Construct	GFI Duration (y)	Number GFI	Age Fusion (y)	Revisions	Complications (Surgery)
1	Bracing	TGR	5.1	9	15.1	3	Rod fracture (planned) Deep infection (planned) Deep infection during spinal fusion (aborted)*
2	No	TGR	10.2	12	14.2	2	Rod fracture (planned) Rod fracture (planned) Conversion to spinal fusion (unplanned)
3	Bracing, casting, HGT	TGR	2.3	4	NA	1	Rod fracture (unplanned) Seroma (nonop)
4	Bracing, casting	MCGR	2.5	10	NA	1	Failure to lengthen rods (unplanned)
5	Bracing, casting	TGR	7.2	12	13.5	4	Rod fracture (planned) Rod fracture (unplanned)
6	Bracing, casting	TGR	5.0	7	NA	3	Rod corrosion (nonop)† Pseudoarthrosis (nonop) Deep infection (unplanned) Superficial infection (nonop) Deep infection (unplanned) Persistent periscapular pain (nonop) L4/L5 disc degeneration (nonop)
7	Bracing, casting	TGR	8.6	12	NA	2	Draining sinus tract (nonop) Persistent paravertebral pain (planned)
8	No	TGR	6.2	10	NA	1	None
9	No	PSF	NA	NA	4.8	0	None
10	No	VEPTR	10.1	18	NA	1	Pneumonia (nonop)
11	No	VEPTR	2.7	2	NA	3	Rod fracture (unplanned)
12	No	MCGR	2.0	7	NA	0	None
13	Bracing	TGR	6.2	7	NA	3	Rod fracture (planned) Progressive kyphoscoliosis (unplanned) Rod fracture (planned) Deep infection (unplanned)

*Aborted surgical procedure.
†Rod corrosion caused systemic inflammatory response with diagnosis based on biopsy.
GFI indicates growth-friendly instrumentation; HGT, halo-gravity traction; MCGR, magnetically controlled growing rods; NA, not applicable; nonop, complication treated nonoperatively; planned, complication treated during planned surgical intervention; PSF, posterior spinal fusion; TGR, traditional growing rods; unplanned, complication treated with unscheduled surgical intervention; VEPTR, vertical expandable prosthetic titanium rib.

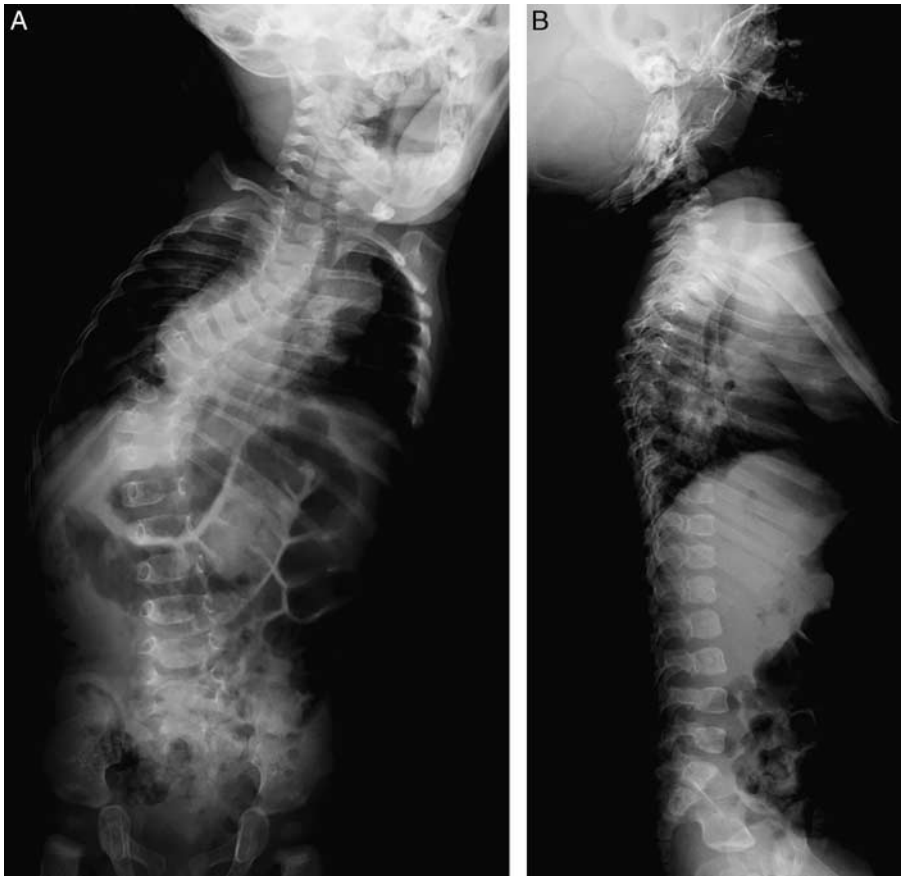

FIGURE 1. A, PA supine spine radiograph of an 8-month-old girl demonstrating a 76 degrees left thoracolumbar curve (case 13). The curve progressed to 90 degrees despite brace treatment with a body jacket and the patient underwent growth-friendly instrumentation with dual traditional growing rods at 2.3 years of age. Titanium 4.5-mm rods were inserted after local fusion of T2-T4 and L4-L5 with crushed cancellous allograft and placement of laminar hooks in a claw configuration. B, Sagittal supine spine radiograph at presentation demonstrating a relative "flat back" with thoracic hypokyphosis measuring 20 degrees.

reported in the literature between 7% and 63%.[3–7,9] The *NSD1* genetic defect in SS results in a heterogeneous phenotype with mutually independent and variable developmental, cardiac, renal, neurological, or musculoskeletal abnormalities.[3]

The diagnosis can be tedious due to the phenotypic variability and the extremely low incidence.[11] Macrocephaly, height/weight ≥ 2 SD, development delay, or hypotonia are common first physical signs that lead to further workup.[7,10,11] Spine involvement is usually recognized before 5 to 10 years old, although children of all ages can be affected.[4,6,10,11] Curve types at presentation are also variable, with a predilection toward thoracolumbar and double major curves.[6,10]

Conflicting reports exist regarding curve severity or management and most studies lack presentation, curve magnitude, or treatment data.[3,4,9] Cole and Hughes[7] observed scoliosis in 3 of 41 SS patients (7%), of which none required treatment. A series of 8 patients by Lim and Yoon[9] found scoliosis in 5 (63%), but exact curve severities and the results of bracing were not included. Tatton-Brown et al[3] studied the genetics of 266 patients with SS and reported scoliosis of variable severity in one third of patients (33%). However, the goal of that study was to identify genotype-phenotype associations and the authors did not mention the exact number of patients with scoliosis, the manner in which severity was defined, or how deformities were managed. Yet other studies include only severe cases requiring spinal fusion.[6,10,11,13]

Most authors agree that early recognition and intervention of EOS is critical in SS due to the accelerated overgrowth and rapidly progressive spinal deformity.[8,10,11] Traditional management consisted of observation, a thoracolumbar sacral orthosis, or definitive spinal arthrodesis. It has been emphasized that precocious spinal fusion should be avoided due to shunted thoracic growth, progressive deformity, the "crankshaft phenomenon," or compromised respiratory function.[10,15–17] Unfortunately, nonoperative treatment is rarely successful, leaving spinal fusion as the only viable option.[6,10,13]

The advent of GFI has provided an alternative in the surgical management of EOS. Before this study, only 1 child with SS has been treated with GFI and described in the literature.[6] In that series by Corrado et al,[6] 8 of 42 children (19%) developed scoliosis (mean age 5.2 y) and 7 of these patients (88%) required surgery. Six underwent

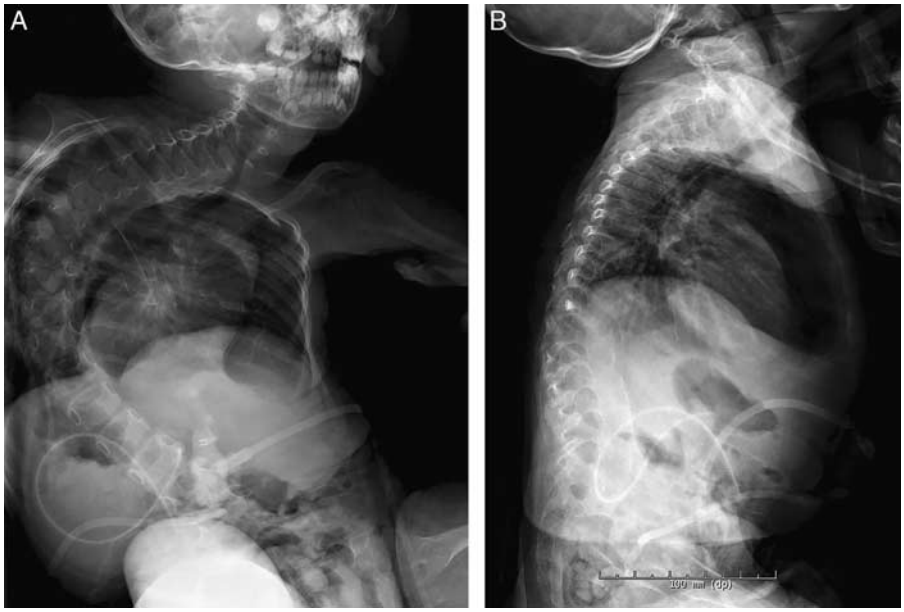

FIGURE 2. A, PA spine radiograph of a 2.6-year-old boy who presented with a right thoracolumbar curve of 75 degrees (case 11). Four months later the patient was treated with growth-friendly instrumentation using an unilateral left-sided rib-to-spine vertical expandable prosthetic titanium rib. Left-sided rib hooks were fixated at ribs 3, 4 and 5 together with placement of left-sided pedicle screws at T11 and T12. B, Sagittal spine radiograph demonstrating 46 degrees of thoracic kyphosis.

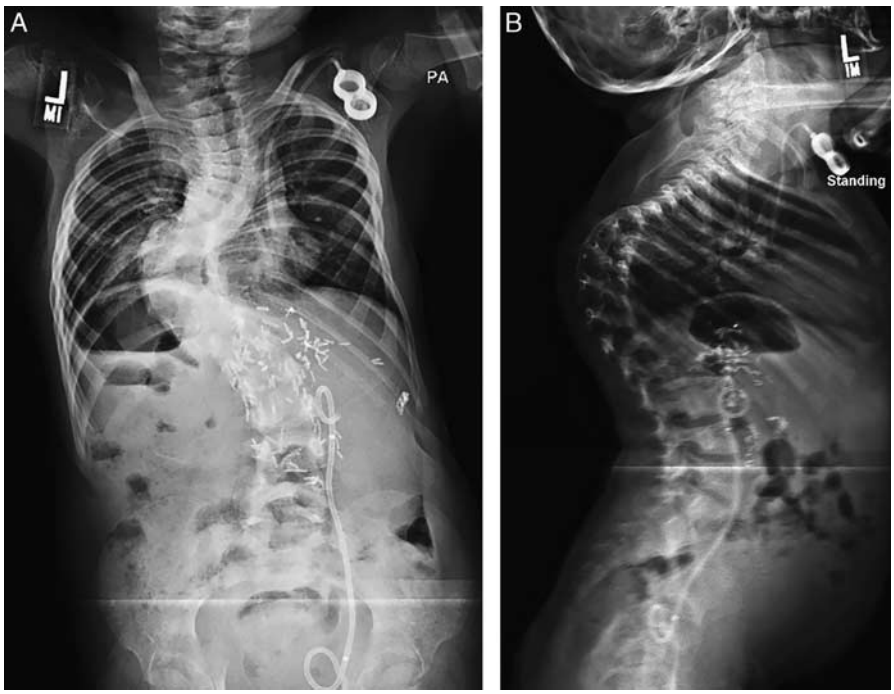

FIGURE 3. A, PA spine radiograph of a 4.8-year-old boy who presented with a left thoracic curve of 89 degrees (case 9). Evidence of metal clips/staples is seen from a previous abdominal neuroblastoma resection. It was elected to perform immediate posterior spinal fusion due to the severe and progressive kyphoscoliosis with rotational deformity. A selective thoracic fusion from T5 to T9 was done that consisted of bilateral pedicle screws at T5, T6, T8, and T9 and an unilateral left-sided pedicle screw at T7. B, Sagittal spine radiograph demonstrating kyphoscoliosis of 82 degrees.

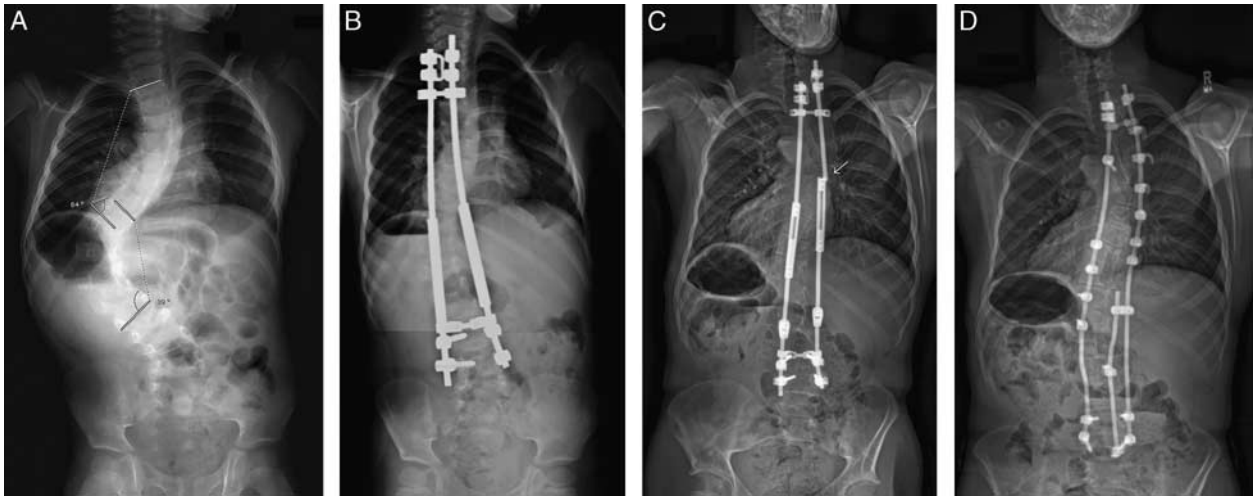

FIGURE 4. A, Preoperative PA spine radiograph of a 4.0-year-old boy who presented with a double major curve (89 degrees left thoracolumbar curve and 64 degrees right thoracic curve) (case 2). B, PA spine radiograph after insertion of dual traditional growing rods (posterior spinal fusion T2-T4 and L3-L4). The major left thoracolumbar has improved to 39 degrees (56% correction) and the minor right thoracic to 32 degrees (50% correction). T1-T12 and T1-S1 lengths are 184 and 295 mm, respectively. C, PA spine radiograph after 10.4 years of growth-friendly surgery with 12 total surgical lengthenings. Adequate correction of the left thoracolumbar curve is seen that has stabilized at 27 degrees, whereas the right thoracic has progressed to 55 degrees. T1-T12 and T1-S1 lengths increased to 264 mm (0.65 mm/mo) and 395 mm (0.81 mm/mo), respectively. A right proximal rod fracture is also observed (white arrow). The patient is now 14 years old and has reached skeletal maturity. D, Postoperative PA spine radiograph after T2-L5 posterior spinal fusion demonstrating improvement of the right thoracic curve to 41 degrees and stabilization of the left thoracolumbar curve at 26 degrees. There is a small increase in T1-T12 and T1-S1 lengths to 270 and 403 mm, respectively.

spinal fusion at an average of 11.2 years. A 7.9-year-old boy was treated with dual TGRs that resulted in a 58% correction (from 57 to 24 degrees), but long-term outcomes or changes in major curve magnitude and thoracic height were not provided.

Outcomes of GFI are traditionally assessed through major curve correctability and deformity progression. Mean major curve correction postindex surgery was 36% in SS patients and is slightly lower than most EOS data that report improvements between 39% and 54%.[18–21] Hung et al[19] evaluated the largest series of 114 MCGR cases and found a mean correction of 40.4%. However, only 37 patients (32%) had an underlying syndrome. Other MGCR studies report similar correctability.[20] Curve improvements of 47% and 39% were seen in 209 TGR cases with tandem or wedding band connectors, respectively, with corrections up to 54% in some cohorts.[18,21] The previously mentioned studies encompassed heterogeneous cohorts with variable frequencies of congenital, idiopathic, neuromuscular, and syndromic diagnoses. Progressive deformity is a concern in patients with SS due to excessive overgrowth. Although a nonsignificant progression was seen, GFI remains an effective method to control spinal deformity in children with SS.

TABLE 4. Effect of GFI on Spinal Parameters Over Time

Curve Characteristic	Preindex	Postindex	Last GFI*	Postfusion
Major curve magnitude (deg.)	71 ± 13.0	46 ± 17.0	52 ± 19.4	36 ± 15.2
T1-T12 length (mm)	162 ± 35.8	186 ± 33.5	210 ± 49.3	240 ± 53.3
T1-S1 length (mm)	280 ± 60.1	300 ± 49.0	348 ± 67.0	368 ± 75.2
Thoracic kyphosis (deg.)	65 ± 16.1	48 ± 10.9	65 ± 23.5	53 ± 29.2
Lumbar lordosis (deg.)	−45 ± 10.9	−39 ± 5.5	−53 ± 13.9	−53 ± 8.5

*Last GFI denotes last GFI, latest follow-up if still actively lengthened, or predefinitive spinal fusion.
GFI indicates growth-friendly instrumentation; NA, not applicable.

Other 2-dimensional radiographic outcome measures of GFI are thoracic height (T1-T12 length) and total spinal height (S1-T1 length). Spinal growth during the first 8 years of life is critical for normal lung development and a minimum T1-T12 length of 18 to 22 cm is required to prevent respiratory insufficiency.[15,16] Dimeglio and Canavese[15] found that T1-T12 growth velocities in children 0 to 5 and 5 to 10 years old were 13 and 7 mm/y, respectively. We found that GFI in SS patients thoracic height increased at a rate of 0.5 mm/mo (6 mm/y), approximating growth in healthy 5 to 10 years old.

Owing to phenotypic differences with healthy children, multiple comorbidities, and absent literature on SS, we felt that GFI outcomes on spinal growth were best compared with well-established data from other EOS etiologies. A recent review evaluated true spinal growth in a heterogeneous cohort of 176 patients with idiopathic, syndromic, congenital, or neuromuscular EOS.[14] Wijdicks and colleagues found that increases in T1-T12 length and S1-T12 length were smaller than anticipated, with growth of 3 and 6 mm/y, respectively. This is lower than growth velocities in SS and may be explained by the accelerated growth in SS. Most other studies incorporate height gained preindex or post-

index surgery and fail to accurately report true spinal growth achieved by growth-friendly systems.[14]

T1-S1 length is important for final trunk height but appears to be less critical for lung development.[22] Furthermore, the accelerated overgrowth gradually declines in children with SS and adolescents often obtain height within the normal range.[8] T1-S1 length increased an average of 0.8 mm/mo (9.6 mm/y) during active treatment. This is less than results by Akbarnia et al[18] who reported growth velocity of 12.1 mm/y in 23 TGR cases, 6 of which were syndromic patients. However, additional length gained after spinal fusion was included in 7 patients, overestimating spinal growth achieved during GFI.

The incidence and types of adverse events in SS are comparable to other EOS etiologies, closely resembling complications seen in children with syndromic diagnoses. Our 77% complication rate is toward the upper limit, but falls within the incidence between 32% and 79% found in the literature.[19,23–25] Consistent with current data, hardware failure accounted for the majority of GFI-related adverse events.[18,20,23–25] It is not uncommon for children with syndromic etiologies to be at greater risk for complications.[23] In a series by Russo et al[23] with a minimum of 5-year follow-up, the syndromic group had an average of 2.7 complications/patient. Syndromic children with hyperkyphosis and curves $\geq$50 degrees were at greatest risk, with 3.4 complications/patient.

Corrado et al[6] reported adverse events in 5 of 7 surgically treated Sotos patients (71%), with 1 patient dying of sepsis, and is equivalent to the 77% complication rate seen in this series. The relatively high incidence of complications seen in patients with SS is comparable to cohorts with higher ratios of syndromic or neuromuscular patients. In a series of children with predominantly neuromuscular, syndromic, or idiopathic EOS, Upasani et al[24] found that 87 of 110 patients (79%) treated with TGR developed complications. The authors identified age below 7.6 years old, thoracic kyphosis $\geq$38 degrees, and initial curve $\geq$84 degrees as risk factors that increased the likelihood of developing an adverse event related to GFI.

In contrast, decreased complications are reported in series that contain fewer syndromic cases. Bess et al[25] observed adverse events in 81 of 140 children (58%) treated with TGR after a minimum of 2 years. Although the relationship between etiology and complication risk could not be proven, the study lacked a syndromic group, and it is possible the number of complications would have been higher with inclusion of syndromic diagnoses. Our data suggest that the incidence of complications in children with Sotos is similar to patients with syndromic or neuromuscular causes of EOS. The presence of genetic defects, multiple comorbidities, younger age at presentation, severe deformities, and excessive overgrowth likely facilitate the development of complications to resemble the incidence seen in syndromes with a comparable disease burden.

Strengths and Limitations

The retrospective design, small sample size, and reliance on radiographic parameters to assess outcomes are the largest limitations of this study. However, a prospective single-center study was not feasible due to the extremely low incidence of SS, and we had to rely on multicenter databases. Another weakness is that GFI outcomes were based on radiographic changes in spinal deformity and thoracic height. Future prospective studies are needed to correlate these results to additional functional outcomes such as respiratory function and quality of life. Databases depend on accurate reporting from all participating sites and radiographs were reevaluated in an attempt to increase measurement consistency. The heterogeneity of constructs is another limitation that resulted from treatment over a 20-year period by different surgeons at various institutions. Lastly, the generalizability of this study may be restricted to tertiary pediatric referral centers with highly specialized spinal deformity services.

The biggest advantage of this study is that it is the first to provide data on the presentation and management of EOS in patients with SS since it was first described more than 50 years ago. Our data suggest that GFI is an effective method to control spinal deformity and avoid precocious spinal fusion in SS, with outcomes comparable to other EOS etiologies. Slightly less curve correction is seen, and the risk of developing complications more closely approaches that of other syndromic patients than children with idiopathic or congenital EOS. This long-term study provides valuable information on the outcomes of GFI for the treatment of EOS in patients with SS and will be an important resource for pediatric spine surgeons who manage these unique cases.

APPENDIX

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