Sotos syndrome and scoliosis surgical treatment: a 10-year follow-up

Romina Corrado · Alejandra Francheri Wilson ·
Carlos Tello · Mariano Noel · Eduardo Galaretto ·
Ernesto Bersusky

Received: 22 March 2010 / Revised: 16 December 2010 / Accepted: 30 December 2010 / Published online: 12 January 2011
© Springer-Verlag 2011

Abstract Sotos syndrome is caused by a gene deletion with an autosomal dominant pattern of inheritance. Cerebral gigantism, hypotonia and joint hyperextensibility are characteristic features of this syndrome. A percentage of these patients develop progressive scoliosis early in life. In the literature, few studies on the evolution of scoliosis in Sotos syndrome have been published. We retrospectively evaluated eight patients diagnosed with Sotos syndrome and scoliosis treated at the Garrahan Children Hospital between 1988 and March 2009. Clinical charts and imaging studies were assessed. Eight patients (19%) presented with scoliosis and seven of them (87.5%) required surgical treatment. The mean follow-up was 9.5 years (range 3–18). Mean age at first consultation was 5.2 years (range 1.1–11.2). Mean Cobb angle for scoliosis at first consultation was 34.3° (range 20°–42°) and the mean Cobb angle for kyphosis was 45.6° (range 30°–90°). Mean age at surgery was 11.2 years (range 3.7–18.10). The surgical procedures performed were instrumented posterior arthrodesis,

alone or combined with anterior arthrodesis, instrumented anterior arthrodesis, while one patient is currently in treatment with growing rods. Preoperative mean Cobb angle for scoliosis was 72.3° (range 54°–130°) and for kyphosis was 59.8° (range 30°–108°); postoperative mean Cobb angle for scoliosis was 45.5° (range 6°–90°) and for kyphosis was 40.2° (range 30°–80°). There were three early complications (pleural effusion in two cases and death due to sepsis in one) and two late complications (kyphosis above the instrumentation area and dislodgement of the proximal hooks). Incidence of scoliosis in Sotos syndrome is high and thus close monitoring of patients with Sotos syndrome during growth is important for early detection of this entity. Joint hyperextensibility and hypotonia that are characteristic of the syndrome should be considered at the moment of surgery to avoid short fusions.

Keywords Cerebral gigantism · Scoliosis deformity

R. Corrado (✉) · A. F. Wilson · C. Tello · M. Noel ·
E. Galaretto · E. Bersusky
J.P. Garrahan Pediatric Hospital, Pichincha,
1889 Ciudad Autónoma de Buenos Aires, Argentina
e-mail: romicdoc@hotmail.com

A. F. Wilson
e-mail: afrancheri@gmail.com

C. Tello
e-mail: Tello@fibertel.com.ar

M. Noel
e-mail: mnoelar@yahoo.com.ar

E. Galaretto
e-mail: eduardogalaretto@gmail.com

E. Bersusky
e-mail: ebersusky@gmail.com

Introduction

In 1964, Juan Sotos first described five patients with early excessive growth and distinctive facial appearance calling it cerebral gigantism, later known as Sotos syndrome [1]. In 1994, Cole and Hughes [2] determined the major diagnostic criteria that define the syndrome.

The excessive growth is global and may reach two or more standard deviations of the percentile with an increased growth rate during the prenatal period and first 5 years of life. Height usually normalizes in adulthood [3]. The patients present with coarse face, prominent superciliary arches, antimongoloid slant of the palpebral fissures, large and long head with high bossed forehead, hypertelorism, a square and pointed chin and macrocephaly [2].

Table 1 Patients, age at first examination, curve pattern, angle value and brace wearing

Patient number	Age at first presentation	Curve pattern		Cobb angle Initial	Age at brace indication	Brace		
		Scoliosis	Kyphosis			Brace	Type	Use
1	6.3	DOUBLE (right thoracic-left lumbar)	40	31°/35°	6.3	31°/35°	MW	4 years
2	11	DOUBLE (right thoracic-left lumbar)	90	41°/30°				
3	2.4	TRIPLE (high right thoracic, left thoracic, right lumbar)	48	25°/40°/40°	2.4	25°/40°/40°	MW	1 years
4	3.5	SIMPLE (right lumbar)	30	30°	5.5	50°	TLSO	4 years
5	4.1	DOUBLE (right thoracic-left lumbar)	50	22°/42°	4.1	22°/42°	MW	6 months
6	1.1	DOUBLE (left thoracic-right lumbar)	40	20°/30°	4.6	25°/37°	MW	9 years
7	2.3	DOUBLE (right thoracic-left lumbar)	35	36°/27°	2.3	36°/27°	MW/TLSO	5 years
8	11.2	SIMPLE (right thoracic)	32	20°	12	26°	TLSO	3 years

TLSO thoracolumbosacral orthosis, MW Milwaukee

Fig. 1 Preoperative and 1-year postoperative PA radiographs of representative patients. **a** and **b** 15-year-old female who presented a left thoracic curve of 60° T4–T10 and right lumbar 50° T10–L3, with 32° of kyphosis (T2–T12). **c** and **d** instrumented posterior arthrodesis of T4–L3 1 year postoperative, with correction of 27° for thoracic curve and 10° for the lumbar curve with 25° of kyphosis

Fig. 2 One patient is currently in treatment with growing rods. **a** and **b** 7.9-year-old patient with left thoracic of 57° T5–T12 and right lumbar curve of 50° T12–L5 and kyphosis of 35° (T2–T12). **c** and

d 5 months after growing rods' placement, with correction of 24° for thoracic curve and 35° for lumbar curve. **e** and **f** Clinical appearance

The disorder is associated with developmental delay, hypotonia, joint hyperextensibility and behavioral and learning disturbances often with mild mental retardation. Hypotonia, joint hyperextensibility and excessive growth in childhood are the main features of the syndrome [4–6].

The incidence of Sotos syndrome is 1/10,000–1/15,000 live births with an autosomal dominant pattern of inheritance [3]. In 2002, a gene deletion was described with *NSD1* (nuclear receptor SET domain containing protein 1 gene) protein insufficiency and a 5q35 microdeletion is the cause of the Sotos syndrome in approximately 90% of the patients [7]. Scoliosis has been reported in about 30% of the affected individuals [3]. There are reports maintaining that scoliosis

develops at an early age with severe and rapidly progressive curves [8] while others state that scoliosis is only rarely severe enough to require treatment [2, 3].

The aim of this study was to show our experience in eight children with Sotos syndrome and scoliosis and evaluate the evolution of the deformity, treatment, either conservative or surgical and complications.

Materials and methods

Between 1988 and March 2009, we analyzed 42 patients diagnosed with Sotos syndrome, confirmed by genetic

Table 2 Data of the patients who required surgical treatment

Patient	Age	Angle value						Surgical treatment
		Pre-op		Post-op		Follow-up		
		Scoliosis	Kyphosis	Scoliosis	Kyphosis	Scoliosis	Kyphosis	
1	12.1	38°/68°	43	46°/57°	40	50°/58°	40	IPA T5–L4
2	12.2	60°/37°	108	31°/21°	50°	34°/24°	70°	AA + IPA T2–L3
3	3.7	40°/85°/95°	61	20°/40°/41°	30	20°/40°/40°	32	AA + IPA T3–L3
4	10	54°	30	6°	32	6°	75	IAA T10–L3
5	18.10	130	108	90°	70	Death		IPA T2–L4
6	15.3	60°/50°	32	27°/8°	30	27°/10	25	IPA T2–L4
7	7.9	57°/50°	35	57°/50°	30	60°/50°	30	GR

PRE-OP preoperative, *POST-OP* postoperative, *IPA* instrumented posterior arthrodesis, *IAA* Instrumented anterior arthrodesis, *AA* anterior arthrodesis, *GR* growing rods

studies. Eight patients (one female and seven male) presented with scoliosis or kyphoscoliosis (19%). The remaining patients (34) were excluded as they did not present with deformity either in the coronal or in the sagittal plane.

The inclusion criteria were a genetic diagnosis of Sotos syndrome and spine deformity at either the coronal or sagittal plane, scoliosis >10° and kyphosis over 40°, respectively.

The patients and their clinical charts and imaging studies were evaluated. The following was investigated: pregnancy control of the mother, complications during delivery, health of parents and siblings, ages of deformity presentation and during evolution, radiographs measuring scoliosis' angular value and kyphosis' angular value. For both, determinations were made at first consultation, including flexibility, at the time of brace indication and surgical treatment and during long-term follow-up as well. Measuring was made with Cobb criteria for scoliosis and kyphosis. All radiographs were performed in standing position while flexibility was performed through active bending test in recumbent position. Curve pattern, brace treatment, surgical procedures, early and late complications, magnetic resonance imaging (MRI) studies of the complete spine and posterior fossa were systematically requested.

Results

Eight of 42 patients with Sotos syndrome presented with scoliosis. All of them were treated. Seven (87.5%) required surgical treatment and only one completed brace treatment successfully.

Mean age at first consultation was 5.2 years (range 1.1–11.2 years) while the mean follow up was 9.5 years (range 3–18 years). Three developed scoliosis before age

3; three between 3 and 10 while two at onset of puberty (Table 1). All pregnancies had been controlled and no remarks were made. In five patients (62.5%) there were complications during the delivery: perinatal asphyxia, amniotic fluid aspiration, failure to progress, umbilical cord hemorrhage and breech presentation. All parents and siblings were healthy. The MRI did not show alterations of the spinal cord in any of the patients.

The curve pattern showed a right thoracic and/or left lumbar curve in five of eight patients with apex between T7–T11 in thoracic curves and between L1–L3 for the lumbar curves. A double curve was seen in five patients, a single curve in two patients and one with triple curve. The mean Cobb angle for scoliosis on the first examination was 34.3° (range 20°–42°) for the major curve and 25.8° (range 20°–31°) for the minor curves. The mean Cobb angle for kyphosis was 45.6° (range 30°–90°), apex T6–T8 (Table 1).

In seven of eight patients brace treatment was prescribed. The indication was based on several parameters: in the angular value of the deformity: scoliosis over 25° and <50°, its flexibility and the age of the patient. Braces were worn for a mean of 3.9 years (range 6 months–9 years). In one patient, surgery was indicated on first examination. Cobb angle at the moment of brace prescription was 36.8° (range 26°–50°). Due to the age of the patients, the Milwaukee brace (MW), what actually avoids modeling of the trunk, was the most frequently used (71.4%). In only one patient, the thoracolumbosacral (TLSO) and Milwaukee braces were alternated (Table 1).

The mean age at surgery was 11.2 years (range 3.7–18.10 years). The surgical interventions were performed between 1993 and 2008, thus causing a disparity in treatment techniques. The choice of approach was based on the age of the patient, structure of the curve, angular value and skeletal maturation. Instrumented posterior arthrodesis alone was performed in three patients, combined with

Fig. 3 **a** and **b** Male of age 12.2 years with right thoracic curve of 60° T7–T11 and left lumbar curve of 37° T11–L3, with 108° kyphosis (T2–L1). **c** and **d** Immediate postoperative arthrodesis of T2–L3 with correction of 50° for kyphosis and 31° for thoracic curve and 21° for

lumbar curve. **e** and **f** 1-year postoperative dislodgement of the proximal hooks with progression of spine deformity in scoliosis and kyphosis

anterior arthrodesis in three other patients. In one patient instrumented anterior fusion only was performed. In the remaining patient, currently in treatment, growing rods were implanted (Fig. 2). Preoperative Cobb angle was 72.3° (range 54°–130°) for the main major curve and 42.2° (range 37°–50°) for the minor curve. Flexibility of the major curve was 48.8° (32.6%) and 18° (37.4%), respectively. Postoperative Cobb angle of the main major curve was 45.5° (range 6°–90°) and 29° (range 8°–50°) of the minor curve. No loss of correction was observed in the long-term follow-up (Fig. 1). Preoperative kyphosis was 59.8° (range 30°–108°) and postoperative was 40.2° (range

30°–80°), with a correction of 33%. Only one patient (patient no. 2) developed loss of kyphosis correction with upper hooks dislodgement. Distally, the fusion ended in the lumbar area in all these cases. None of them needed the sacrum to be involved (Table 2).

There were three early postoperative complications: pleural effusion secondary to anterior arthrodesis in two cases and death due to sepsis after instrumented posterior arthrodesis in one. There were two late complications. Dislodgement of the proximal hooks occurred in one patient with kyphosis above the instrumentation area that did not require treatment (Fig. 3). In the patient who

Fig. 4 **a** and **b** Male patient of age 6.11 years with scoliosis of T10–L3 of 54° with kyphosis of 30°. **c** and **d** Immediate postoperative arthrodesis of T10–L3 with correction of 6° for scoliosis and 32° for kyphosis. **e** 1-year-old postoperative instrumented anterior arthrodesis

with kyphosis above the instrumentation. **f** and **g** Post surgery, he required simple anterior arthrodesis from T3 to T10 and instrumented posterior fusion from T2 until L3. The previous implants were not removed with correction of kyphosis of 43°

underwent lumbar instrumented anterior arthrodesis, kyphosis developed above the instrumented area. Eight years postsurgery he required simple anterior arthrodesis from T3 to T10 and instrumented posterior fusion from T2 until L3. The previous implants were not removed (Fig. 4).

Discussion

In the literature, scarce data were found on the incidence of scoliosis in Sotos syndrome [3]. The percentage of spinal deformities was 19% in 42 patients.

Close monitoring of these patients during growth is important for early diagnosis of scoliosis. Deformity develops early in life. Three of our patients developed scoliosis before 3 years of age, three patients between 3 and 10 years of age and two at onset of puberty. In five of eight patients, right thoracic–left lumbar curves were found. On first examination scoliosis angular value was

remarkably high averaging 34.3° (range 20°–42°) and orthotic management was needed in seven patients while surgical treatment in one.

Literature data about the progression of the deformity is also scarce [8, 9]. Most publications present a small number of patients with rapidly progressive curves without treatment [2]. In our series, one patient presented a quick curve progression. In the remaining seven patients, however, curve progression was <5°/years.

It is important to emphasize that the majority of our patients started to wear a brace at a very early stage. This factor may have influenced curve progression.

The elapsed mean time between the first consultation and surgery was 6.9 years (range 1–18 years). Nevertheless, 50% of the patients who underwent surgery already had a surgical indication at that moment, but received orthotic management to postpone the arthrodesis because of their young age [the mean age at first consultation was 5.2 years (range 1.1–11.2)].

Most of our patients underwent surgical treatment. In the literature there are reports where majority of patients did not require surgery [8–10]; however Tsirikos et al. [4] recently reported five patients with Sotos syndrome that required surgical treatment.

Regarding the complications seen in surgical treatment, we believe that they are not specific to the syndrome. It is necessary to consider that the causes are multifactorial. The kyphosis above the instrumentation area and also the dislodgement of the proximal hooks may be linked to short fusion in a case while the wrong choice of fusion level, technical problems, hybrid instrumentation, and lack of assessment of the sagittal plane may be involved factors among others as well. Hyperextensibility and hypotonia that are characteristic of the syndrome for sure may play a role too. For this reason we advocate not to perform short fusions as in idiopathic scoliosis but arthrodesis long enough to avoid that complication.

In summary, incidence of scoliosis in Sotos syndrome is high and thus close monitoring of patients with Sotos syndrome during growth is important for early detection of this entity. Scoliosis is generally severe, as 87.5% of our patients required surgery. We believe that early indication for brace wearing allows control of the curve progression and delay of definitive arthrodesis until the onset of puberty. Joint hyperextensibility and hypotonia that are characteristic of the syndrome should be considered at the moment of surgery to avoid short fusions.

Conflict of interest None of the authors has any potential conflict of interest.

References

1. Sotos JF, Dodge PR, Muirhead D (1964) Cerebral gigantism in childhood: a syndrome of excessively rapid growth with acromegalic features and a nonprogressive neurologic disorder. *New Eng J Med* 271:109–116
2. Cole TRP, Hughes HE (1994) Sotos syndrome: a study of the diagnostic criteria and natural history. *J Med Genet* 31:20–32
3. Pagon RA, Bird TC, Dolan CR, Stephens K (2009) Sotos syndrome. *GeneReviews* [Internet]. University of Washington, Seattle
4. Tsirikos AI, Demosthenous N, McMaster MJ (2009) Spinal deformity in patients with Sotos syndrome (Cerebral gigantism). *J Spinal Disord Tech* 22:149–153
5. Bravo M, Chacon J, Bautista E, Perez-Camacho I, Trujillo A, Grande MA (1999) Sotos syndrome associated with focal dystonia. *Rev Neurol* 28:971–972
6. Carlo W, Dormans JP (2004) Cervical instability in Sotos syndrome: a case report. *Spine* 29:E153–E156
7. Tatton-Brown K, Rahman N (2007) Sotos syndrome. *Eur J Hum Genet* 15:264–271
8. Sweeney E, Fryer A, Donnai D (2002) Sotos syndrome: two cases with severe scoliosis. *Clin Dysmorphol* 11:121–124
9. Haga N, Nakamura S, Shimode M, Yanagisako Y, Iwaya T (1996) Scoliosis in cerebral gigantism, Sotos syndrome. A case report. *Spine* 21:1699–1702
10. Suresh D (1991) Posterior spinal fusion in Sotos syndrome. *Br J Anaesth* 66:728–732