Scoliosis Associated with Proteus Syndrome: Report of 2 Cases and Review of the Literature

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Key words
- Proteus syndrome
- Scoliosis
- Spinal fusion
- Spine/surgery

Abbreviations and Acronyms
CA: Cobb angle
CT: Computed tomography
DTT: Devices for transverse traction
HRQoL: Health-related quality of life
PS: Proteus syndrome
SRS-22 scale: Scoliosis Research Society Outcomes Questionnaire

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BACKGROUND: **Proteus syndrome (PS) is a complex genetic disorder, characterized by the sporadic appearance of hamartomatous lesions that follow a mosaic pattern and have a progressive evolution. It affects most of the mesodermal origin tissues, including the bones. Scoliosis is a common manifestation, with great variability and specific peculiarities, but little about it has been published.**

CASE DESCRIPTION: **Presentation of 2 clinical cases of patients with PS that underwent scoliosis surgery and literature review.**
Two patients aged 17 years, a girl (patient 1) and a boy (patient 2), both diagnosed with PS, were being followed-up for scoliosis. Patient 1 had a right thoracic curve with a Cobb angle of 69.1°, whereas patient 2 also had a right thoracic curve of 106.8°. In both patients a posterior fusion was performed, associating rib and ponte osteotomies at the level of the apex in patient 2. A minimum 2-year follow-up was done.
Both patients had a satisfactory evolution without neurologic or other complications, with a high degree of correction of their curves (Cobb angle 29.2° and 55.6°, respectively). Their total SRS-22 (Scoliosis Research Society Outcomes Questionnaire) score at the last visit was 4.77 and 4.64, respectively.

CONCLUSIONS: **Both PS and scoliosis are conditions associated with deformities and physical limitations that decrease the health-related quality of life of these patients. Because of the severity of the spinal deformities and their risk of progression, early diagnosis and prompt treatment is recommended.**
Despite being highly complex, scoliosis surgery allows a satisfactory deformity correction and consequently improves the health-related quality of life of patients with PS.

INTRODUCTION

Proteus syndrome (PS) is a complex and very rare congenital hamartomatous overgrowth, characterized by the sporadic appearance of hamartomatous lesions that follow a mosaic pattern and have a progressive evolution disorder.[1,2] It affects most of the mesodermal origin tissues, including the bone, skin, fat, and central nervous system.[3] Only approximately 200 cases have been reported in the literature.[4]

Patients usually have a normal appearance at birth, emerging the main phenotypic manifestations around the first year of age (6–18 months)[3] with an asymmetric and disproportionated growth of hands and feet, macrodactyly, cerebriform masses of the plantar or palmar surfaces, and hemihypertrophy.[1,2,5,6] There is a wide variety of malformations, along with epidermal and connective tissue nevi, and an increased occurrence of tumors. It has recently been associated with mosaicism with a somatic activating mutation in the AKT1 gene, located at chromosome 14q32.3.[7]

PS diagnosis is currently based on the criteria of Biesecker et al.[6] that includes the presentation of all general criteria (mosaic distribution of lesions, progressive curse, and sporadic occurrence) added to one category A sign (cerebriform connective tissue nevus), 2 of category B (linear epidermal nevus, disproportionate overgrowth, and specific tumors before the second decade of life), or 3 category C (dysregulated adipose tissue, vascular malformations, lung cysts, and peculiar facial phenotype). Currently, a genetic test can confirm the diagnosis. It is also imperative to do a differential diagnosis with other congenital overgrowth syndromes, such as Klippel-Trenaunay-Weber syndrome, multiple enchondromatosis (Ollier disease and Maffucci syndrome), neurofibromatosis, and Bannayan syndrome, which often have similar characteristics.[8]

Spinal deformity is a common manifestation not very well documented in the literature because of the scarcity of cases published. It is included as 1 of the 5 major criteria of Samlaska et al.,[9] although it was not incorporated into the posterior approved diagnostic criteria. Despite its great variability, in some cases, specific anatomic peculiarities are detected, such as the irregularity of the vertebral bodies,

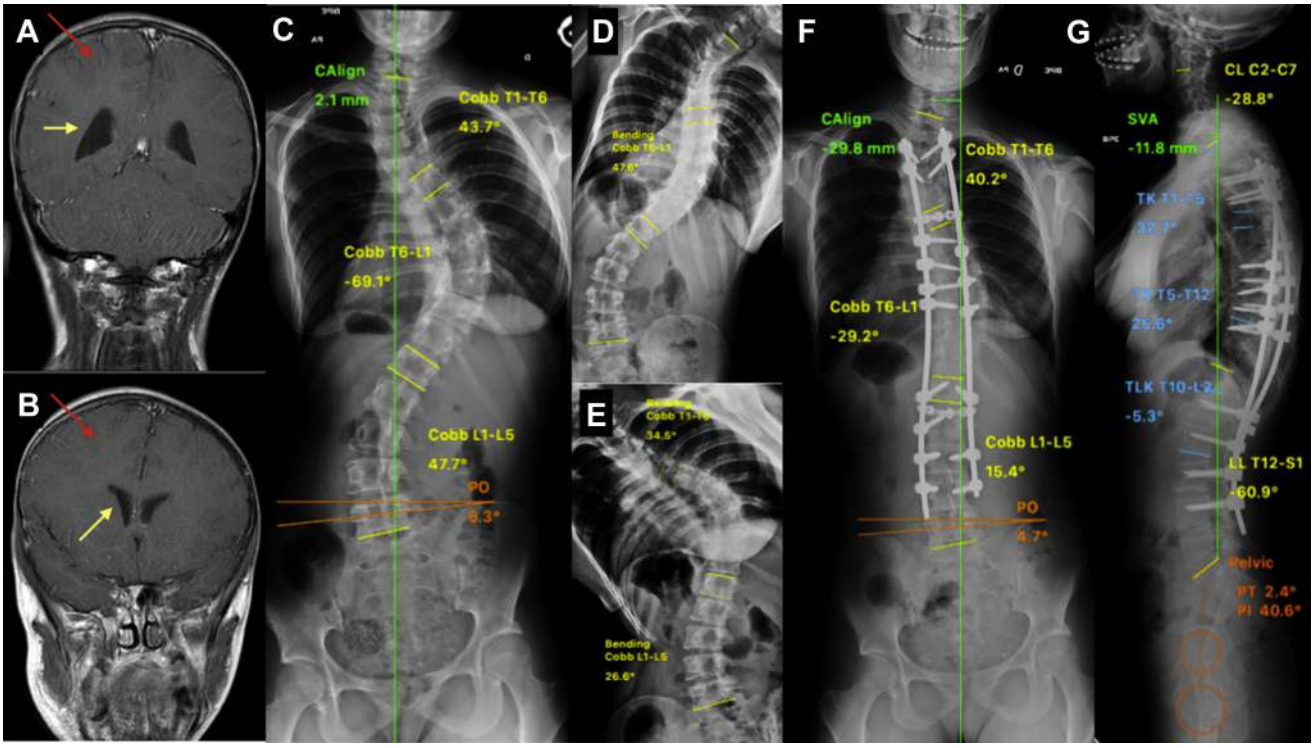

Figure 1. Radiologic images from patient 1. (**A** and **B**) Head magnetic resonance imaging revealing hemimegalencephaly, with overgrowth of the right cerebral hemisphere (*red arrows*), and asymmetrical enlargement of the right lateral ventricle (*yellow arrows*). (**C**) Preoperative standing posteroanterior (PA) radiography view of the whole spine in which a right thoracic T6-L1 curve (Cobb angle [CA] 69.1°), a proximal thoracic T1-T6 curve (CA 43.7°), and a left lumbar L1-L5 curve (CA 47.7°) are observed, pelvic obliquity of 6.3°, and coronal balance of +2.1 mm. (**D** and **E**) Bending test to the right with a main thoracic curve of 47.6°, and to the left with a proximal thoracic of 34.5° and lumbar curve of 26.6°. (**F**) Postoperative PA radiography view of the whole spine, T2-L3 posterior instrumentation, right thoracic T6-L1 curve (CA 29.2°) and left lumbar L1-L5 (CA 15.4°), pelvic obliquity of 4.7°, and coronal balance of −29.8 mm. (**G**) Postoperative lateral radiography view of the whole spine showing harmonic sagittal alignment.

hemihypertrophy of the facet joints and pedicles, and rigid and rapidly progressive curves.[5,6,10,11] The anatomic features encountered at the vertebral spine cause other problems, in particular, spinal canal stenosis and cord compression, tether cord, or hyperkyphosis.[12,13] Spinal tumors are also a frequent cause of spinal cord compression, scoliosis, and rapid curve progression in these patients.[14,15] Consequently, all these must be rigorously considered for an optimal management of spinal abnormalities associated with PS.

Very few single case reports regarding scoliosis in patients with PS have been published. We present 2 cases managed in a multidisciplinary approach at our institution, focusing on the surgical management of the spinal deformity characteristic of this syndrome, and also describing their mid-term radiologic results and health-related quality of life (HRQoL) at a minimum follow-up of 2 years after the intervention. Furthermore, we checked over the current literature and summarized the main characteristics described by other authors concerning scoliosis in patients with PS.

CASE DESCRIPTION

This study was carried out in accordance with the World Medical Association Declaration of Helsinki (JBJS 79A:1089–98,1997). Patients confidentiality was protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA).

Case Report 1

The first patient is a girl, born without complications after a controlled pregnancy, weighing 3750 kg and without milestone developmental abnormalities, apart from a slight delayed walking start at 15 months, attributed to an earlier diagnosis of right hemihypertrophy. Other clinical manifestations appearing consecutively were hemimegalencephaly and mild intellectual disability, epidermal nevus, left facial lipoatrophy, and various hemangiomas. These provided the basis to make the diagnosis of PS at the age of 3 years. There was no family history of similar conditions.

Because the leg length discrepancy her main problem, she did not need any orthopedic surgery during her childhood. However, several abnormalities were observed on a routine medical check-up at the age of 11 years, which were a prominent shoulder blade, uneven shoulders, flank asymmetry, and pelvic obliquity, added to a right thoracic gib when bending, being measured on a vertebral column radiography a right thoracic T6-L1 curve of 49° of Cobb angle (CA) and a

Table 1. Registered Data of the Presented Cases

	Patient 1		Patient 2	
	Preoperative	**Postoperative**	**Preoperative**	**Postoperative**
Age PS diagnosis	3 years		1 years	
Age scoliosis diagnosis	11 years		10 years	
Age surgical treatment	17 years		17 years	
Main thoracic CA	T6-L1 69.1°	29.2°	T5-T10 106.8°	55.6°
Main thoracic BC	47.6°	—	72.9°	—
Lumbar or TL CA	L1-L5 47.7°	15.4°	T10-L4 52.6°	31.9°
Lumbar or TL BC	24.4°	—	17°	—
Coronal alignment (mm)	+2.1	−29.8	−37.5	−31.2
Sagittal alignment (mm)	—	−11.8	+84.2	+28.8
PSF levels	T2-L3		T3-L1	
Implants/material	Pedicular bilateral screws, bilateral rods, allograft, 2 DTT		Pedicular bilateral screws, bilateral rods, allograft, 2 DTT	
Correction techniques	Premodeled extra strong chrome-cobalt rod applied in the concavity and en bloc derotation maneuvers		Ponte and 7–9 left rib osteotomies at the apex. Two chromium-cobalt modeled rods and en bloc and segmental vertebral derotation	
Complications	None		None	
Follow-up	26 months		34 months	
SRS-22 function	4.6	5	3.2	4.8
SRS-22 pain	5	4.4	2.8	4.8
SRS-22 self-image	3	4.8	1.8	4
SRS-22 mental health	4.4	4.8	4.6	4.8
SRS-22 satisfaction	—	5	—	5
SRS-22 total score	4.25	4.77	3.1	4.64

PS, Proteus syndrome; CA, Cobb angle; BC, bending Cobb; PSF, posterior spinal fusion; T, thoracic; L, lumbar; TL, thoracolumbar; DTT, devices for transverse traction; SRS-22, Scoliosis Research Society Outcomes Questionnaire.

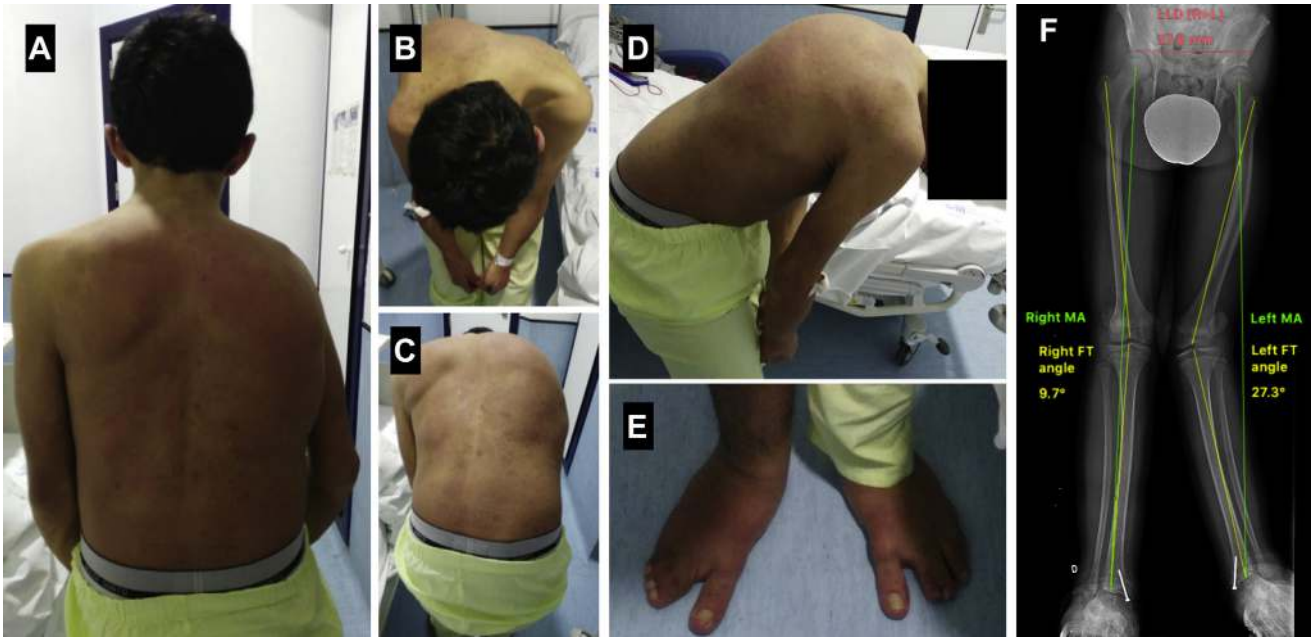

Figure 2. Clinical and radiologic images from patient 2. (**A**) Back picture in which patchy hyperpigmentation can be seen, uneven shoulders, and prominent left scapula. (**B**–**D**) Adams forward bending test evidencing right thoracic gib. (**E**) Disproportionate foot overgrowth and syndactyly of second, third, and fourth right foot toes, and second and third left foot toes. (**F**) Lower limbs measurement on a standing posteroanterior radiography view, demonstrating leg length discrepancy of 2.76 cm, bowing of the left femur, and severe left genu valgus (left femorotibial angle of 27.3°).

compensatory L1-L5 left lumbar curve of 33°, without notable alterations in the sagittal plane. At that moment, she exhibited a Risser 0 grade of skeletal maturity, therefore orthopedic management was recommended, and a 2-cm shoe lift for pelvic balance plus a Boston brace for scoliosis control were prescribed.

Clinical and radiologic follow-up was made, with slow progression of the curves, reaching at the age of 17 a T1-T6 CA of 43.7°, a T6-L1 CA of 69°, and a L1-L5 CA of 47.7°, being all structural curves as seen in the bending test (proximal thoracic of 34.5°, main thoracic of 47.6°, and lumbar curve of 26.6°), a coronal balance of +2.1 mm, 6.7° of pelvic obliquity due to leg length discrepancy (right larger than left), and normal sagittal plane morphology (Figure 1). Hence surgical treatment was advised. Under neurophysiological and fluoroscopic control, a posterior spinal T2-L3 fusion was performed using bilateral pedicle screws. As derotation maneuvers a premodeled extra strong chrome-cobalt rod in the concavity was applied, and once the correction with the bar was obtained, an en bloc derotation maneuver was subsequently performed. For additional stiffness, 2 devices for transverse traction (DTT) and allograft were added.

The patient evolved in a satisfactory manner, without incidents occurring during the postoperative follow-up and achieving an adequate correction in both planes, satisfactory coronal and sagittal balance, and a harmonic sagittal profile. Neurologic symptoms did not appear either pre- or postoperatively. Her reported total SRS-22 (Scoliosis Research Society Outcomes Questionnaire) score at the last follow-up 34 months postoperative was of 4.77 points (whereas previous score was 4.25), and she was very satisfied with the results of the surgery (Table 1).

Case Report 2

The second patient is a boy born in Ecuador where he was diagnosed with Klippel-Trenaunay-Weber syndrome. Reports inform a normal pregnancy, cephalic presentation and eutocic delivery, weighing 4 kg. No family history of overgrowth syndromes or skeletal abnormalities was acknowledged. Being evaluated for the first time at our institution at the age of 1 year, he exhibited a syndromic face, short neck, thoracic and abdominal hemangiomas, patchy hyperpigmentation on his back, right hip dysplasia, disproportionate foot overgrowth, and syndactyly of the second, third, and fourth right foot toes, and second and third left foot toes (Figure 2). During the first years, he also presented with some developmental milestone abnormalities, as delayed conversation and ambulation. Gathering all these characteristics, he was diagnosed with PS.

He was surgically treated for hip dysplasia with a right Dega pelvic osteotomy at age 5 years. During his childhood, he also developed subcutaneous neurinomas, right supraclavicular, axillar and dorsal paraspinal bilateral soft tissues tumors, right hemihypertrophy, painful vascular malformation in the dorsum of the foot, and patellar instability, with a need for surgery for patellar instability at the age of 7 years, and for leg length discrepancy and bilateral ankle valgus at age 13 years, performing a right distal femur and proximal tibial epiphysiodesis, and a bilateral medial distal tibial hemiepiphysiodesis.

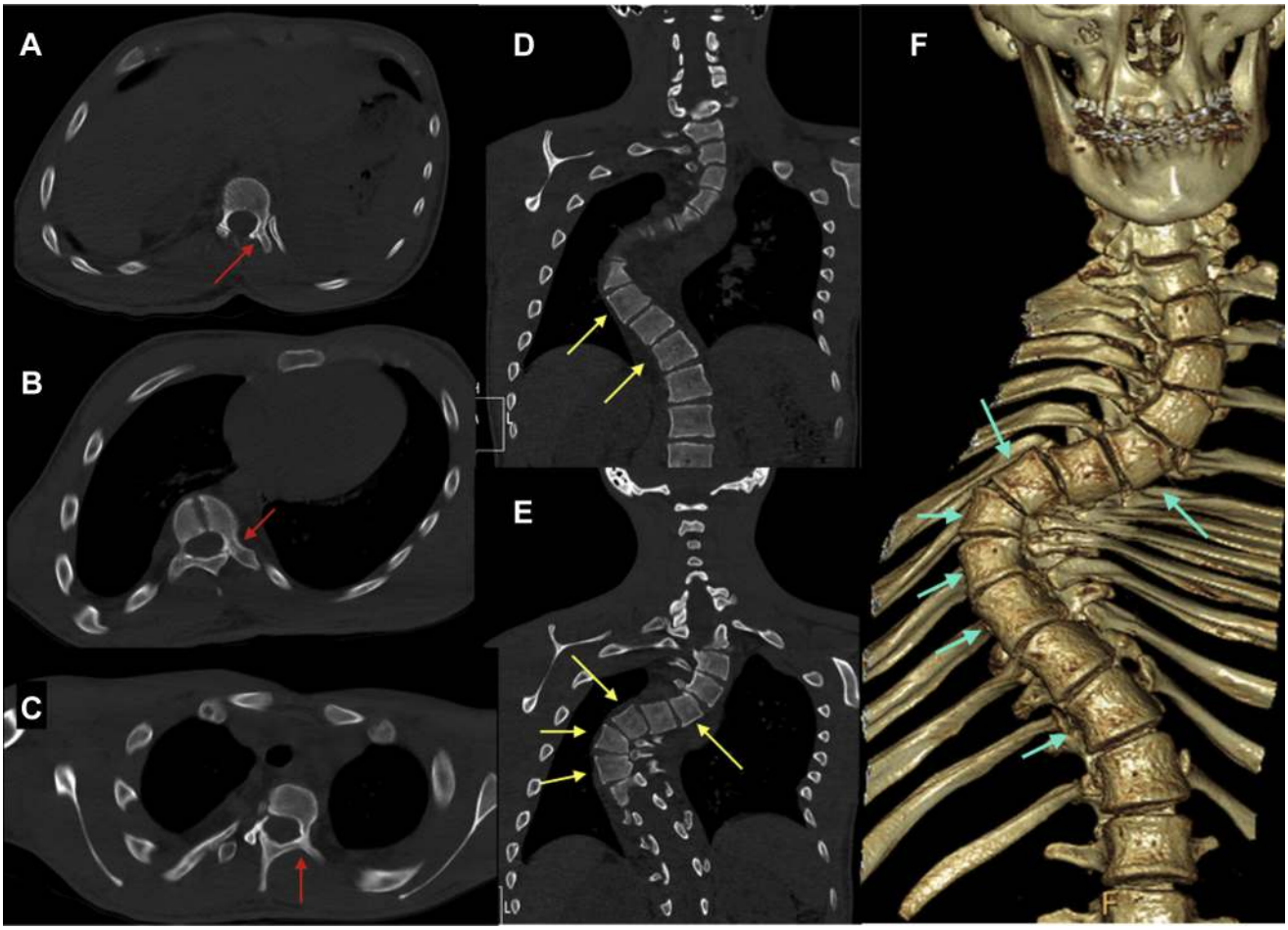

Figure 3. Spinal column computed tomography (CT) scan images from patient 2. (**A**–**C**) Axial plane cuts demonstrating left asymmetric pedicle and facet joint overgrowth of several thoracic and thoracolumbar vertebra (*red arrows*). (**D** and **E**) Coronal plane cuts in which lateral wedge vertebrae can be seen (*yellow arrows*). (**F**) Three-dimensional CT reconstruction showing asymmetric overgrowth of thoracic and thoracolumbar vertebral bodies (*green arrows*) with resultant scoliosis.

Scoliosis was detected at age 10 years, presenting on physical examination a right thoracic and a left lumbar gib, and on radiography a proximal thoracic T1-T5 curve of 21° of CA, a principal right thoracic T5-T10 curve of 26°, and a lumbar T10-L4 curve of 22° were measured, his triradiate cartilage remained open. He discontinued the medical check-ups during the following years and consulted again at age 16 years having significantly worsened scoliosis, being his T5-T10 CA of 106° and sagittal vertebral alignment of +84.2 mm. Thus surgical treatment was recommended. On a preoperative computed tomography (CT) scan, several thoracic lateral wedge vertebrae were visualized, secondary to vertebra hemihypertrophy (Figure 3), as well as asymmetric pedicle and facet overgrowth of multiple vertebrae. A mild thrombopenia without other cytopenia or morphologic alterations and normal coagulation indices were detected during the preoperative study, which was linked to his underlying disease and required no additional treatment prior to surgery.

As in the first patient, in this boy a posterior spinal T3-L1 fusion with bilateral pedicle screws and rods, 2 DTT, and allograft was accomplished when he was age 17 years. Ponte osteotomies at the level of the apex, as well as 7–9 left rib osteotomies were essential to make the thoracic curve more flexible to help in correction. To achieve an adequate coronal and sagittal alignment, chromium-cobalt rods were previously modeled in an appropriate manner. After attaining an increase in mean arterial pressure to ensure a correct spinal cord vascularization, derotational maneuvers were executed, first, derotation with the 2 bars, and then en bloc and segmental derotation were completed. The main complication during surgery was excessive bleeding during the initial approach, appropriately controlled with intravenous tranexamic acid, as well as relaxation of the patient while dissection was being done, once the baseline potentials had been obtained. Also, topical hemostats, vasoactive drugs, and autologous blood recovery were used in this patient. No

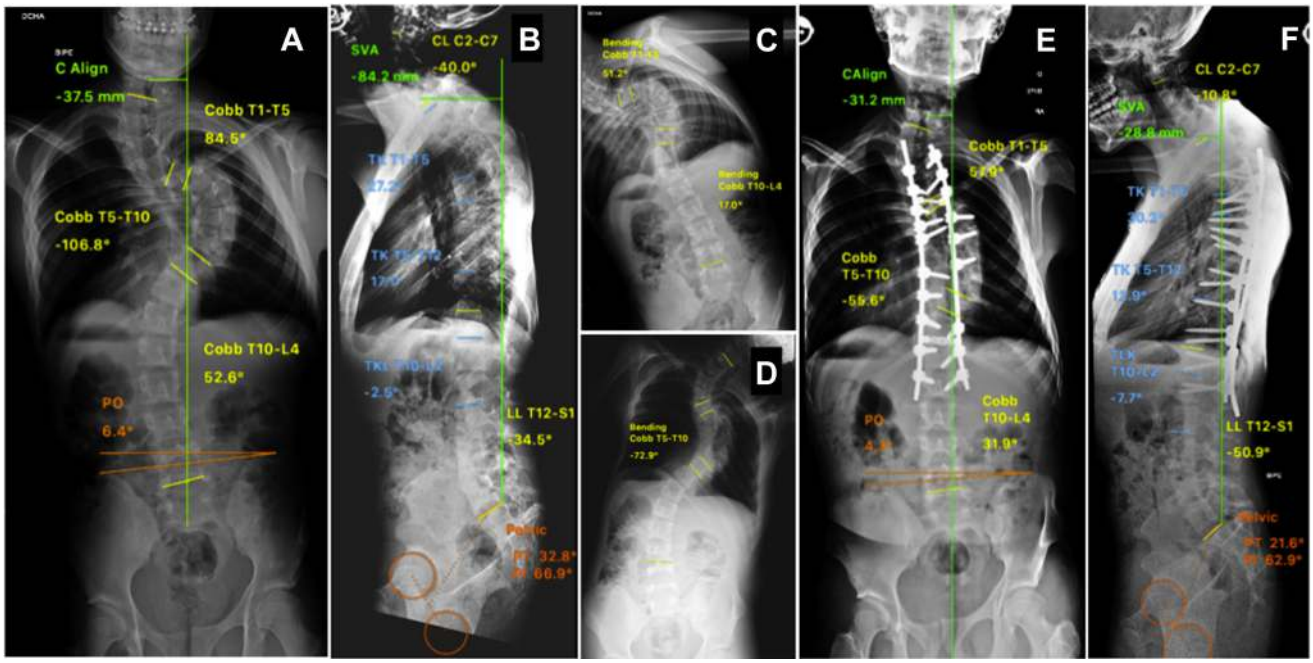

Figure 4. Standing whole-spine radiographs from patient 2. (**A**) Preoperative posteroanterior (PA) radiography view, showing a right thoracic T5-T10 curve (Cobb angle [CA] 106.8°) and left thoracolumbar T10-L4 (CA 52.6°) curve, pelvic obliquity of 6.4°, and coronal balance of −37.5 mm. (**B**) Preoperative lateral radiography view demonstrating a sagittal imbalance of +84.2 mm. (**C** and **D**) Bending test radiography, displaying a flexible thoracolumbar curve (bending CA 17°). (**E**) Postoperative PA radiography view that demonstrates T3-L1 posterior instrumentation and a high degree of curve correction with a right thoracic T5-T10 curve CA of 55.6° and left lumbar T10-L4 of 31.9°, pelvic obliquity of 4.3°, and coronal balance −31.2 mm. (**F**) Postoperative lateral radiography view showing improved sagittal profile, being the sagittal vertebral alignment of +28.8 mm.

other intraoperative or immediate postoperative incidents occurred.

In the postoperative period, thromboprophylaxis was indicated for having a higher risk of thrombosis. At the periodic outpatient clinic examinations, the patient was found to have recovered adequately. In the last visit, 26 months after surgery, his coronal and sagittal profile had improved, being his sagittal vertebral alignment +28.8 mm (Figure 4). He had an active life without pain or functional limitations and scoring a total of 4.64 points on the SRS-22 scale, being the previous score of 3.1, and showing great satisfaction with the treatment (Table 1).

DISCUSSION

As previously described, PS is a complex and rare hamartomatous disease with a wide range of malformations. The literature regarding scoliotic deformities in patients with PS and their optimal management is currently limited. This report contributes to the literature with 2 new cases of scoliosis associated with PS that underwent surgical treatment for spinal deformity correction. Both cases had previously been diagnosed with PS based on application of revised diagnostic criteria and developed scoliosis at approximately age 10–11 years, being followed up during their adolescence until surgical management was performed. Posterior instrumentation fusion was satisfactorily accomplished, and mid-term follow-up showed good clinical, radiologic, functional, and HRQoL results.

The oddity of PS, the wide spectrum of manifestations, and the confusion with other overgrowth syndromes makes the PS diagnosis arduous. Biesecker et al.[6] proposed diagnostic criteria based on clinical features and radiologic findings. Our patients met all the general diagnostic criteria (mosaic distribution of lesions, progressive course during childhood, and sporadic occurrence) and various category B and C criteria: in the first patient, 2 category B (epidermal nevus, disproportionate overgrowth of the limbs) and 2 category C (left facial lipoatrophy and various hemangiomas), whereas in the second patient, 3 category B (right hemihypertrophy, subcutaneous neurinomas, right supraclavicular, axillar and dorsal paraspinal bilateral soft tissues tumors) and 2 category C (syndromic face, thoracic and abdominal hemangiomas, and vascular malformation in the foot). None of our patients displayed the single sign in category A, however, because this sign is pathognomonic for the diagnosis, it is not a common finding in patients with PS.[16] Dysregulation of fatty tissue is common in PS, and it can include atrophy of fatty tissues,[17] as seen in patient 1. Also, brain abnormalities may be present in PS,[18] as hemimegalencephaly and the concomitant dilatation of ipsilateral ventricle appreciated in the first patient. Furthermore, knee or ankle valgus and

foot malformations, which exhibited in the second patient, have been reported by other authors.[6,10,16] Although molecular testing can be done,[7] the clinical criteria for PS alone may be sufficient for the diagnosis without identifying the mutation.[19]

After a detailed literature review work-up, 5 published single-case reports that describe the scoliosis pattern and its management in patients with PS were found (Table 2).[13,20-23] Some other authors name scoliosis as a common manifestation in PS,[5,6,10,14,16,24] without focusing their manuscript on this condition. PS malformations are variable among the analyzed patients, being hemihypertrophy, foot gigantism, and vascular malformations the most predominant manifestations among them.

Spinal pathology, apart from scoliosis described in these patients, include spinal stenosis, tether cord, thoracic kyphosis, paraspinal tumors, and acute spinal cord compression. Additionally, some patients show particular anatomic spine anomalies, such as, wedge vertebrae, hemihypertrophy of pedicles, and facet joint or mega-spondylo-dysplasia, as described by other authors,[5,6,10,11] that certainly contribute to the pathogenesis of the scoliotic deformity and is related to the main characteristics of the curves and risk of progression.

The type of main curves presented by the patients are all right thoracic except for one left thoracolumbar curve, ranging from mild to severely angulated curves using the CA method. The concavity of the curve matches with the side of the asymmetrical overgrowth of the vertebral bony structures. Most of them also describe a lumbar or thoracolumbar compensatory curve. In all of these patients, the direction of the main curve coincides with the side of the extremity hemihypertrophied argument that sustains the idea that the asymmetric changes arising from the mesodermal disorder intrinsic to the syndrome have a great influence on the spinal curvature.[14,20] Despite not happening in the cases we exposed, cord tethering, spinal stenosis, and spinal tumors should be ruled out when detecting an atypical or rapidly progressing curve, and in the event of neurologic deterioration.[13-15] Clinical and radiologic follow-up should be made until skeletal maturity, and continued later if a moderate or severe curve is present. Preoperatively, we recommend performing magnetic resonance imaging to rule out intraspinal abnormalities and spinal cord status, as well as CT scans in complex cases to assess the vertebrae anatomy for surgical planning.

Only 3 articles[20,21,23] describe the surgical management of the scoliosis deformity, whereas the 2 remaining published case reports[13,22] deal with scoliosis associated to other spinal problems, such as spinal stenosis, tether cord, and spinal cord compression that required focal laminectomy decompression without correction or instrumentation of scoliosis deformity. In 2 cases added to one of ours, an orthopedic treatment was used before going through with surgery. Despite not being well established in the literature, we contemplate that bracing may delay the surgical treatment in skeletally immature patients.

When analyzing the articles that describe a surgical management (Table 3), our approach agrees with previously reported articles about deformity correction and fusion using a posterior spinal instrumentation, whereas Takebayashi et al.[20] used a combined anterior release and posterior approach for vertebral fusion. Also, in one of our cases, because of the severe angulation exhibited by the patient, ponte and rib osteotomies at the apex of the deformity were required. This may have probably helped in the degree of correction obtained and the absence of recurrence in our patient, as opposed to the patient described by Yazar et al.[21] The age at which this surgical intervention is performed is also analogous among the published literature, being adolescence as a common period for intervention in the reported cases.

Complication reported rate after deformity surgical intervention remains low, being the recurrence of deformity described in one case.[21] The only complication in one of our patients was bleeding but was adequately controlled and had no consequences. We recommend the use of intravenous tranexamic acid, as well as relaxation of the patient while dissection is being done, to reduce bleeding, once the baseline potentials have been obtained by the neurophysiologist. Neurologic impairment has not been described in relation to scoliosis surgery in the 5 patients analyzed, however, it is a common complication in patients with PS due to spinal stenosis, tether cord, or paraspinal tumors that may or may not have accompanying scoliosis. This complication rate after scoliosis surgery in patients with PS should be taken cautiously as the number of patients reviewed remains low.

Because PS and scoliosis are 2 conditions associated with physical limitations and loss of self-esteem that additionally have a negative impact on the HRQoL of these patients, early diagnosis and prompt treatment is recommended. Scoliosis surgery in these patients is considered highly complex, sometimes requiring various osteotomies to achieve adequate correction of the deformity, but our experience and results demonstrate that satisfactory deformity correction, and consequently improved quality of life of patients with PS can be achieved.

Conclusions

To the best of our knowledge, this is the first report that describes the surgical management of scoliosis deformity in 2 consecutive patients diagnosed with PS, and their 2-year clinical and radiologic results together with their reported HRQoL. The overgrowth potential and vertebrae abnormalities of the tissues may be responsible for the particular characteristics and rapid progression of the spinal deformities in these patients. Magnetic resonance imaging and preoperative CT scans are recommended for proper surgical planning. In very severe deformities, surgical tips, such as different types of osteotomies, are necessary to achieve an optimal outcome. Corrective spinal surgery should be performed when required by an experienced team, to avoid potential functional and respiratory limitations and to improve the HRQoL of these patients.

ACKNOWLEDGMENTS

All authors made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; drafted the work or revised it critically for important intellectual content; gave final approval of the

Table 2. Compilation of Scoliosis Cases Associated to Proteus Syndrome Published in the Literature

Study	Number	Age PS Dx	Sex	PS Anomalies	Associated Spine Problems	Anatomic Spine Anomalies	Main Scoliosis Curve CA	Other Scoliosis Curves CA	Spine Surgical Treatment	Last Status
Takebayashi et al., 2001[20]	1	<1	M	Epidermal nevi, lesion, macrodactyly, right hemihypertrophy	Scoliosis, thoracic kyphosis	Wedge vertebrae, pedicle and facet joint hemihypertrophy, extra lumbar vertebrae	Right Thoracic T5-L1 79°	L1-L6 50°	Anterior release + PSF for scoliosis	NR
White et al., 2005[13]	1	2	M	Lymphangiomatosis, bilateral foot gigantism, right lobster claw deformity, patellar instability	Acute spinal cord compression, paraspinal tumor, scoliosis	Paraspinal mass in the midthoracic region with extradural extension	Right thoracic 30°	Lumbar 18°	Laminotomy and decompression for spinal cord compression	Healthy 12 months PO
Yazar et al., 2005[21]	1	8	F	Lipoma, foot gigantism, left hemihypertrophy, nevus, hemangioma, nephrolithiasis	Scoliosis	NR	Left TL T7-L2 44°	NR NR	PSF for scoliosis	Recurrence 20 months PO
Yamamoto et al., 2012[22]	1	NR	F	Lipomas, hemangiomas, rib deformity, hypoplasia first metatarsal	Lumbar spinal stenosis, tether cord, kyphosis, scoliosis	Mega-spondylo-dysplasia, tether cord, lumbar stenosis	Right thoracic T4-T12 NR	NR NR	Laminectomy L2-L3 for spinal stenosis	Died 7 months PO
Li et al., 2015[23]	1	17	F	Right hemihypertrophy, multiple exostosis	Scoliosis	No vertebral or canal abnormalities	Right TL T5-L4 100°	PT 70°	PSF for scoliosis	Healthy 3 months PO
Current research 2020	2	3	F	Right hemihypertrophy	Scoliosis	No vertebral or canal abnormalities	Right T6-L1 69.1°	Left L1-L5 47.7°	PSF for scoliosis	Healthy 34 months PO
		1	M	Hemangioma, neurinoma, right hemihypertrophy, syndactyly, foot gigantism, hip dysplasia, subcutaneous mass, patella instability	Scoliosis	Lateral wedge vertebra, right pedicle and facet joint hemihypertrophy	Right T5-T10 106.8°	Left TL T10-L4 52.6°	PSF for scoliosis + osteotomies at apex	Healthy 26 months PO

PS, Proteus syndrome; Dx, diagnosis; CA, Cobb angle; M, male; F, female; NR, not registered; TL, thoracolumbar; PT, proximal thoracic; PSF, posterior spinal fusion; PO, postoperative.

Table 3. Scoliosis Deformity-Specific Data of Surgically Treated Patients with Proteus Syndrome Reported in the Literature

Study	Number	Age of Scoliosis Dx	Sex	Anatomic Spine Anomalies	Main Scoliosis Curve CA	Main Curve Apex	Other Scoliosis Curves CA	Orthopedic Treatment	Scoliosis Surgical Treatment	Fusion Levels	Age Surgery	Post-CA Main curve	Complications	Follow-Up (months)
Takebayashi et al., 2001[20]	1	6	M	Wedge vertebrae, right pedicle and facet joint hemihypertrophy, extra lumbar vertebrae	Right Thoracic T5-L1 79°	T9/T10	L1-L6 50°	None	Anterior release + PSF	T2-L3	18	60°	NR	NR
Yazar et al., 2005[21]	1	8	F	NR	Left TL T7-L2 44°	T10/T11	NR NR	Brace	PSF	T6-L3	NR	22°	Recurrence	20
Li et al. 2015[23]	1	3	F	No vertebral or canal abnormalities	Right TL T5-L4 100°	T12	PT 70°	TLSO	PSF	T2-L4	17	77°	NR	3
Current research 2020	2	11	F	None	Right T6-L1 69.1°	T8	Left L1-L5 47.7°	Boston brace	PSF	T2-L3	17	29.2°	None	34
		10	M	Lateral wedge vertebra, right pedicle and facet joint hemihypertrophy	Right T5-T10 106.8°	T7/T8	Left T10-L4 52.6°	None	PSF + Ponte + 7–9 left rib osteotomies	T3-L1	17	55.6°	None	26

Dx, diagnosis; CA, Cobb angle; M, male; F, female; NR, not registered; TL, thoracolumbar; PT, proximal thoracic; TLSO, thoracolumbosacral orthosis; PSF, posterior spinal fusion.

version to be published; were in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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