

## Surgical management of high-grade lumbar spondylolisthesis associated with Hajdu-Cheney syndrome: illustrative case

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**BACKGROUND** Hajdu-Cheney syndrome (HCS) is a rare connective tissue disorder characterized by severe bone demineralization. In the spine, it is associated with the early onset of severe osteoporosis and can cause spondylolisthesis. Spinal instrumentation in the setting of severe osteoporosis is challenging because of poor resistance of vertebrae to biomechanical stress.

**OBSERVATIONS** A 59-year-old woman with known idiopathic HCS presented with a grade 4 L5-S1 spondylolisthesis and right L5 pedicle fracture associated with a left L5 pars fracture, causing a progressive L5 radiculopathy that was worse on the left side than the right side and bilateral foot drop. The authors performed decompressive lumbar surgery, which included a complete L5 laminectomy and resection of the left L5 pedicle. This was followed by multilevel lumbosacral instrumentation using cement-augmented fenestrated pedicle screws as well as transdiscal sacral screws and bilateral alar-iliac fixation. Postoperatively, the radicular pain resolved, and the left foot drop partially recovered.

**LESSONS** Stabilization of high-grade spondylolisthesis in the setting of bone demineralization disorders is challenging. The use of different instrumentation techniques is important because it increases biomechanical stability of the overall instrumentation construct.

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**KEYWORDS** Hajdu-Cheney syndrome; acro-osteolysis; spondylolisthesis; spinal instrumentation

Hajdu-Cheney syndrome (HCS) is a rare, autosomal dominant connective tissue disorder.<sup>1</sup> It occurs as a result of a mutation in the NOTCH2 gene, which leads to increased bone demineralization and resorption.<sup>2</sup> Patients with HCS may present with a wide range of clinical features such as acro-osteolysis, premature loss of teeth, thoracic deformities, fractures of long bone, and osteoporosis.<sup>3</sup> To this date, approximately 100 cases of HCS have been reported, with only two reported cases associated with spondylolisthesis as a result of HCS.<sup>4,5</sup> First, Shah et al. described a patient with grade 4 L5-S1 spondylolisthesis associated with HCS that was treated surgically.<sup>4</sup> Unfortunately, the patient later developed an adjacent segment fracture of S1-S2 requiring revision surgery.<sup>4</sup> Second, Mattei et al. described a patient with a focal cervical kyphosis, associated with a C6-C7 spondylolisthesis and surgical management of the case.<sup>5</sup> Due

to bone demineralization and ligamentous laxity, spondylolisthesis is a possible complication of HCS.<sup>4-7</sup> This underscores the challenge associated with spondylolisthesis surgery in patients with disorders of bone demineralization.

### Illustrative Case

#### History

A 59-year-old woman was diagnosed with HCS on the basis of hand and foot deformities and repeated pathological fractures due to early-onset severe osteoporosis. She tested positive for NOTCH2 mutation as part of the FORGE Canada Consortium study.<sup>8</sup> Despite ongoing treatment for her osteoporosis with alendronate, forteo, zoledronic acid, and denosumab, severe osteoporosis with moderate to high risk of fractures remained.

**ABBREVIATIONS** CT = computed tomography; HCS = Hajdu-Cheney syndrome; PMMA = polymethylmethacrylate.

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**FIG. 1. A:** Preoperative EOS radiographs. **B:** Preoperative sagittal spine CT scan. **C:** Preoperative sagittal T2-weighted spine magnetic resonance imaging.

She was first referred for a neurosurgical evaluation at the age of 48 years for the surgical management of her high-grade L5-S1 spondylolisthesis associated with bilateral sciatica pain. However, given her multiple severe comorbidities, which included oral anticoagulation medication for repeated pulmonary

embolisms, supraventricular tachycardia, asthma, and severe osteoporosis (all in the absence of any motor or sphincter dysfunction) and relative pain control with analgesia, it was decided that she would be best treated with conservative management at that time.



**FIG. 2. A:** Postoperative EOS radiographs. **B:** Postoperative sagittal CT scan with cement-augmented screws. **C:** Postoperative sagittal view of S1 transdiscal screw. **D:** Postoperative axial view of S1 transdiscal screw.

She had yearly clinical and imaging follow-up with her family physician. However, 11 years later, she presented with increased bilateral sciatica worse on the left side than right, and new-onset partial bilateral foot drop, with her left dorsiflexors and extensor hallucis longus graded at 3/5. Her physical examination otherwise did not reveal any other weakness, paresthesia, or hyperreflexia.

Imaging revealed a high-grade Meyerding grade 4 spondylolisthesis associated with right L5 pedicle fracture and a left L5 pars fracture. She had a dysplastic Wiltse-Newman type 1 pars fracture on the left, with a Wiltse-Newman type 4 fracture disconnecting her vertebral body from the pedicle on the right. There was obvious bone demineralization and old pathological wedge fractures at T8 and L1. Preoperatively, bone density at the femoral neck was  $0.660 \text{ g/cm}^2$  with a T score of  $-2.7$  despite being on denosumab. A previous bone density scan in 2013 had revealed a bone density of the femoral neck of  $0.754 \text{ g/cm}^2$  with a T score of  $-2.0$ .

EOS radiography, spine computed tomography (CT), and spine magnetic resonance imaging were performed prior to surgery (Fig. 1, Supplementary Figure 1).

### Surgical Intervention

Under neuromonitoring, including motor and sensory evoked potentials, the patient was in the ventral position on a Jackson

spine top table. She received an open bilateral L5 and S1 laminectomy, with a complete left L5 pedicle resection to allow for a complete decompression of the left L5 nerve root. Multiple Smith-Peters osteotomies at the L4-L5 and L5-S1 levels were also performed. Fenestrated pedicle screws (Xia 3 Spinal System, Stryker) were then placed from L2 to L4 bilaterally under fluoroscopy guidance. No L5 pedicle screws were placed. The S1 bilateral screws were then placed using the transdiscal pedicle screw technique, crossing the midline (Fig. 2). Bilateral S2 alar-iliac screws were finally placed. Each screw was then filled with 1 to 2 mL of high viscosity polymethylmethacrylate (PMMA). Fusion was achieved by decorticating the remaining joints, lamina, and transverse processes and by adding autologous bone graft for a poster. This was augmented as well with demineralized bone matrix (Grafton, Medtronic) and recombinant human bone morphogenetic protein-2 (Infuse Bone Graft, Medtronic).

One month after surgery, CT-guided vertebroplasty was performed on L1, which had an old L1 osteoporotic fracture associated with a 35% height loss. This was performed to decrease the biomechanical stress given the adjacent instrumentation construct.

Postoperative imaging confirmed a partial reduction of the spondylolisthesis to a grade 2. Her EOS radiography revealed a balanced spine in the sagittal and coronal plane.



**FIG. 3. A:** Six-month postoperative EOS radiographs. **B:** Six-month postoperative axial view of S1 transdiscal screw. **C:** Six-month postoperative sagittal view of S1 transdiscal screw.

## Follow-Up

After a 1-month stay in the rehabilitation center, the left-sided dorsiflexion weakness partially improved and the sciatic pain decreased significantly, leading to weaning of opioid and neuropathic pain medications.

Postoperative imaging revealed a partial correction of her listhesis to a grade 2, all while having her sagittal parameters well balanced on standing EOS radiographs.

A CT scan of the lumbar spine at 6 months postoperatively did not reveal any instrumentation complications or any rod fracture or screw pull out. We also visualized beginning of a bony posterior fusion via the facets bilaterally (Fig. 3).

## Discussion

### Observations

HCS affects less than 1 in 1 million newborns<sup>9</sup> and is caused by a mutation in the NOTCH2 gene, which plays a key role in skeletal development and bone remodeling by acting on the differentiation of osteoclasts and osteoblasts.<sup>2</sup> It is an autosomal dominant disorder, but sporadic cases, such as with our patient, have been described.<sup>10,11</sup>

The gold standard for its diagnosis is genetic sequencing of exon 34 of NOTCH2 gene.<sup>3</sup> However, HCS is often suspected due to the presence of aforementioned clinical and radiological findings.<sup>3</sup> It is important to note that these clinical and radiological findings, such as acro-osteolysis, in which there is osteolysis of the distal phalanges,<sup>12</sup> are not exclusive to HCS. Therefore, clinicians must have a wide differential diagnosis and perform extensive evaluations to differentiate HCS from other disorders such as hyperparathyroidism, scleroderma, psoriasis, and neuropathic disorders, which are all causes of acro-osteolysis.<sup>13</sup>

Spondylolisthesis can be encountered in disorders of bone demineralization, such as HCS, osteogenesis imperfecta, and pycnodysostosis. The surgical treatment of high-grade spondylolisthesis associated with these conditions is challenging, with a higher risk of instrumentation failure or pathological fractures adjacent to the instrumentation.<sup>4,5,14</sup> Falls et al. reported their experience with the correction of complex cervicothoracic deformity in three patients with HCS, highlighting the distorted craniovertebral anatomy (prominent occiput, persistently open cranial sutures, atypical pedicle anatomy, poor bone quality) and advising an extension of the construct to achieve adequate fixation.<sup>14</sup>

The use of bone cement-augmented pedicle screws for transforaminal lumbar interbody fusion has been validated by two independent retrospective studies in patients with nonsyndromic osteoporosis.<sup>15,16</sup> PMMA leakage is a rare complication of vertebroplasty through fenestrated pedicle screw.<sup>17</sup>

Because our goal was not to achieve a complete reduction of spondylolisthesis, our patient's spondylolisthesis was fused in situ after a partial reduction using the cement-augmented pedicle instrumentation. Because placement of L5 pedicle screws was not possible, we opted for S1 transdiscal screws crossing the midline. A recent biomechanical study by Kerr et al. found that transdiscal screws were superior biomechanically when compared to the Bohlman technique and even the modified Bohlman technique.<sup>18</sup>

### Lessons

This case highlights the surgical challenges of high-grade spondylolisthesis surgery in patients with genetic disorders of bone demineralization. To improve long-term biomechanical stability of

the instrumentation in patients with these conditions, we have used cement-augmented pedicle screws, bilateral S1 transdiscal screws, and bilateral alar-iliac screws. We hope that describing the surgical management of this patient contributes to optimizing the management and outcome of these difficult spondylolisthesis cases.

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### Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

### Author Contributions

Conception and design: Wang, Shedid, Yuh. Acquisition of data: Bergeron, Shedid, Yuh. Analysis and interpretation of data: Ndongo Sonfack, Bergeron, Wang, Yuh. Drafting the article: Ndongo Sonfack, Wang. Critically revising the article: Bergeron, Shedid, Yuh. Reviewed

submitted version of manuscript: Ndongo Sonfack, Bergeron, Boubez, Yuh. Approved the final version of the manuscript on behalf of all authors: Ndongo Sonfack. Statistical analysis: Yuh. Administrative/technical/material support: Yuh. Study supervision: Yuh.

### Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

*Supplementary Figure 1.* <https://thejns.org/doi/suppl/10.3171/CASE.22171>.

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