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Minimally Invasive Lumbar Decompression and Removal of Symptomatic Heterotopic Bone Formation After Spinal Fusion with Recombinant Human Bone Morphogenetic Protein-2

***Fabio Roberti*[1,2] *and Katie Arsenault*[1]**

We present a case of symptomatic heterotopic bone formation following revision of posterolateral lumbar fusion/instrumentation and "off-label" use of recombinant human bone morphogenetic protein-2, treated successfully with the use of a minimally invasive tubular approach.

INTRODUCTION

The use of recombinant human bone morphogenetic protein-2 (rhBMP-2) as an osteoinductive factor in spine surgery has been approved by the U.S. Food and Drug Administration for single-level anterior lumbar fusion with tapered cages in skeletally mature patients.[1] Due to its proven effectiveness in increasing postoperative fusion rates,[2,3] the "off-label" use of these proteins has gained widespread popularity among spine surgeons dealing with various spinal conditions,[4-9] and a published review of administrative data found that 85% of rhBMP-2 used in spinal surgery fell under the "off-label" definition.[10] Notwithstanding the proven benefits, several studies regarding complications associated with the use of rhBMP-2 have been so far published. Increased rates of infection, postoperative seromas and hematomas, delayed wound healing, dysphagia and neck swelling, retrograde ejaculation, symptomatic radiculitis, vertebral osteolysis, cage subsidence, as well as heterotopic bone formation have all been reported following the use of rhBMP-2 in spine surgery.[11-18] We report a case of symptomatic heterotopic bone formation following lumbar spinal revision surgery and posterolateral fusion with rhBMP-2, successfully treated using a minimally invasive tubular approach and provide documentation of the technical aspect of the procedure.

CASE PRESENTATION

A 65-year-old female patient with obesity underwent an open lumbar laminectomy with instrumented allograft posterolateral fusion using iliac bone graft, local bone, calcium phosphate augmentation, and pedicle screws instrumentation at L4—L5 at an outside institution, with clinical improvement. Three years after the initial surgery, she experienced recurrent low back pain and was diagnosed with pseudoarthrosis and hardware failure (fractured left L5 pedicle screw) that prompted a revision surgery with fractured hardware removal and extension of the instrumented fusion to S1, bilaterally. At the time of the revision surgery, rhBMP-2 was used "off-label" to promote a successful postoperative posterolateral arthrodesis. Both initial and revision procedures were performed at the same hospital and by the same surgeon. Three years after the revision surgery, the patient started experiencing recurrent episodes of severe L5 and S1 left radiculopathy and medical management and lumbar steroid injections failed to reduce the severity of the symptoms. This is when we first saw the patient.

A clinical examination confirmed the presence of radicular signs and symptoms with no neurologic deficits or significant back pain. Lumbar radiographs and computed tomography (CT) scan were performed and revealed the presence of new broken hardware on the left side (fractured S1 pedicle screw) as well as significant heterotopic bone formation mainly involving the left L5—S1 lateral recess, leading to severe stenosis and nerve root compression (**Figures 1—3**).

Despite the findings of broken hardware, there were no signs of mechanical instability on a flexion—extension radiograph, and the CT documented the presence of a solid joint arthrodesis, especially on the right (**Figures 4**, **5**, and **6A** and **B**). Magnetic resonance imaging also was performed, which confirmed the diagnosis of

Key words
- Ectopic bone formation
- Heterotopic bone formation
- Minimally invasive surgery
- rhBMP-2

Abbreviations and Acronyms
CT: Computed tomography
MISS: Minimally invasive spine surgery
rhBMP-2: Recombinant human bone morphogenetic protein-2

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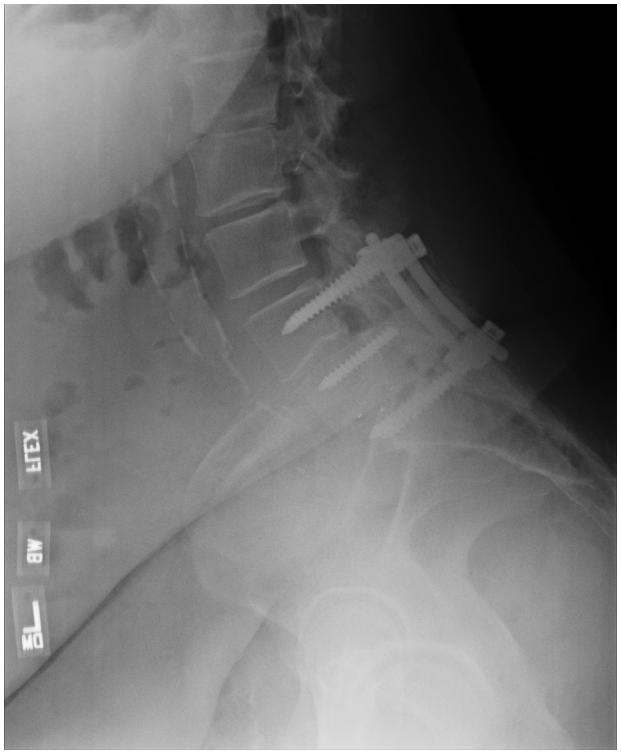

Figure 1. Lateral preoperative lumbar radiograph showing fractured hardware.

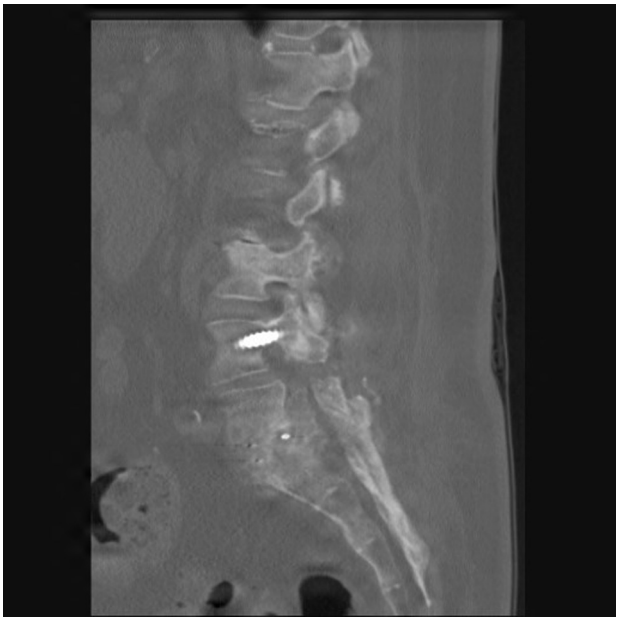

Figure 2. Preoperative sagittal computed tomography scan showing heterotopic bone formation within the left L5–S1 lateral recess.

severe lateral recess stenosis at L5–S1 due to heterotopic bone formation (**Figure 7**).

Clinically, she had only minimal axial low back pain and no radiologic signs of mechanical instability, with most of the symptoms being radicular in nature. She had severe obesity, with a BMI of 40.10, and a history of hyperlipidemia, hypertension, and coronary artery disease. After discussing the surgical options with the patient, we elected to explore the fusion, remove the broken instrumentation, and decompress the involved nerve roots by removing the heterotopic bone formation using a minimally invasive tubular approach. Open surgery with complete revision of instrumentation and redo-arthrodesis also was discussed. In light of the absence of significant low back pain, the predominance of radicular symptoms, the absence of mechanical instability, and the presence of bilateral facet arthrodesis, as well as the history of previous lumbar surgeries and associated medical comorbidities, we felt a minimally invasive approach was an appropriate option to be selected in this case, and the patient concurred with this informed decision.

The patient was positioned on a standard prone position on a Wilson frame. The METRx tubular system (Medtronic, Minneapolis, Minnesota, USA) and anteroposterior and lateral intraoperative fluoroscopy guidance were used. A 3-cm incision was made over the anteroposterior radiographic projection of the L5–S1 broken screws on the left side, and the fascia was opened approximately 3–4 cm lateral to the midline, as guided by the radiographs. An Xtube expandable tubular retractor (Medtronic) was used to expose the L5–S1 hardware. The rod was exposed and any surrounding newly formed bone was carefully drilled away. The rod was then cut using a carbide drill bit and

Figure 3. Preoperative axial computed tomography scan showing heterotopic bone formation within the left L5–S1 lateral recess.

Figure 4. Preoperative axial computed tomography scan showing heterotopic bone formation within the left L5–S1 lateral recess as well as facet arthrodesis on right.

removed. The lower broken screw (S1) was then used as landmark to start our microscopic dissection (Figure 8).

The borders of the previous laminectomy were the identified, epidural scarring removed, and the dura and nerve roots displaced by the presence of the heterotopic bone formation

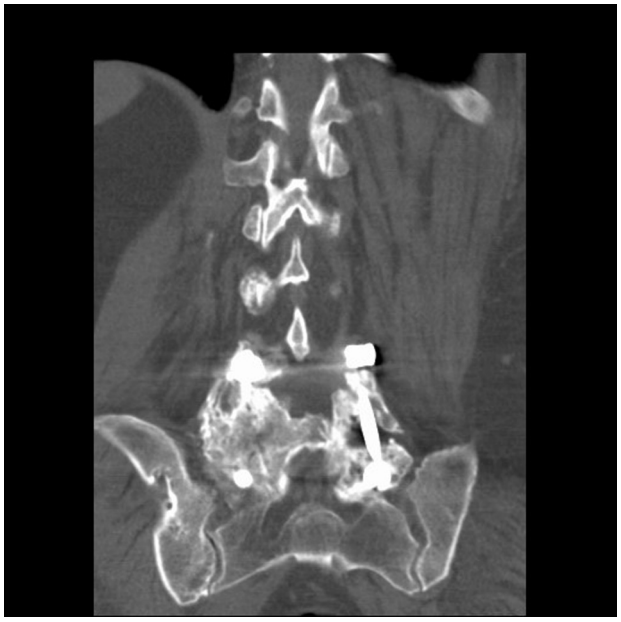

Figure 5. Preoperative coronal computed tomography scan showing facet arthrodesis on right.

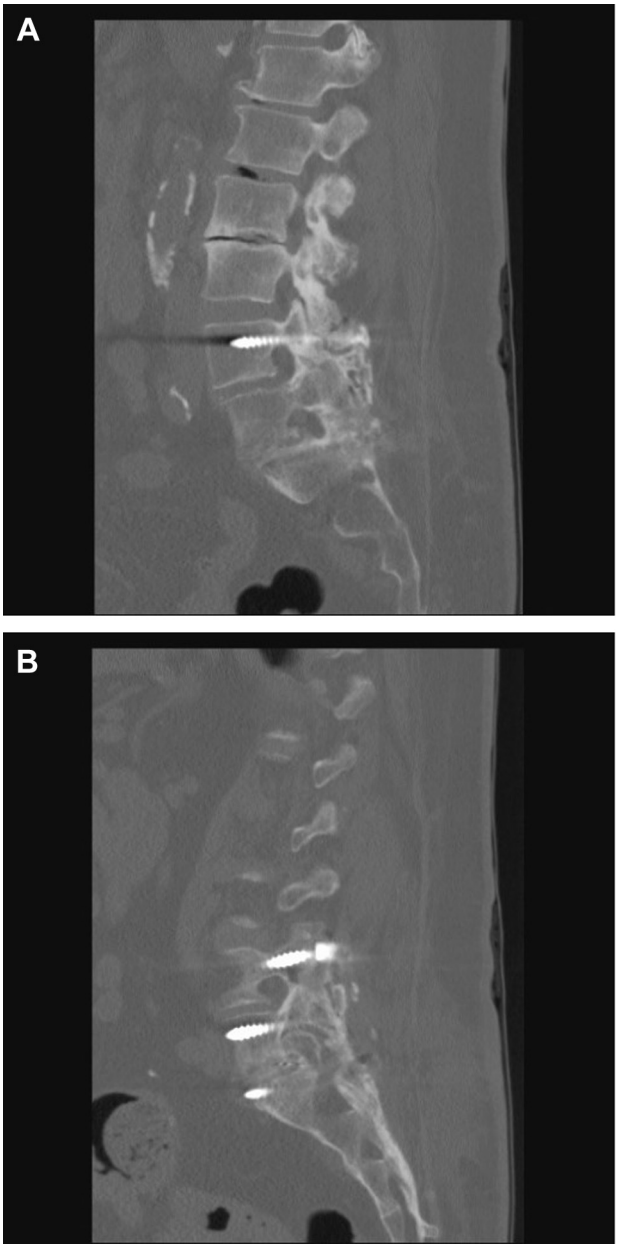

Figure 6. (**A**) Preoperative sagittal computed tomography scan showing facet arthrodesis on right. (**B**) Preoperative sagittal computed tomography scan showing facet arthrodesis on left as well as severe foraminal stenosis due to heterotopic bone formation.

identified. The traversing nerve root was decompressed below the area involved by the ectopic bone formation, and the exiting nerve root was isolated and decompressed above it (Figures 9–11). Once the nerve roots and the lateral dura were identified, the heterotopic bone was removed by gentle drilling and use of Kerrison rongeurs until complete decompression was achieved (Figure 12).

After hemostasis was achieved and any dural leak ruled out, the remaining loosened hardware (S1 screw head that was kept in

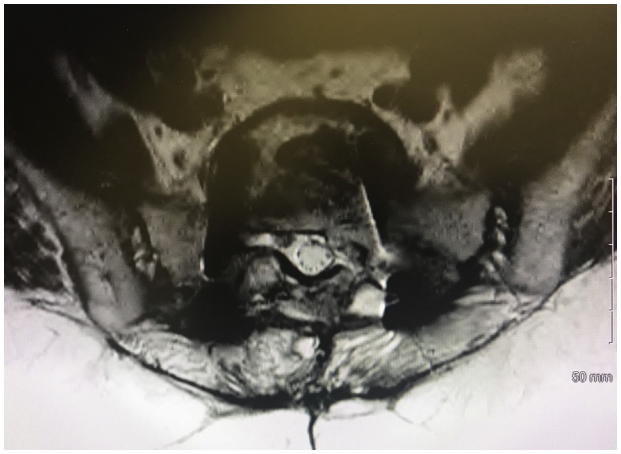

Figure 7. Preoperative axial T2-weight magnetic resonance imaging showing heterotopic bone formation involving the L5—S1 lateral recess with severe stenosis.

place as landmark) was removed. The Xtube was removed and the fascia and wound closed using standard techniques. The procedure lasted approximately 90 minutes, and blood loss was minimal (<50 cc). In light of the absence of significant low back or radiologic signs of mechanical instability, the documented solid arthrodesis on the contralateral side, as well as the presence of retained fractured screws within the L5 and S1 pedicles, we elected not to place supplemental instrumentation.

A postoperative CT confirmed good neural decompression (**Figure 13**), and the patient was discharged home on postoperative day 1. The radicular symptoms resolved and no recurrent symptoms or complications were recorded at a 1-, 3-, and 6-month follow-up. At the most recent clinical follow-up (7 years after the minimally invasive surgery), the patient still remains pain free without any significant recurrent radicular symptoms or axial back pain and has been able to resume recreational sport activities. In light of the ongoing coronavirus disease 2019 (COVID-19) pandemic and following institutional protocols and policies while dealing with this event, long-term follow-up radiologic examinations were not obtained.

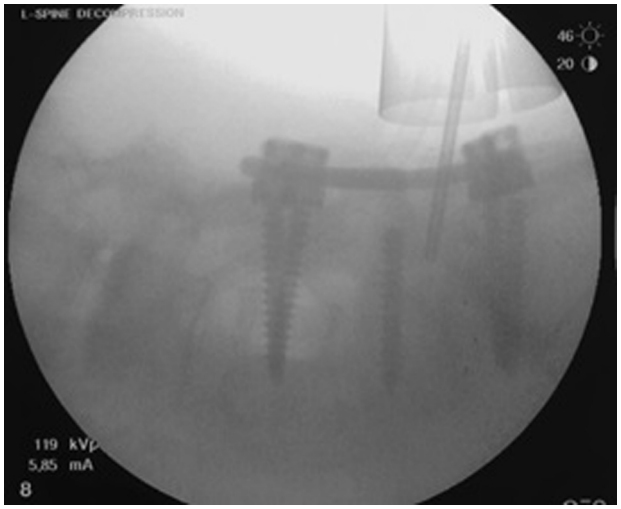

Figure 8. Lateral radiograph after minimally invasive removal of titanium rod. S1 screw head left in place as landmark. Suction cannula was placed on the heterotopic bone to confirm its localization.

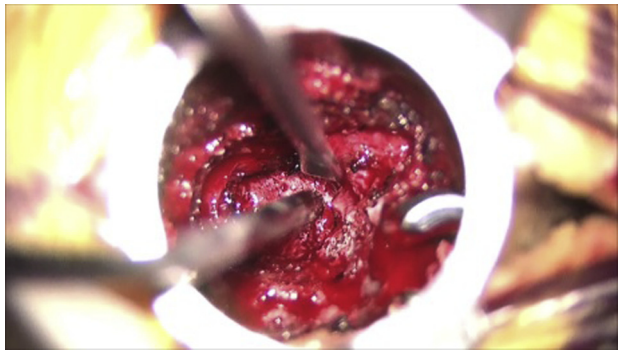

Figure 9. Heterotopic bone formation (under the tip of the suction cannula) and traversing nerve root (gently mobilized by nerve root retractor).

DISCUSSION

Heterotopic (or ectopic) bone formation is a known complication associated with the use of rhBMP-2 during spinal fusion surgery,[19-21] and due to its possible compressive nature, this condition may lead to recurrent or worsening symptoms in the postoperative period. Depending on the size, symptoms, and location of the ectopic bone formation, surgical treatment may be needed, posing sometimes a technical challenge especially in patients who already have undergone revision surgery or who carry multiple medical comorbidities. In such patients, the use of minimally invasive decompressive techniques may be beneficial in tailoring the treatment to the symptomatic condition, while minimizing possible adverse effects sometimes associated with open revision surgery.

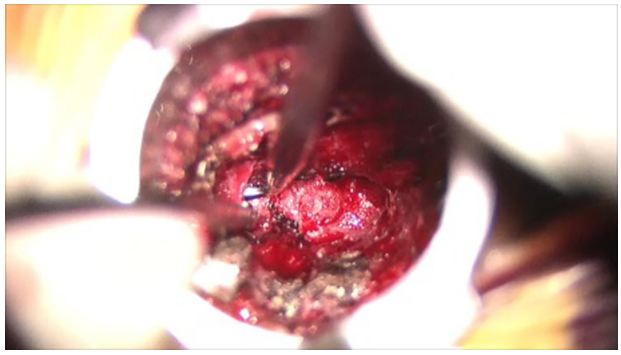

Figure 10. Exiting nerve root (back angled curette) just above heterotopic bone formation.

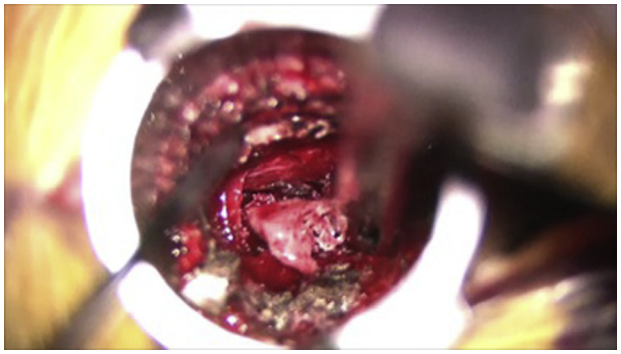

Figure 11. Heterotopic bone formation removed with Kerrison rongeurs.

Minimally invasive spine surgery (MISS) techniques are nowadays used by many surgeons as an alternative or adjunct to open spine surgery in the treatment of various degenerative pathologies involving the cervical, thoracic, and lumbosacral spine,[22-25] as well as trauma- and tumor-related conditions.[26,27] Centers and surgeons familiar with these novel techniques also have expanded the use and indications of these lesser invasive techniques to deformity correction surgery and revision surgery as well.[28-30]

In our practice we too have expanded the use of MISS techniques, as we live in a community in which many patients are seen in consultation in their seventh and eighth decade of life. Spine surgery in elderly patients may be at time challenging, as multiple comorbidities, osteopenia/osteoporosis, as well as history of multiple previous spine surgeries need to be carefully considered while selecting the most effective and safe surgical (or nonsurgical) approach. Revision spine surgery also may prove challenging, as several factors may contribute to render some of these procedures more complicated than others.

Lack or paucity of information related to previous surgeries, diagnostic limitation of radiologic studies available (e.g., patients with spinal cord stimulators or non-magnetic resonance imaging—compatible implanted devices), and postsurgical anatomical changes and fibrosis, do in fact play an important role during the preoperative and operative decision-making process in such patients. Anatomical landmarks may be difficult to recognize during revision surgery, as postoperative changes, associated deformity, and epidural fibrosis may all render the surgeon's evaluation of the operative field at times challenging. This is especially true in MISS, where the anatomical exposure is usually limited to the surgical area of interest, and in such cases an optimal use of preoperative and intraoperative imaging plays a very important role in facilitating the surgeon during the various steps of the selected approach. MISS offer many benefits in this cohort of patients (elderly, revision surgery, multiple comorbidities), as limited tissue dissection, minimal blood loss, shorter surgery time, faster and easier mobilization, and lesser and shorter need for postoperative narcotics are all in favor of the use of such techniques when deemed feasible and appropriate.

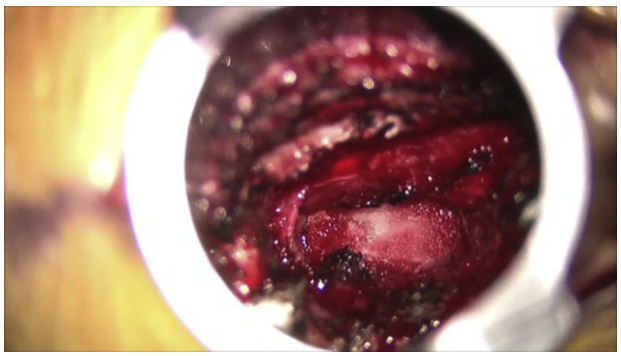

Figure 12. Final intraoperative view of decompressed dura and nerve roots.

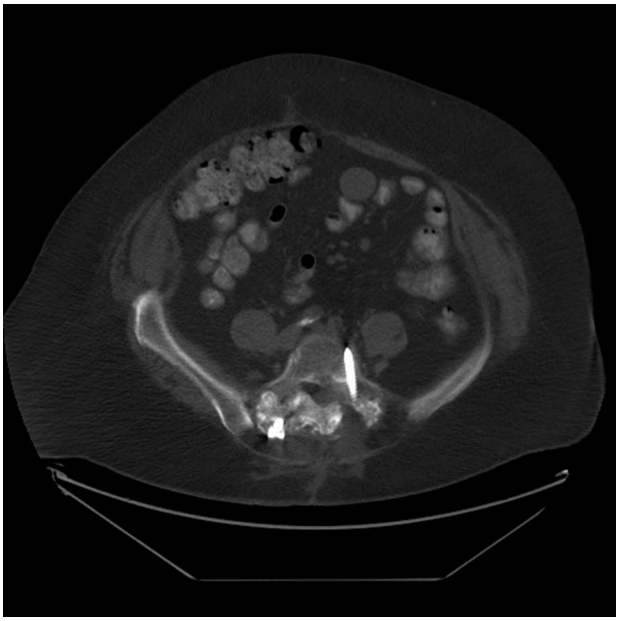

Figure 13. Postoperative computed tomography scan showing good decompression.

In the presented case, it is unclear when the hardware failed/refractured, as the patient did not complain of significant low back pain at the time of our initial evaluation. It is indeed possible that the hardware failure happened before the arthrodesis was complete and solid and before the ectopic bone formation became symptomatic. Also, we were unable to directly confirm what dose of rhBMP-2 was used at the time of the revision surgery; therefore, we cannot comment on this specific issue as a cofactor for the onset of the heterotopic bone formation. Review of previous operative reports revealed that the initial posterolateral fusion was performed with the use of iliac crest and local bone autograft as well as calcium phosphate allograft augmentation. In light of the recurrence of radicular symptoms and evidence of fractured hardware at L5, the patient underwent a revision surgery with "exploration of fusion, removal of L5 instrumentation, bilateral transverse process fusion with local

bone graft and 'off-label' use of BMP," as well as "left transforaminal lumbar interbody fusion at L5—S1 with polyetheretherketone allograft and L4—S1 bilateral pedicle screw instrumentation." According to the operative report, there was no presence of heterotopic bone formation at L5—S1 at that time of the revision surgery, and the BMP sponges were "morcellized and placed in smaller pieces, combined with the local bone graft, into both posterolateral gutters." The amount of BMP used was not recorded. The colleague also commented that the "fixation of the L5 screw on the left side was extremely good and had sustained a fatigue fracture at its base, indicating a solid anchorage in the L5 pedicle." Therefore, such fractured screw was not retrieved at that time.

In light of the documented absence of heterotopic bone formation at the time of the revision surgery, the addition of calcium phosphonate to promote the arthrodesis during the initial lumbar fusion does not appear to have played a role in the genesis of the ectopic bone formation in this case, and it appears that this condition is to be associated with the use of rhBMP-2, as previously described.[11]

In the presented case, an open procedure of revision/decompression/lysis of adhesions could have certainly been used, but in light of the patient's expectations, the absence of significant low back pain and radiologic instability, as well as the presence of numerous medical comorbidities, we chose a minimally invasive approach, which proved to be successful in providing long-lasting relief of the preoperative symptoms. Although the treatment of heterotopic bone formation associated with the use of rhBMP-2 may be challenging, the use of a minimally invasive tubular decompression may facilitate a tailored and safe approach to this condition and should be kept in the armamentarium of spine surgeons as one of the many valid techniques to be considered and discussed with these patients.

CONCLUSIONS

In the presented case, we found the use of minimally invasive techniques to be of benefit for the removal of heterotopic bone formation following lumbar spine fusion with rhBMP-2. This approach remains consistent with the concept that minimally invasive surgery should not equal lesser effective surgery and that final recommendation on the technique to be adopted should be tailored on a case-by-case scenario, keeping in mind patient's expectations, safety issues, and goals to be achieved.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Fabio Roberti: Conceptualization, Methodology, Writing - original draft, Validation, Writing - review & editing. **Katie Arsenault:** Data curation.

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