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Case Reports

Vertebral osteolysis after posterior interbody lumbar fusion with recombinant human bone morphogenetic protein 2: A report of five cases

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Abstract

BACKGROUND: Recombinant human bone morphogenetic protein 2 (rh-BMP-2) is frequently used in an off-label fashion. Its application for posterior interbody fusion appears intuitive because its use obviates the need for iliac crest bone graft and shows higher fusion rates than with the use of local autologous bone graft. To date, there is no report of adverse outcomes with such use of rh-BMP-2.

PURPOSE: To draw attention to this unusual complication of posterior interbody lumbar fusion and to review the relevant literature.

STUDY DESIGN: Clinical report of five cases of vertebral osteolysis that developed postoperatively from lumbar transforaminal interbody fusion of the L5/S1 motion segment using cages and rh-BMP-2.

METHODS: Sixty-eight patients underwent transforaminal lumbar interbody fusion for spondylolisthesis or degenerative disc disease with discogenic back pain. Five of these 68 patients developed vertebral osteolysis within 4 months from their surgery. Their clinical presentation and radiographic findings are presented in this case series.

RESULTS: Each one of these five patients had uneventful surgery and postoperative recovery. Their back and leg pain improved in the immediate postoperative period. However, each patient reported worsening back pain with variable radicular pain as early as 4 weeks and as late as 3 months after the index procedure. Diagnostic workup revealed evidence of vertebral osteolysis typically involving the L5 vertebral body. In all five patients, osteolytic defects filled in spontaneously, and symptoms typically resolved within an additional 3 months of nonoperative care.

CONCLUSIONS: Vertebral osteolysis can occur with the use of rh-BMP-2 in posterior lumbar interbody fusions. Violation of the end plate during decortication may be a contributing factor. Symptoms often resolve spontaneously.

Keywords: Bone morphogenetic protein; Interbody fusion; Bone resorption

Introduction

Recombinant human bone morphogenetic protein 2 (rh-BMP-2) supersedes the use of iliac crest autograft bone because it induces the body to grow its own bone [1–4]. In 2000, the Food and Drug Administration approved the use of rh-BMP-2 for anterior interbody fusion when used in conjunction with the Lumbar Tapered Fusion Device; LT cage (Sofamor Danek) [5]. Since then, clinical studies have indicated equivalent interbody fusion rates between rh-BMP-2 and iliac crest bone graft [4,6]. As a result, rh-BMP-2 has found a number of ''off-label'' applications, one of which includes its use for posterior interbody lumbar fusions [7].

The BMPs belong to the transforming growth factor super family [8]. They are involved in development and differentiation of skeletal tissues, as well as the brain, spinal cord, liver, kidneys, skeletal muscle, eyes, and epithelium [3,9]. Physiologic concentrations of BMP-2 are quite low. Although sufficient for normal fracture healing, only 0.002 mg of BMP-2 can be extracted from 1 kg of

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Table 1

#	Sex	Age	Preoperative diagnosis	Procedure	Previous surgery
1	F	50	L5/S1 adjacent level disease	L3–SI TLIF	L3–L5 PSF, L4/5 PLIF
2	M	50	L5/S1 Spondylolisthesis	L5/S1 TLIF	
3	M	50	L5/S1 Spondylosis	L5/S1 TLIF	
4	F	50	L5/S1 Spondylosis	L5/S1 TLIF	
5	M	51	L5/S1 Spondyolisthesis	L5/S1 TLIF	

TLIF = transforaminal lumbar interbody fusion; PLIF = posterior lumbar interbody fusion.

normal powdered bone [10]. To achieve demonstrable enhancement of fracture healing, much higher BMP-2 concentrations ranging from 0.01 mg/mL in rodents to 1.5 mg/mL in nonhuman primate models are necessary. The commercially available form of rh-BMP-2, Infuse, contains 1.5 mg/mL of reconstituted collagen sponge [9,11]. More recently, even higher numbers have been suggested for posterolateral fusions. Boden et al. [12] found successful posterolateral lumbar spinal fusion with or without the use of internal fixation when rh-BMP-2 was delivered at a dose of 20 mg per side. It has been suggested that only these "…supraphysiologic concentrations…" are in fact capable of inducing the desired clinical effect by overcoming the tight regulation of BMP and its inhibitors [8].

Reports on complications related to the application of rh-BMP-2 in posterior lumbar interbody fusions are now emerging. Therefore, we describe five cases of vertebral osteolysis after transforaminal interbody fusion with rh-BMP-2 (Infuse; Medtronic Sofamor Danek) used in conjunction with local bone graft and a single interbody fusion cage.

Materials and methods

Study design and patients

From November 2004 to March 2006, 68 patients consisting of 43 females and 25 males underwent minimally invasive lumbar fusions (TLIF) through 1-inch paraspinal incisions using the Wiltse approach. Surgical indications included spondylolisthesis (48 patients), degenerative disc disease resulting in discogenic low back pain (18 patients), recurrent herniated nucleus pulposus (1 patient), and adjacent level disease (1 patient). The procedures were performed by the senior author. Five of the 68 patients showed signs of vertebral osteolysis postoperatively. We retrospectively analyzed the operative reports, X-ray films, and medical records of these 5 consecutive patients.

Instrumentation

Sixty-three patients had bilateral posterior pedicle screw-rod instrumentation with Pathfinder titanium implants (Abbott Spine). An additional five patients had unilateral posterior pedicle screw-rod instrumentation with Pathfinder titanium implants (Abbott Spine) and with ipsilateral percutaneous placement of a translaminar facet screws (AO Synthes 4.0-and 4.5-mm cannulated partially threaded screws). Two types of interbody fusion cages were used in conjunction with local bone graft and recombinant bone morphogenic protein 2 (Infuse): Traxis cage (Abbott Spine) made from polyetheretherketone (PEEK) and Saber cage (Depuy Spine) made from carbon fiber.

Surgical technique

Bilateral or unilateral Wiltse-type muscle-splitting approaches were used to perform the TLIF and to place the pedicle screws. In general, the TLIF was performed through the side on which the patients' radicular symptoms were more severe. This involved removal of the entire facet joint, discectomy, and end plate preparation. Before inserting the interbody fusion cage, approximately 1.5 to 2 mL of morselized local bone graft and one Infuse collagen sponge were placed into the interspace. This was followed by insertion of one interbody fusion cage, which was filled with an additional Infuse collagen sponge and local bone graft. Cage position was checked under biplanar fluoroscopy to ensure anterior position across the midline. Then, Gel foam was injected into the disc interspace and the facetectomy site to minimize postoperative blood loss and leakage of rh-BMP-2 into the neuroforamen. It was removed by suction before wound closure.

In this entire series of 68 patients, only small and medium kits with 2 and 4 absorbable collagen sponges (ACSs; 1" x 2") were used. These kits come with a vial 4.9 mg of rh-BMP-2. According to the manufacturer, only 4.2 mg of the 4.9 mg of rh-BMP-2 is applied to the ACS after reconstitution.

Postoperative care

Postoperatively, mobilization began as soon as tolerated by the patient either immediately postoperatively or on postoperative day 1 with formal gait training by the physical therapist. Most patients were discharged to their home on postoperative day 1. None of the patients received any lumbar supports or braces. Low-impact exercising, walking to tolerance, and swimming were encouraged immediately on the patients' discharge to home. Heavy lifting and any other type of strenuous activity were discouraged for at least 6 weeks postoperatively. Patients were otherwise permitted to return to work as soon as they could tolerate it. All patients were counseled to avoid over-the-counter