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Case Report

Histopathologic inflammatory response induced by recombinant bone morphogenetic protein-2 causing radiculopathy after transforaminal lumbar interbody fusion

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Abstract

BACKGROUND CONTEXT: A significant increase in off-label use of recombinant human bone morphogenic protein-2 (rhBMP-2) in posterior lumbar interbody fusion techniques has been seen in the spine community. Numerous reports have demonstrated complications with use of this proinflammatory agent; however, the in vivo response caused by rhBMP-2 has not been characterized on a cellular level.

PURPOSE: To report the case of lumbar radiculopathy and the associated histopathologic findings stemming from the inflammatory response to rhBMP-2 used in transforaminal lumbar interbody fusion (TLIF) surgery.

STUDY DESIGN/SETTING: Case report.

PATIENT SAMPLE: Single patient case report of rhBMP-2 off-label use causing an inflammatory response that resulted in radiculopathy after TLIF surgery.

OUTCOMES MEASURES: Clinical, radiologic, and histopathologic evidence was used to determine outcomes in this report.

METHODS: A 27-year-old male presented with low back pain and radiculopathy and radiographic evidence of degenerative disc disease and foraminal stenosis. Four weeks after L4−L5 TLIF surgery augmented with rhBMP-2, the patient developed right-sided lower extremity radiculopathy. Magnetic resonance imaging of the lumbar spine demonstrated bilateral fluid collections with the larger right-sided mass compressing the right L4 nerve root.

RESULTS: Surgical decompression of this mass resulted in resolution of his right-sided radicular symptoms. Histologic analysis of the surgical pathology demonstrated diffuse osteoid and woven bone amidst a fibrovascular stroma densely populated by lymphocytes and eosinophils.

CONCLUSIONS: Off-label rhBMP-2 use in posterior interbody fusion techniques can lead to complications. This case serves to identify potential hazards of this growth factor and highlight areas for further study to better understand its in vivo behavior.

Keywords: BMP; Inflammatory; Transforaminal lumbar interbody fusion; Radiculopathy

Introduction

Although the use of recombinant human bone morphogenetic protein-2 (rhBMP-2) has only been Food and Drug Administration-approved for anterior lumbar interbody fusion, there has been widespread use in off-label augmentation of spine fusion in anterior cervical and posterior lumbar procedures [1−12]. However, complications attributed to the use of rhBMP-2 have raised prudent questions involving its mechanism of action in vivo and possible untoward effects to patients. Examples of adverse events

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when rhBMP-2 has been used in posterior lumbar interbody fusion include local bone resorption [10,13,14], postoperative radiculitis [3,4,14,15], and ectopic bone formation [8,14–17].

In vitro studies suggest that the mechanism of action by which rhBMP-2 augments spine fusion involves a notable host inflammatory response to initiate the bone healing cascade. The mechanism of osteoinduction via bone morphogenic protein (BMP) has been associated with the in vitro release of local cytokines, such as Tumor necrosis factor-α, interleukin-1α, interleukin-1β, and interleukin-6 [18,19]. Because the current doses of rhBMP-2 used in patients are 1 millionfold greater than concentrations seen physiologically in humans [20], it stands to reason that a potent local inflammatory response occurs in vivo. However, this mechanism of action has not been proven in a clinical setting.

We report the case of a 27-year-old male who developed right- and left-sided lumbar radiculopathy after the off-label use of rhBMP-2 following L4–L5 transforaminal lumbar interbody fusion (TLIF). Magnetic resonance imaging (MRI) 3 months postoperatively demonstrated bilateral fluid-filled masses compressing the traversing nerve roots. To our knowledge, this is the first case report with the use of rhBMP-2 in spine fusion that includes postoperative histopathologic analysis and MRI that intimates its in vivo mechanism of action. The patient was informed of and gave consent to allow this case to be submitted for publication.

Case report

A 27-year-old, otherwise healthy, male carpenter was referred to our institution for consultation regarding progressive low back pain that radiated into his left lower extremity. There were no associated traumatic or work-related incidents. The pain was exacerbated by activity. Conservative therapies—including ice, anti-inflammatory and narcotic pain medication, ultrasound, physical therapy, and chiropractic adjustment—were pursued for over a year without obtaining any relief. The patient reported smoking 1.5 packages of cigarettes per day. Despite suggesting extensive smoking cessation measures including outpatient therapy and medication, the patient was unsuccessful at quitting.

Physical examination revealed an obese male (body mass index=38.3), slight scoliosis of the lumbar spine and a normal gait. Neurologic examination demonstrated 5 of 5 strength throughout the bilateral lower extremity myotomes and intact light touch and pinprick sensation throughout the L2–S1 dermatomes. Patellar tendon and Achilles tendon reflexes were normal. A straight leg raise was positive on the left as was a Lasègue maneuver and a contralateral straight leg raise.

Radiographs of the lumbar spine demonstrated rotatory subluxation and levoscoliosis at L4–L5, mild levoscoliosis at L3–L4, and mild degenerative disc disease at L4–L5 and L5–S1 (Fig. 1, left). Magnetic resonance imaging showed degenerative disc disease at L4–L5 with a central disc herniation and subarticular stenosis and degenerative disc disease at L5–S1 with a bulging disc (Fig. 1, right). The MRI did not demonstrate any scoliosis on coronal imaging indicating dynamic instability.

Surgical technique

We discussed with the patient potential treatment options. Conservative treatment measures were recommended, and further physical therapy was offered. Additional smoking

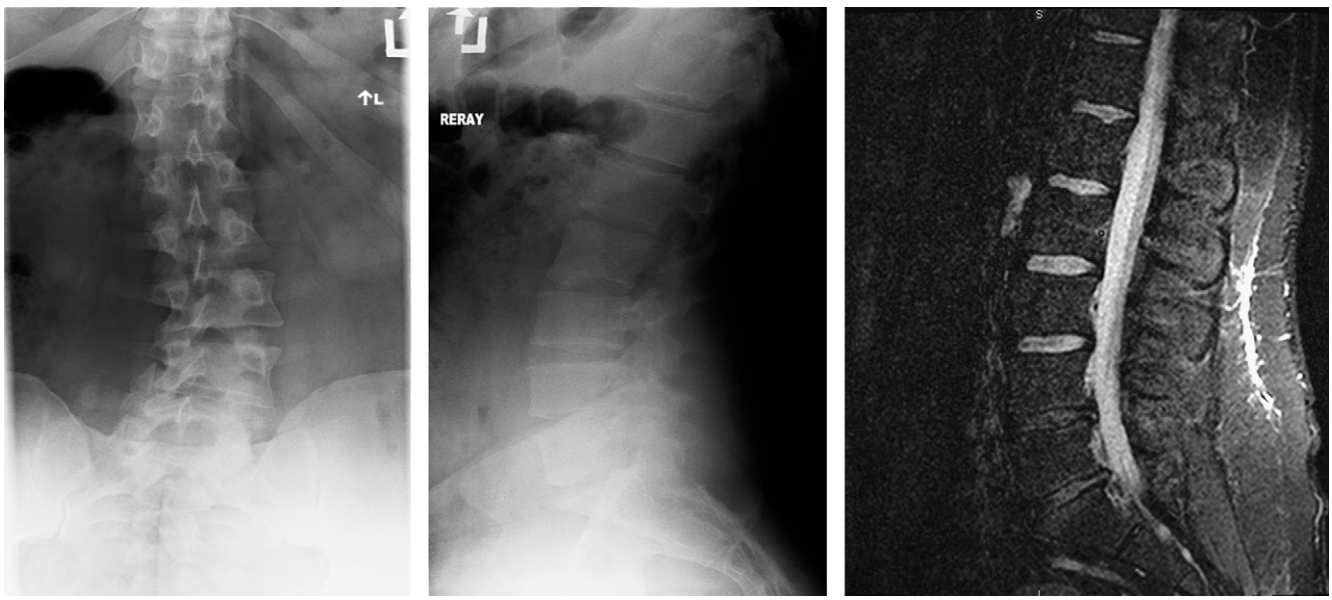

Fig. 1. (Left and Center) Anteroposterior and lateral radiographs of the lumbar spine demonstrate mild L4–L5, L5–S1 disc-space narrowing and lumbar levoscoliosis. (Right) Sagittal proton density/T2-weighted image of the lumbar spine in the midsagittal plane demonstrating degenerative disc disease.