

Case Report

# Neuroforaminal chondrocyte metaplasia and clustering associated with recombinant bone morphogenetic protein-2 usage in transforaminal lumbar interbody fusion

Thomas J. Christensen, MD<sup>a</sup>, Prokopis Annis, MD<sup>a</sup>, Justin B. Hohl, MD<sup>a</sup>,  
Alpesh A. Patel, MD, FACS<sup>b,\*</sup>

<sup>a</sup>Department of Orthopaedics, University of Utah, 590 Wakara Way, Salt Lake City, UT 84108, USA

<sup>b</sup>Department of Orthopaedic Surgery, Northwestern University School of Medicine, 676 N St Clair St, Suite 1350, Chicago, IL 60611, USA

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**Abstract**

**BACKGROUND CONTEXT:** Recombinant human bone morphogenetic protein-2 (rhBMP-2) is commonly used to augment posterior and interbody spinal fusion techniques and has many reported side effects. Neuroforaminal heterotopic ossification (HO) is a known cause of postoperative leg pain, but the pathohistologic composition of this material is not well understood.

**PURPOSE:** The purpose of this article was to report the histologic composition of a case of HO and lumbar radiculopathy after transforaminal lumbar interbody fusion with rhBMP-2.

**STUDY DESIGN/SETTING:** This is a case report.

**PATIENT SAMPLE:** This is a single patient case report.

**OUTCOME MEASURES:** The outcomes considered were physician-recorded clinical, physiological, and functional measures.

**METHODS:** A retrospective review of a single patient was performed. Clinical, radiographic, and pathologic specimens were reviewed and are reported.

**RESULTS:** A 69-year-old woman presented with low back pain and right leg radicular pain associated with L4–L5 stenosis and a recurrent facet cyst. After attempted nonsurgical care, she underwent an L4–L5 revision decompression with interbody and posterolateral fusions including off-label rhBMP-2. Postoperatively, her symptoms resolved for approximately 7 months but then returned in association with right L4–L5 foraminal HO. The ectopic tissue was notably larger than suggested by preoperative computed tomographic scan. It was decompressed, which then improved her symptoms. Histologic examination of the specimen revealed three discrete tissue types: a nonspecific fibrovascular stroma; immature osteoid and woven bone; and chondrocyte metaplasia with chondrocyte clustering.

**CONCLUSIONS:** Neuroforaminal HO formation is a reported side effect associated with the off-label use of rhBMP-2 for posterior lumbar interbody fusion. The mechanism of formation and the composition of this material are not well understood but may involve a chondrocyte differentiation pathway. © 2014 Elsevier Inc. All rights reserved.

**Keywords:**

BMP-2; TLIF; Complication; Heterotopic bone; Radiculopathy; Chondrocyte metaplasia

FDA device/drug status: Not approved for this indication (rhBMP-2 [Infuse, Medtronic, Memphis, TN]).

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The disclosure key can be found on the Table of Contents and at [www.TheSpineJournalOnline.com](http://www.TheSpineJournalOnline.com).

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\* Corresponding author. Department of Orthopaedic Surgery, Northwestern University Feinberg School of Medicine, 676 North St Clair St, Suite 1350, Chicago, IL 60301, USA. Tel.: (312) 695-5902.

## Introduction

Recombinant human bone morphogenetic protein-2 (rhBMP-2; Medtronic, Memphis, TN, USA) is currently FDA approved for anterior lumbar interbody fusions in a threaded cage [1]. Over the last decade, the “off-label” usage of rhBMP-2 to achieve osseous healing has increased dramatically by many different surgical subspecialties, particularly spinal surgery for transforaminal lumbar interbody fusion, posterior lumbar interbody fusion, and posterolateral lumbar fusions [2–8]. Despite improved fusion rates compared with traditional bone grafting techniques, rhBMP-2 has a significant side effect profile including, but not limited to, heterotopic bone formation, bone resorption/osteolysis, radiculopathy, and wound complications [9–18]. The mechanism of these side effects is poorly understood as are the potential effect on the surrounding tissues. Prior reports have implicated a local inflammatory response associated with the release of tumor necrosis factor- $\alpha$ , interleukin-1 $\alpha$ , interleukin-1 $\beta$ , and interleukin-6, which may be associated with supraphysiological BMP-2 doses over a million-fold greater than physiological concentrations [19,20]. Only one case has, to date, reported histologic findings in the setting of rhBMP-2 [20]. Muchow et al. reported diffuse osteoid, woven bone, and a fibrovascular stroma populated by lymphocytes and eosinophils. We herein report the first case of rhBMP-2-associated heterotopic ossification (HO) with chondrocyte metaplasia and clustering.

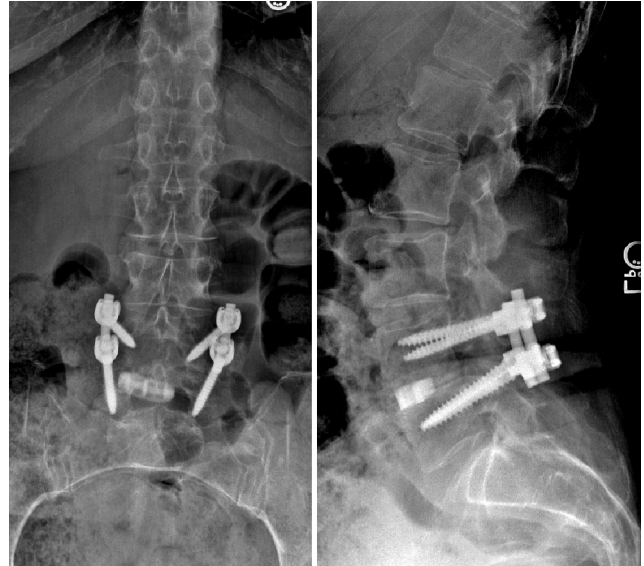


Fig. 1. Upright postero-anterior (Left) and lateral (Right) radiographs of the lumbar spine performed 7 months after surgery demonstrate no instrumentation or interbody complications and suggest stable fusion.

## Case report

This case report was approved by our institutional review board. The patient is an otherwise healthy 69-year-old retired woman with a history of a left-sided L4–L5 foraminotomy 22 years prior who presented with 18 months of

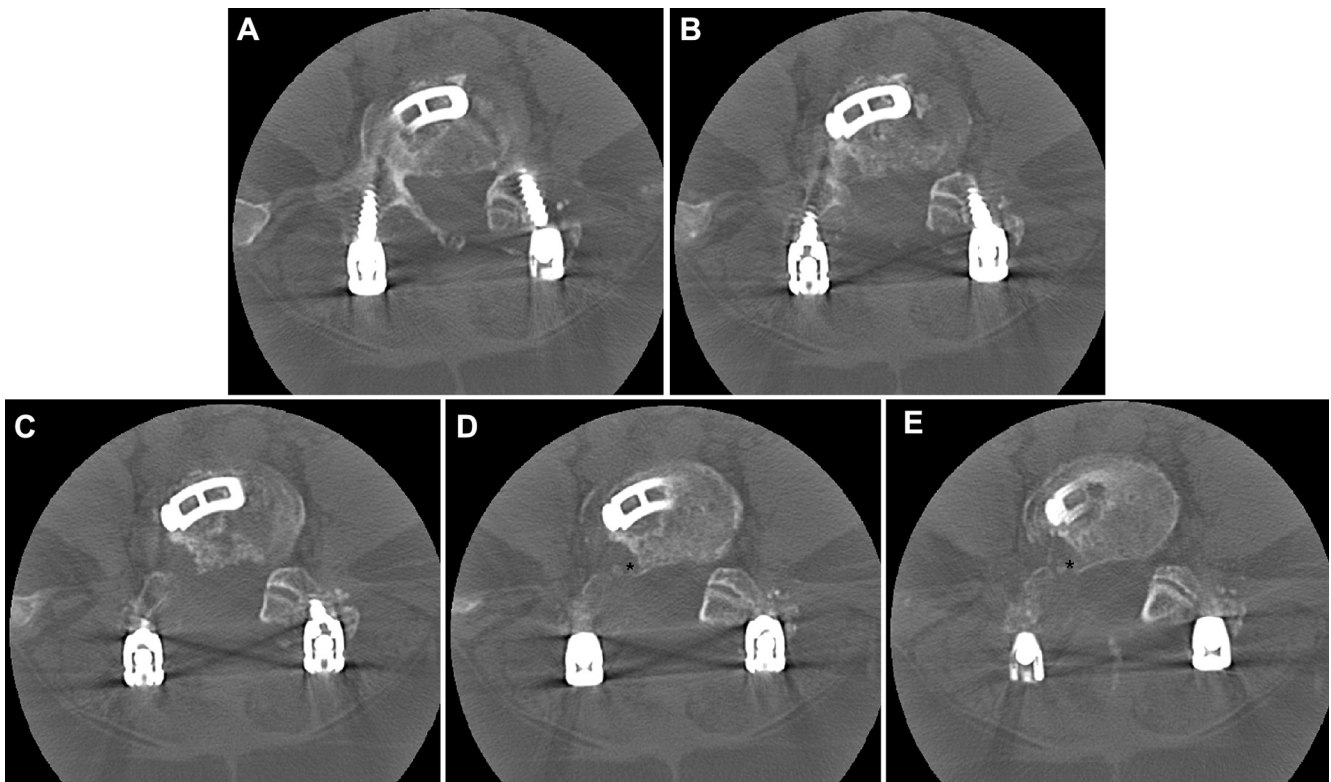


Fig. 2. Axial computed tomography scan images through the L4–L5 level demonstrating heterotopic ossification in the right neuroforamina moving cranially from the L5 pedicle (A–E). Asterisks denote bone/tissue formation near prior annulotomy that is compressing the exiting nerve root.

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