Tumor extravasation following a cement augmentation procedure for vertebral compression fracture in metastatic spinal disease

Report of 2 cases

JUAN PABLO CRUZ, M.D., ARJUN SAHGAL, M.D., CARI WHYNE, PH.D., MICHAEL G. FEHLINGS, M.D., PH.D., F.R.C.S.C., AND ROGER SMITH, M.D.

1Department of Medical Imaging, Toronto Western Hospital, University of Toronto; 2Department of Radiation Oncology, Princess Margaret Hospital, University of Toronto; 3Department of Radiation Oncology, Sunnybrook Health Sciences Center, University of Toronto; 4Holland Musculoskeletal Research Program, Sunnybrook Research Institute, Department of Surgery, IBBME and IMS, University of Toronto; and 5Department of Neurosurgery, Toronto Western Hospital, University of Toronto, Ontario, Canada

Balloon kyphoplasty (BKP) has been proven to be safe and effective in the management of pathological vertebral compression fracture (VCF) due to metastatic spinal disease. The most common serious complications related to BKP include cement extravasation and new fractures at adjacent levels. Although the potential for "tumor extravasation" has been discussed as a potential iatrogenic complication, it has yet to be confirmed. The authors report on 2 cases of tumor extravasation following BKP, which they base on an observed unusual rapid tumor spread pattern into the adjacent tissues. They postulate that by increasing the vertebral body internal pressure and disrupting the tissues during balloon inflation and cement application, a soft-tissue tumor can be forced beyond the vertebral bony boundaries through pathological cortical defects. This phenomenon can manifest radiologically as subligamentous spread and/or extension into venous sinusoids, resulting in epidural venous plexus involvement, with subsequent tumor migration into the adjacent vertebral segments. Accordingly, the authors advise caution in using BKP when significant epidural tumor is present. The complication they encountered has caused them to modify their preference such that they now first use radiosurgery and subsequently BKP to ensure the target is appropriately treated, and they are currently developing possible modifications of procedural technique to reduce the risk.

(https://thejns.org/doi/abs/10.3171/2014.4.SPINE13695)

KEY WORDS • balloon kyphoplasty • pathological vertebral compression fracture • tumor spread • tumor extravasation • metastatic disease • oncology

Abbreviations used in this paper: BKP = balloon kyphoplasty; SRS = stereotactic radiosurgery; VCF = vertebral compression fracture.

Vertebral compression fractures (VCFs) have been observed in up to 39% of patients with metastatic spine disease, and the risk depends on various tumor-related factors, spine-specific factors, and the radiation dose/approach used.4,5,19-21 In the treatment of VCFs, surgical management has shifted from open invasive surgery that can put the patient at moderately high risk of developing complications2 to minimally invasive percutaneous procedures.3,9,10,15 This change in practice has been driven largely by the intent of providing pain relief and vertebral stability while minimizing the interruption in patients’ overall oncological care. In addition, for certain patients the extent of metastatic disease in the spine can be so profound that instrumentation is not an option, and vertebral augmentation procedures have an invaluable role in palliating mechanical pain. At our institution, balloon kyphoplasty (BKP) has been a procedure commonly offered to patients with painful pathological VCFs.

Although BKP is a percutaneous technique, the potential for serious iatrogenic complications remains. The most significant adverse events tend to be cement extravasation (local and systemic) and the development of new fractures at adjacent levels. Although tumor spread, much like what we observe in the extravasation of cement, has been discussed theoretically, its occurrence has yet to be
confirmed in humans. In this report, we describe 2 cases of what we describe as post-BKP “tumor extravasation.” This paper seeks to alert clinicians to this potential complication of BKP in the setting of epidural tumor.

Case Reports

Case 1

A 73-year-old man with a history of non–small cell lung cancer was subsequently diagnosed with metastatic spinal disease after presenting with sudden unprovoked back pain. Spine MRI confirmed the presence of a pathological T-9 VCF with > 50% disc height loss, bulging of the anterior and posterior vertebral wall, and complete replacement of the vertebral body marrow with tumor. The tumor extended to both pedicles and the paravertebral soft tissues, and there was focal cortical disruption of the posterior wall (Tomita Classification Type 5 and a Spinal Instability Neoplastic Score of 9) (Fig. 1A). There was no involvement of the adjacent vertebral levels.

Because the pain was mechanical and refractory to analgesics (opioids and nonsteroidal antiinflammatory drugs) and because the patient was medically inoperable, a decision was made to proceed with BKP prior to radiotherapy. Using bipedicular 8-gauge kyphoplasty cannulas, 20 × 3–mm kyphoplasty balloons (Kyphon Balloons, Medtronic) were inflated to a maximum volume of 3 cm³. The balloons were placed anteriorly within the vertebral body prior to inflation to avoid increased posterior bulging of tumor and epidural cement extravasation. A total of 4.5 ml of bone cement (KyphX HV-R, Medtronic) was injected through each cannula without any venous extravasation (Fig. 1B).

Complete pain relief was achieved for approximately 2.5 weeks after the BKP procedure. At that point, the patient complained of recurrent back and bilateral flank pain. A 4-week follow-up MRI study obtained for radiotherapy planning suggested anterior subligamentous tumor spread to the immediate adjacent cranial and caudal vertebral levels (Fig. 1C), as well as extension into the paravertebral soft tissues beyond the boundaries of the T-9 vertebral body cortex. There was also involvement of the pedicles along the path of the BKP cannulas (Fig. 1D). Given the time course and unusual pattern of spread for adenocarcinoma metastases, we considered that this pattern of disease extension occurred secondary to the increased vertebral body internal pressure and disruption of the tissue during balloon inflation and cement application, such that soft-tissue tumor was forced beyond the vertebral bony boundaries through pathological cortical defects and subsequently involving the adjacent levels mainly via subligamentous spread.

The patient was subsequently treated with palliative conventional radiotherapy at a dose of 20 Gy given over 5 daily fractions. It was not felt that the target was amenable to stereotactic radiosurgery (SRS) because the target volume was no longer delineable with the precision required for SRS. One month later the patient was discharged to a palliative care unit where he finally died of his systemic disease.

Fig. 1. Case 1. Images obtained in a 75-year-old man who harbored a T-9 metastatic lesion from non–small cell lung cancer with rapid subligamentous spread to the adjacent levels after BKP. A: Sagittal T1-weighted MR image of thoracic spine revealing a metastatic T-9 VCF and complete replacement of the vertebral body marrow with tumor. B: Lateral plain radiograph acquired immediately after T-9 BKP showing no cement extravasation. C: Sagittal T1-weighted MR image 4 weeks after BKP demonstrating rapid tumor spread, predominantly anterior subligamentous spread to the adjacent levels. Note how the anterior longitudinal ligament bulges in the segment located between the points of bony attachment (arrows). D: Axial T1-weighted MR images through T-9 before and 4 weeks after BKP, showing the rapid disease progression, with soft-tissue extension beyond the boundaries of the bone cortex.
Case 2

A 48-year-old woman with a history of diffuse metastatic melanoma within the axial skeleton, liver, and lungs was ultimately diagnosed with multifocal spinal metastases. She presented with unprovoked acute back pain, and MRI confirmed a T-10 VCF. Her pain was refractory to opioids and nonsteroidal antiinflammatory drugs, and she had clear mechanical pain such that she could not ambulate or lie down flat. Full-spine MRI revealed complete replacement of the marrow of the T-10 vertebral body by tumor, focal cortical disruption of the posterior vertebral body wall, soft-tissue extension of tumor into the epidural space, VCF with < 50% vertebral body height loss, and bulging of the posterior wall into the spinal canal (Tomita Type 7 and a Spinal Instability Neoplastic Score of 8). In the rest of the spine, there were only 2 other small metastases in the anterior aspect of the T-6 and T-9 vertebral bodies (Fig. 2A).

A decision was made to proceed with BKP followed by SRS (24-Gy dose in 2 fractions). Using a bipedicular approach and 15 × 3–mm balloons inflated to a maximum volume of 3 cm³, BKP was performed. A total of 3.0 ml of bone cement (KyphX HV-R) was injected through each cannula. There was minor posterior epidural venous cement extravasation and some migration of cement along the path of the left cannula into the pedicle. Using SRS, radiation was delivered to T-10, but target volume delineation was compromised. It was felt still best to proceed with SRS because melanoma is radioresistant, and a generous “donut”-type contour was applied to encompass as much tissue into the target volume at the T-10 level as possible, as opposed to a more focal target volume.

The subsequent standard-of-care 2-month follow-up MR images (4 weeks following spine SRS) suggested that the tumor had spread cranially and caudally to T-9 and T-11. This is indicated in Fig. 2 by involvement of the epidural fat at T-9 and T-11 as well as the opening of the basilar vein, from where tumor propagated to the posterior aspect of the T-9 vertebral body (Fig. 2B). No disease progression in the rest of the spine was observed. This unusual pattern of spread into the adjacent levels in a short period following spine SRS suggested that tumor venous extravasation could be the potential mechanism to explain the imaging findings.

As a result of the tumor spread, the patient underwent conventional radiotherapy (SRS could not be repeated), and 6 months later, she was discharged to palliative care and finally died of her extraspinal metastatic disease.

Discussion

In this paper, we describe for the first time an iatrogenic complication secondary to BKP that we characterize as “tumor extravasation.” Our 2 cases highlight the importance of this complication as the plan radiation treatment might change from SRS to conventional radiotherapy and/or subject patients to further radiation given the change in tumor distribution. In addition, these cases support the need for careful follow-up MRI of patients with residual or persisting epidural tumor who have undergone BKP for VCF.

Vertebral compression fracture has been reported to occur in 5%–39% of patients with spinal metastasis. In our cases, the tumor spread was via the epidural plexus, extending to involve the adjacent vertebral levels through the epidural space. The follow-up MR images showed extravasation of the cement into the epidural space, indicating potential mechanisms for tumor spread.

Fig. 2. Case 2. Images obtained in 48-year-old woman with a history of diffuse metastatic melanoma and a treated T-10 VCF, showing successive tumor involvement of the adjacent levels through epidural spread. Sagittal T1-weighted images and axial T1-weighted images through T-9 and T-10 obtained before BKP (A and B) and 8 weeks after T-10 BKP and 4 weeks after SRS (C and D). There is a T-10 metastatic VCF with posterior epidural extension. The follow-up MR images show tumor spread to the adjacent levels via the epidural plexus (open arrows, C), infiltrating the posterior part of the vertebral bodies via the opening of the basilar vein. Note that the original anterior T-9 metastasis has remained stable in size. Note how the tumor has infiltrated the previously uninvolved epidural space at the level of T9 (arrowheads, B).
Tumor extravasation following balloon kyphoplasty

Although radiation treatment provides pain relief in general, it is not effective in palliating mechanical pain related to spinal instability or fracture. Rather than subjecting patients with advanced cancer to a major open surgery, procedures like BKP have evolved as an attractive minimally invasive solution to provide both spinal stability and mechanical pain palliation. However, the optimal sequence of whether to perform BKP preirradiation or postirradiation is unknown.

The first group to report on the exclusive use of BKP in a series of cancer patients was from the MD Anderson Cancer Center. These authors observed postoperative pain relief and no significant complications in 84% of patients treated. Since then, other nonrandomized series have replicated their reported rates of efficacy with similar low rates of serious complications. Most recently, a randomized controlled trial confirmed both the efficacy and safety of BKP in the management of painful VCFs in cancer patients when compared with nonoperative therapies. The BKP group had superior functional outcomes at 1 month, reductions in back pain, improvements in quality of life, and lower requirements of pain medications compared with the nonsurgical management group. Importantly, in those who crossed over to the BKP group following nonsurgical management, similar benefits were observed following the procedure, and improvement in functional status, quality of life, and pain continued until the end of the study (12 months). A meta-analysis of complications from BKP in cancer patients showed that the 2 main complications were cement extravasation (rarely symptomatic) and adjacent-level VCF, which occurred in 6.1% and 16% of patients, respectively.

The purpose of our investigation was to describe a new complication secondary to BKP that we characterize as “tumor extravasation.” This phenomenon has been largely discussed as a theoretical complication, but no reports have been published until now. In our 2 cases, we observed MRI-confirmed tumor spread into adjacent vertebral levels 4 weeks following BKP in Case 1, and 2 months following BKP (and postirradiation) in Case 2. In both cases, we are confident that we were not visualizing true tumor progression, as in the first case the period between BKP and presentation was very short, and in the second the interval between BKP and high-dose spinal SRS, which maximizes local tumor control, was again short. In addition, in both cases metastatic lesions at other levels were assessed for evidence of progression during the same period as a benchmark for tumor aggressiveness, and no evidence of spread was observed.

Two possible synergistic mechanisms may explain this unusual pattern of tumor spread after BKP. The first is based on our observation of anterior subligamentous tumor spread. We postulate that this is directly linked to physical displacement of the soft tumor tissue, which is pushed beyond the vertebral bony boundaries through defects in the fractured cortex. In contrast to osteoporotic VCFs, metastatic VCFs may exhibit disruption of the endplates as well as compromise of the vertebral body cortex and internal trabecular structure. These multiple areas of disruption represent paths of least resistance for flow of cement and/or tumor. Bony destruction has been used to explain the greater propensity for cement leakage in augmentation procedures performed on metastatically involved vertebrae. Hence, tumor cells may be physically displaced by the inflated balloons/cement beyond the boundaries of the vertebral body and into the adjacent paravertebral soft tissues. Case 1 may be illustrative of this mechanism, where there is rapid tumor spread to the paravertebral soft tissues shortly after BKP (Fig. 1C). Anterior subligamentous extension to the adjacent vertebral bodies is also seen and the anterior longitudinal ligament bulges in the segment located between the points of attachment (Fig. 1D).

The second mechanism may be the result of a physical increase in intravertebral pressure that is generated during balloon inflation and/or cement injection, leading to venous extravasation. The rate of asymptomatic cement venous extravasation during vertebral augmentation procedures is underestimated by fluoroscopy when compared with inspection of the gross specimen in cadaveric histopathological studies. When osteolytic tumor is present in the spine, there is a loss of mechanical barriers resulting from the destruction of the trabecular network, which may increase the potential communication points with the venous sinusoids. Similar to the spread pattern of venous extravasation of cement during balloon inflation or cement injection, as local pressure increases, tumor cells may migrate into the lumen of the venous sinusoids. Viable tumor cells entering these venous spaces may continue to spread through the basilar vein into the anterior internal venous plexus. Unlike displacement of venous blood from the sinusoids, tumor under increased pressure would be displacing tumor along the path of least resistance. Once the neoplastic cells reach this network of valveless veins, they may propagate along the cranio-caudal axis to involve adjacent vertebral bodies. Evidence of such a mechanism is present in both cases and may be best illustrated in Case 2, where soft-tissue infiltration of the epidural space was seen at the treated level as well as both the adjacent inferior and superior levels. The tumor also infiltrated the opening of the basilar vein and, at T-9, extended to the posterior aspect of the vertebral body (Fig. 2B).

Both postulated mechanisms of action are based on MRI findings, the relatively short interval between BKP and tumor spread, and the unusual pattern of spread for solid tumor metastases. In both cases, the unusual pattern of tumor spread was seen with no associated increase in the global disease burden or spine-specific disease burden. Risk factors for this phenomenon may include complete replacement of the vertebral body marrow (high tumor cell load), baseline VCF, cortical bone disruption, and visible tumor extension into the prevertebral/epidural spaces. We surmise that this complication is more frequent than is reported in literature, as it is not typical that patients undergo follow-up MRI so early. With respect to our imaging protocol, it is important to note that at our institution gadolinium contrast is not routinely administered because enhancement can mask the infiltration of tumor into fatty marrow or tissue planes unless a fat saturation technique is routinely employed. More commonly, follow-up imaging is performed with radiography or CT.
scanning, which are far less sensitive to soft-tissue visualization. Also, in the absence of other reported cases, this phenomenon may be easily misinterpreted as general disease progression.

Strategies to avoid this complication may include a slower rate of balloon inflation, which would avoid any sudden marked increases in pressure within the vertebral body; underinflation of the balloons; or injection of smaller amounts of cement to reduce the potential for mechanical tumor displacement. While high-viscosity cements have been shown to be associated with reduced rates of extravasation than lower-viscosity cements, their use does not reduce the likelihood of tumor extravasation. Performing BKP after radiation treatment may also be considered to be a strategy for those patients deemed at risk, since radiation would reduce the tumor bulk that might create a cavitory space for balloon/cement placement and, hence, reduce the internal vertebral body pressure upon subsequent BKP. Radiation also has the added benefit of inducing remineralization, which may heal cracks in the vertebral cortex to reduce the potential for direct tumor extravasation. Of note, we have changed our practice of using radiation pre-BKP when possible because we are also concerned with targeting, given that we preferentially use SRS, the success of which depends on accurate tumor delineation. Other therapeutic options may include tumour ablation to create a cavitory defect prior to cement injection, thereby reducing the potential for increased pressurization and mechanical displacement of viable tumor cells. Minimally invasive techniques that can destroy tumor cells using a BKP cannula or percutaneous vertebroplasty cannula for access, such as laser-induced thermal therapy, radiofrequency ablation, or photodynamic therapy, may prove viable options for this purpose. While considering all of these options, it is important not to lose sight of the objectives involved in performing the BKP procedure—that is, the pain relief obtained by stabilizing a metastatic vertebral fracture by using a minimally invasive technique.

Conclusions

We present the first report of 2 cases of contiguous tumor spread following single-level BKP. We are confident that this represents a distinct pattern of tumor spread related to BKP, as opposed to usual tumor progression, explained by mechanical/pressure-induced spread through cortical defects in the vertebral body and/or into the venous plexus.

Disclosure

Both Drs. Sahgal and Smith have received honoraria for past educational seminars directly related to BKP. Otherwise none of the authors have any conflicts of interest to disclose.

Author contributions to the study and manuscript preparation include the following. Conception and design: Smith, Cruz, Sahgal. Analysis and interpretation of data: Smith, Cruz, Sahgal. Drafting the article: Cruz, Sahgal. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Smith. Study supervision: Smith, Cruz, Sahgal.

References


Manuscript submitted July 22, 2013.
Accepted April 30, 2014.

Please include this information when citing this paper: published online June 6, 2014; DOI: 10.3171/2014.4.SPINE13695.
Address correspondence to: Roger Smith, M.D., Department of Medical Imaging, Toronto Western Hospital, University of Toronto, 3 McLaughlin Wing, 3MC-428, 399 Bathurst St., Toronto, ON M5T 2S8, Canada. email: roger.smith@uhn.on.ca.