J Neurosurg Spine 17:263–267, 2012

A single spinal lesion arising from an intradural meningioma contiguous with an extradural lymphoma

Case report

Pawel P. Jankowski, M.D.,[1] Lissa C. Baird, M.D.,[1] Sassan Keshavarzi, M.D.,[1] Mary E. Goolsby, M.D.,[2] William R. Taylor, M.D.,[1] and Andrew D. Nguyen, M.D., Ph.D.[1]

Departments of [1]Neurosurgery and [2]Pathology, University of California, San Diego, California

The authors describe here a unique case of contiguous, synchronous meningioma and lymphoma in the spinal column. Both tumors were present at the same vertebral level, one intradural and the other extradural. A patient presented with bilateral leg pain, acute weakness, and sensory loss in the lower extremities. Magnetic resonance imaging revealed an intradural mass at T6–7 with ambiguous boundaries relative to the thecal sac and compressing the spinal cord. The patient underwent resection of the epidural and intradural mass at T6–7. Histopathology revealed the epidural specimen to be a double-hit B-cell lymphoma and the intradural mass to be a transitional meningioma. Postoperatively, the patient did well, with an immediate return of strength and sensation. A postoperative MR image showed complete resection of the intradural mass. The authors suggest that biopsy may be prudent in patients with known systemic lymphoma presenting with a spinal lesion that has unclear boundaries relative to the thecal sac prior to commencing radiation and chemotherapy.
(http://thejns.org/doi/abs/10.3171/2012.6.SPINE11913)

Key Words • **double-hit lymphoma** • **spine** • **oncology** • **transitional meningioma** • **contiguous and synchronous tumor**

The association of different primary tumors with one another or with metastases in the spinal cord is rare.[3,16] Without predisposing conditions, such as phacomatoses or prior radiotherapy, the presence of an aggressive lymphoma and slow growing meningioma is uncommon.[3,13,16,24] Patients with meningioma or glioma, the most prevalent primary CNS tumors, manifest multiple lesions in less than 10% of cases.[3]

We report on a case of contiguous, synchronous meningioma and lymphoma in the spinal column. Both tumors were present at the same vertebral level, one intradural and the other extradural. To the best of our knowledge such a case has not been reported in the literature.

Case Report

History and Examination. A 63-year-old woman presented to us with a 7-month history of bilateral leg pain. The pain had initially been isolated to her left leg, but it eventually progressed to both legs. She reported worsening weakness and numbness and had recently begun using a wheelchair given her difficulty with walking. The remainder of the neurological examination was unremarkable. Her medical history was negative. On neurological examination she had full strength in her upper extremities. Significant proximal weakness was noted in her lower extremities, worse on the left: hip flexion 1/5, knee extension 1/5, dorsiflexion and plantar flexion 4/5. Sensation was diminished equally on the right and left lower extremities, while proprioception remained intact. Her Babinski reflex was absent, and her patellar and ankle deep tendon reflexes were both +2.

An MRI study of the spine revealed multiple abnormal osseous, extradural, intradural, and paraspinal masses. Most concerning was an intradural mass at T6–7 (Figs. 1 and 2), which compressed the spinal cord. Tumor involvement of the posterior bony and cartilaginous elements at T-4, T-5, and T-12 with adjacent epidural extension was also noted.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

Abbreviation used in this paper: NHL = non-Hodgkin lymphoma.

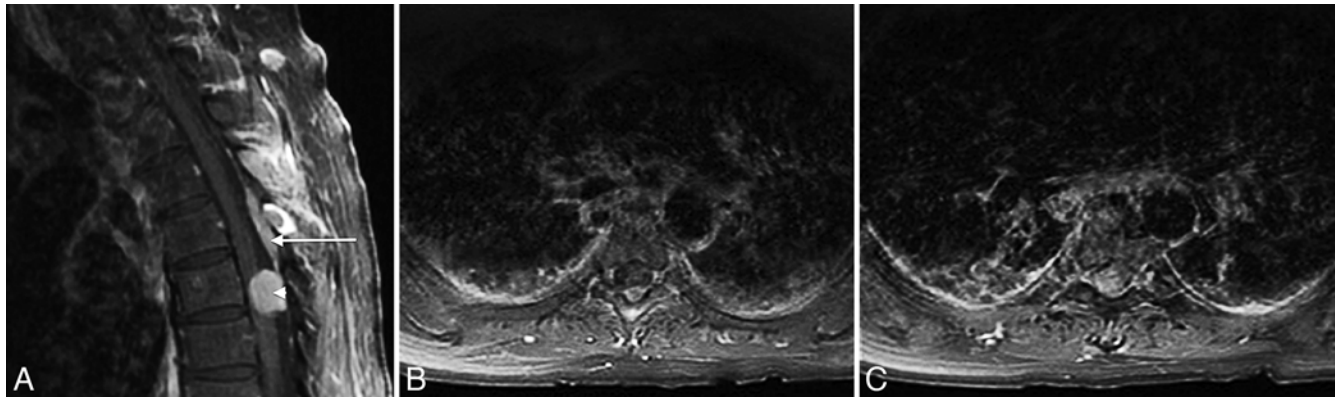

Fig. 1. **A:** Sagittal T1-weighted postcontrast MR image demonstrating a 12 × 21–mm enhancing intradural mass at T6–7 compressing the spinal cord *(arrowhead)* as well as epidural thickening and enhancement extending superiorly 3.6 cm to the level of T4–5 *(arrow)*. **B:** Axial T1-weighted postcontrast MR image showing epidural enhancement representative of the lymphoma. **C:** Axial T1-weighted postcontrast MR image showing a meningioma occluding the majority of the canal.

Operation. Treatment options were discussed with the patient, and she agreed to proceed with surgical removal of the compressive intradural lesion at T6–7. Neurophysiological monitoring preflip baseline recordings were obtained. Fluoroscopy was used to localize the T6–7 level. An 8-cm skin incision was made, and a subperiosteal dissection was performed to expose the medial facet joints of T-6 and -7. During the laminectomy and bone removal at T-6 and -7, abnormal tissue was encountered in the spinous processes and subsequently in the epidural space. Biopsy samples were sent, and preliminary frozen pathology demonstrated lymphoma. After removing the epidural mass, the dura was opened and reflected laterally. A distinct intradural mass was identified and noted to be adherent to the right lateral dura. The appearance of this mass was distinct from the bony and epidural lesion previously encountered. After dissecting the mass away from the lateral dural wall, it was easily elevated off of the spinal cord and dissected away from surrounding nerve roots. Neuromonitoring remained stable without any changes to motor or sensory evoked potentials. The dura was closed with a DuraGen Plus patch (Integra), and a watertight seal was achieved. In total, 3 specimens were sent for pathological evaluation: the intradural mass, the epidural mass, and the bony lesion. The duration of the procedure lasted 2 hours, and there was less than 100 ml of blood loss.

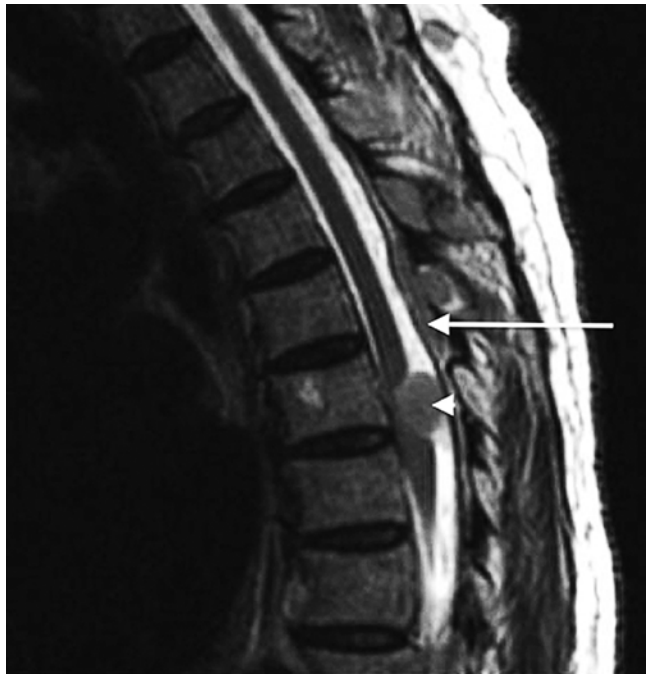

Fig. 2. Preoperative sagittal T2-weighted MR image demonstrating the epidural lymphoma *(arrow)* and intradural meningioma *(arrowhead)*.

Histopathology. Histological examination of the tissue confirmed 2 tumor types. The epidural and bony specimens revealed high-grade B-cell lymphoma (Fig. 3) with abundant monotonous small- to medium-sized lymphocytes intermixed with occasional macrophages. Numerous apoptotic figures and occasional mitoses were identified. Cells were strongly positive for the B-cell markers CD20 and BCL-2. The Ki 67 staining was 90%–95%, indicating the aggressive nature of this lesion. Flow cytometry was performed and demonstrated CD5-negative and CD10-positive B-lineage NHL with monotypic surface kappa

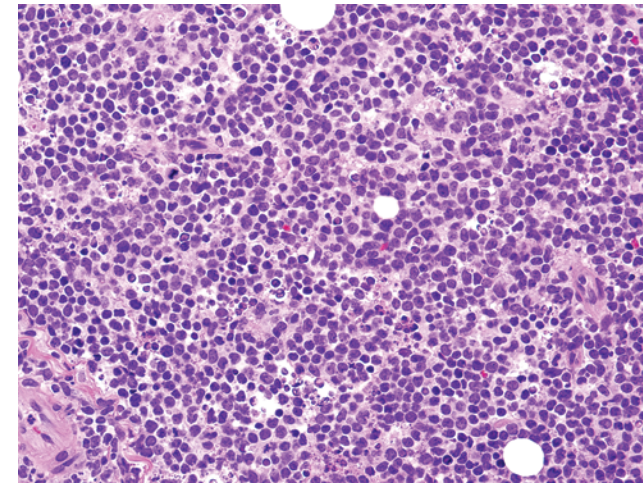

Fig. 3. Photomicrograph demonstrating a lymphoma. H & E, original magnification × 25.2.

light chain restriction. Fluorescence in situ hybridization analysis showed evidence of both MYC translocation and IGH/BCL-2 translocation, findings that support a diagnosis of aggressive B-cell lymphoma with features between diffuse large B-cell lymphoma and Burkitt lymphoma, also known as a "double-hit lymphoma" (WHO classification: B-cell lymphoma, unclassifiable). The second specimen (Fig. 4), from the intradural mass, demonstrated a meningioma with a transitional appearance including both meningotheliomatous and fibrous patterns with frequent psammoma bodies. No significant atypia or mitoses were identified.

Postoperative Course. The patient experienced immediate improvement in her motor strength following surgery. Sensation in both lower extremities returned to normal. No new neurological dysfunction was noted in the postoperative period. At the time of discharge, her strength in the left lower extremity improved: hip flexion 3/5, knee extension 4/5, dorsiflexion and plantar flexion 4/5.

She was ambulating well with moderate assistance. Postoperative MRI of the thoracic spine revealed complete resection of the intradural mass at T6–7.

A bone survey performed after resection of the spine tumors revealed a pathological fracture in the right femur, accounting for the lack of recovery to full strength in that extremity. The patient underwent stabilization and pinning 2 weeks after the spine surgery. Also after surgery, an Ommaya reservoir was placed for CSF sampling and the administration of intrathecal chemotherapy. Approximately 1 month after the spine surgery she started the first of 3 cycles of hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone). She was also started on intrathecal methotrexate followed by arabinofuranosyl cytidine. She responded well to the chemotherapy, and follow-up CSF sampling was negative for residual lymphoma cells. Follow-up brain MRI demonstrated multifocal lymphomatous infiltration of the meninges. As a result, the patient received whole-brain radiation. A follow-up spine MRI survey showed no recurrence or any additional spinal lesions. After 4 months of adjuvant therapy the patient elected to enter hospice care instead of continuing her chemotherapy. At that time her neurological examination remained stable; she was ambulatory and required minimal assistance.

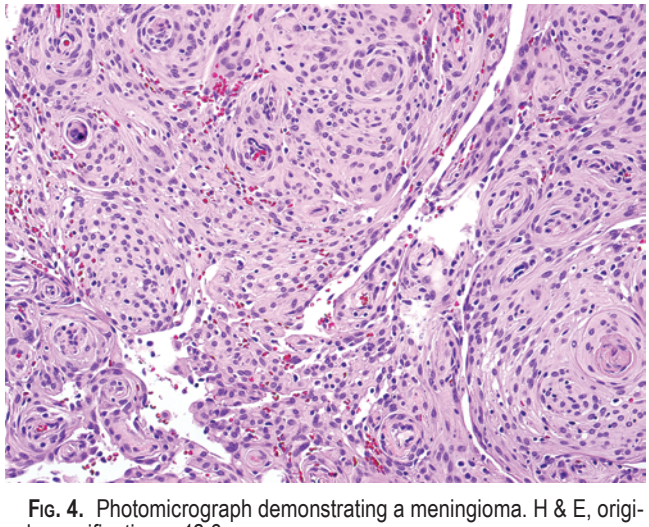

Fig. 4. Photomicrograph demonstrating a meningioma. H & E, original magnification × 12.6.

Discussion

Lymphoma occurring in adults in conjunction with other tumors is rare. Eight cases have been reported in the literature, 5 of which were associated with meningiomas.[1,3,6,7,10] Of the 5 meningioma-lymphoma associations, 4 were noncontiguous and none were in the spine. Our case is unique since it is the first report of an extradural lymphoma and intradural meningioma coexisting contiguously at the same level in the spinal column.

Meningiomas are one of the most common CNS neoplasms, and while the majority are intracranial or intraspinal, ectopic sites have been reported in the literature. Previous radiation exposure, genetic factors such as neurofibromatosis Type 2, and hormonal factors have been implicated in the growth and development of meningiomas. Spinal meningiomas represent approximately 25% of all primary tumors of the spine, second only to schwannomas in frequency.[18,21] Both intracranial and spinal meningiomas are typically found to have a dural base stretching the arachnoid as they grow. Sometimes they will incorporate the arachnoid but rarely the pia.[4,22,23] Approximately 80% of meningiomas in the spinal cord occur in the thoracic spine.[11,17,25] The highest prevalence of meningiomas is seen in middle-aged females with a 2:1 ratio for intracranial lesions and a 9:1 ratio for spinal lesions as compared with males.[17,22] Meningiomas in the spinal cord and in the brain are slow-growing tumors, and patients initially present with back pain in 50% of cases.[5,13] The clinical manifestations usually progress slowly and tend to be widely variable, ranging from weakness, sensory disturbances, and radicular pain.[20] From the literature, the common tumor associations found in conjunction with meningiomas include meningioma-glioma and meningioma-pituitary adenoma, all intracranial.[5,17,25]

Lymphomas may be primary or secondary. Non-CNS lymphoma, a secondary lymphoma, is the fifth most common cause of cancer deaths in the US, with 63% of new cases attributed to NHL.[15] Central nervous system involvement tends to occur late in the course of the disease. Primary or secondary lymphomas affecting the CNS show singular or multiple lesions; however, it is rare to find them in concurrence with other tumors affecting the CNS. The most common pathogenesis of spinal cord compression in patients with NHL is metastases to the lymph nodes.[9] When paraspinal lymph nodes are involved, the tumor can extend into the spinal epidural space through the neural foramina.[9] The peripheral nervous system is frequently affected in patients with NHL, as a consequence of either a paraneoplastic syndrome or direct infiltration. A key determinant of CNS involvement relates to the histopathology of the lymphoma, with higher-grade tumors exhibiting greater CNS disease.[9,12] Additional risk factors for CNS involvement include elevated serum lactate dehydrogenase, hypoalbuminemia (< 35 g/L), an age < 60 years, retroperitoneal lymph node

involvement, and more than one extranodal lymph node involvement.[12] Aside from her age, our patient had all of the above features.

Lymphomas with recurrent chromosomal breakpoints activating multiple oncogenes are referred to as "double-hit" lymphomas.[2] The term is typically used for mature B-cell lymphomas with a chromosomal breakpoint affecting the *myc* locus. The median age for double-hit lymphomas ranges from 51 to 65 years, and the disorder is rarely found in patients younger than 18 years of age.[19] Typically one will find elevated lactate dehydrogenase, and if the disease is advanced, extranodal spread will be present.[2,19] The bone marrow and CNS are commonly affected sites, and the frequency of CNS involvement has been reported to be between 9% and 50%.[2,19] Our patient had a lymphoma that was unique, containing features between diffuse large B-cell lymphoma and Burkitt lymphoma. The conditions that placed our patient's diagnosis in this category included a Ki 67 proliferation index > 90%, a cohesive growth pattern, and the expression of CD10.[2] The prognosis for the above NHL classification and features is poor.

The cause and the pathogenesis of the association between diffuse lymphoma and meningioma occurring contiguously and synchronously in the spine remain unclear. The rarity of this association may indicate that it is purely coincidental. However, as meningiomas are common and slow growing, there is an increased risk of their concurrence with a second neoplasm.[6] Other plausible explanations include a local carcinogenic agent giving rise to a slow-growing meningioma, and later causing a lymphoma,[3,8,16] or an irritative effect of the meningioma facilitating the development of lymphoma,[3,16] especially given the synchronous occurrence of the 2 lesions at the same spinal level.

Recognizing multiple tumors located contiguously along with their clinical presentation is influenced by the sensitivity of the diagnostic test used. Magnetic resonance imaging is the most sensitive test for detecting spinal lesions, both intra- and extradural based. However, when the lesions are adjacent to one another, it may be problematic to distinguish their location in relation to the thecal sac, as occurred in our case.

Our patient had no previous imaging studies that would aid in determining whether one lesion was present before the other. Furthermore, her first clinical symptoms were back pain and myelopathy, not systemic lymphoma-related symptoms. Her first MR image revealed one homogeneous lesion occupying the epidural and intradural space at the T6–7 vertebral level with another epidural lesion at T4–5, suggesting the possibility of only one tumor. As the lymphoma was extradural and probably unrelated to her neurological symptoms, the diagnosis was not established until the intradural meningioma grew large enough to create myelopathic symptoms. This case may provide further support to the theory that an irritative effect of the meningioma facilitates the development of a lymphoma in a contiguous location.[3,7,8] However, it may be that the two tumors are completely unrelated, and the diagnosis of lymphoma was established early and incidentally because of the patient's symptomatic meningioma.

Conclusions

We report here a unique case of an extradural lymphoma and intradural meningioma coexisting contiguously at the same level in the spinal column. The pathogenesis of these two tumors coexisting contiguously and synchronously at the same level in the spine remains speculative. Imaging techniques were unable to differentiate two unique tumors within the same spinal level. We suggest that in patients with known systemic lymphoma presenting with a spinal lesion that has unclear boundaries relative to the thecal sac, it may be prudent to obtain a biopsy prior to commencing radiation and/or chemotherapy.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Jankowski. Acquisition of data: Jankowski. Analysis and interpretation of data: Jankowski. Drafting the article: Jankowski. 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: Jankowski. Administrative/technical/material support: Jankowski.

References

1. Andrioli GC, Zuccarello M, Scanarini M, d'Avella D: Concurrent primary intracranial tumors of different histogenesis. **Acta Neuropathol Suppl 7:**111–115, 1984
2. Aukema SM, Siebert R, Schuuring E, van Imhoff GW, Kluin-Nelemans HC, Boerma EJ, et al: Double-hit B-cell lymphomas. **Blood 117:**2319–2331, 2011
3. Buccoliero AM, Taddei GL, Caldarella A, Mennonna P, Ammannati F, Taddei A, et al: Meningioma-primary brain lymphoma association. **Neuropathology 24:**336–340, 2004
4. Ciappetta P, Domenicucci M, Raco A: Spinal meningiomas: prognosis and recovery factors in 22 cases with severe motor deficits. **Acta Neurol Scand 77:**27–30, 1988
5. Compston A: Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationary Office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 figures. **Brain 133:**2838–2844, 2010
6. Ederli A, Lo Russo F, Vesentini G: Glioblastoma of the brainstem associated with Hodgkin lymphoma. **Ital J Neurol Sci 4:**349–353, 1983
7. Fewings PE, Bhattacharyya D, Crooks D, Morris K: B cell non-Hodgkin cerebral lymphoma associated with an anaplastic oligodendroglioma. **Clin Neuropathol 21:**243–247, 2002
8. George B, Kumar R, Johns P, Bartlett RJU, O'Brien D: Contiguous synchronous occurrence of primary cerebral lymphoma and meningioma. **Br J Neurosurg 21:**35–38, 2007
9. Giglio P, Gilbert MR: Neurologic complications of non-Hodgkin's lymphoma. **Curr Hematol Malig Rep 1:**214–219, 2006
10. Giromini D, Peiffer J, Tzonos T: Occurrence of a primary Burkitt-type lymphoma of the central nervous system in an astrocytoma patient. A case report. **Acta Neuropathol 54:**165–167, 1981
11. Griffiths IR, Trench JG, Crawford RA: Spinal cord blood flow and conduction during experimental cord compression in normotensive and hypotensive dogs. **J Neurosurg 50:**353–360, 1979
12. Hollender A, Kvaloy S, Nome O, Skovlund E, Lote K, Holte

H: Central nervous system involvement following diagnosis of non-Hodgkin's lymphoma: a risk model. **Ann Oncol 13:**1099–1107, 2002
13. Hollis PH, Malis LI, Zappulla RA: Neurological deterioration after lumbar puncture below complete spinal subarachnoid block. **J Neurosurg 64:**253–256, 1986
14. Ildan F, Bağdatoğlu H, Boyar B, Haciyakupoğlu S, Gönlüşen G, Tunali N: Combined occurrence of primary cerebral lymphoma and meningioma. **Neurosurg Rev 18:**45–48, 1995
15. Jellinger K, Radiaszkiewicz T: Involvement of the central nervous system in malignant lymphomas. **Virchows Arch A Pathol Anat Histol 370:**345–362, 1976
16. Lee EJ, Chang CH, Wang LC, Hung YC, Chen HH: Two primary brain tumors, meningioma and glioblastoma multiforme, in opposite hemispheres of the same patient. **J Clin Neurosci 9:**589–591, 2002
17. Levy WJ Jr, Bay J, Dohn D: Spinal cord meningioma. **J Neurosurg 57:**804–812, 1982
18. Nittner K: Spinal meningiomas, neurinomas and neurofibromas and hourglass tumors, in Vinkin PJ, Bruyn GW (eds): **Handbook of Clinical Neurology.** New York: Elsevier, 1976, Vol 20, pp 177–322
19. Oschlies I, Salaverria I, Mahn F, Meinhardt A, Zimmermann M, Woessmann W, et al: Pediatric follicular lymphoma—a clinico-pathological study of a population-based series of patients treated within the Non-Hodgkin's Lymphoma—Berlin-Frankfurt-Munster (NHL-BFM) multicenter trials. **Haematologica 95:**253–259, 2010
20. Pansini A, LoRe F, Conti P, Conti R, Montali E, DeLuca G: **Spinal Meningiomas.** Berlin: Springer, 1996
21. Rasmussen TB, Kernohan JW, Adson AW: Pathologic classification with surgical consideration, of intraspinal tumors. **Ann Surg 111:**513–530, 1940
22. Schaller B, Heilbronner R, Pfaltz CR, Probst RR, Gratzl O: Preoperative and postoperative auditory and facial nerve function in cerebellopontine angle meningiomas. **Otolaryngol Head Neck Surg 112:**228–234, 1995
23. Schaller B, Merlo A, Gratzl O, Probst R: Premeatal and retromeatal cerebellopontine angle meningioma. Two distinct clinical entities. **Acta Neurochir (Wien) 141:**465–471, 1999
24. Slowik F, Jellinger K: Association of primary cerebral lymphoma with meningioma: report of two cases. **Clin Neuropathol 9:**69–73, 1990
25. Solero CL, Fornari M, Giombini S, Lasio G, Oliveri G, Cimino C, et al: Spinal meningiomas: review of 174 operated cases. **Neurosurgery 25:**153–160, 1989

Manuscript submitted October 25, 2011.
Accepted June 19, 2012.
Please include this information when citing this paper: published online July 20, 2012; DOI: 10.3171/2012.6.SPINE11913.

Address correspondence to: Pawel P. Jankowski, M.D., Moores Cancer Center, 3855 Health Sciences Drive, San Diego, California 92093-0987. email: pjankowski@ucsd.edu.