Neck Pain in a 27-year-old Man

Addisu Mesfin MD, Jacob M. Buchowski MD, MS,
Mitra Mehrad MD, Jianwen Xu MD, PhD

Received: 18 October 2012 / Accepted: 6 February 2013 / Published online: 15 February 2013
© The Association of Bone and Joint Surgeons® 2013

History and Physical Examination

A 27-year-old man presented to the emergency room with a 1-month history of progressive neck pain and left upper-extremity weakness. He had no history of antecedent trauma. He also reported numbness over the left index finger and left thumb and radiating neck pain into the left forearm and index finger. He had no difficulties with

balance or tripping and no problems with fine motor tasks. He had no medical conditions and never had surgery. He did not smoke and he worked in a supermarket. His family history was notable for melanoma on his maternal side.

On physical examination, the patient was afebrile with stable vital signs. He had posterior neck tenderness to palpation. On motor testing, his left deltoid and biceps were 4 +/5 in strength, left triceps was 3/5 in strength, and left wrist flexion, wrist extension, and grip were 4/5 in strength. Hoffmann sign was negative. His right deltoid, biceps, triceps, wrist flexion, and grip strength were 5/5. Reflexes in the bilateral biceps, brachioradialis, and triceps were +2. On sensory examination, he had diminished sensation in the left radial forearm, left thumb, and left index finger.

His CBC showed a white blood count of 10.6 mm^3 (normal, $3.8\text{--}9.8 \text{ mm}^3$), C-reactive protein of 17 mg/dL (normal, $< 10 \text{ mg/dL}$), and erythrocyte sedimentation rate of 17 mm/hour (normal, $< 12 \text{ mm/hour}$). His basic metabolic panel was within normal limits.

Radiography (Fig. 1) and MRI (Fig. 2) of the cervical spine were performed.

Based on the history, physical examination, laboratory studies, and imaging studies, what is the differential diagnosis at this point?

The institution of one or more of the authors (JMB, JX) has received, during the study period, funding from K2 M, Inc/Complex Spine Study Group (Malvern, PA, USA) and from the Orthopaedic Research and Education Foundation (Rosemont, IL, USA). One of the authors (JMB) has or may receive payments or benefits, during the study period, an amount of less than USD10,000 from CoreLink, Inc (St Louis, MO, USA), USD10,000 to USD100,000 from Globus Medical, Inc (Audubon, PA, USA), and USD10,000 to USD100,000 from Stryker, Inc (Mahwah, NJ, USA), USD10,000 to USD100,000 from DePuy, Inc (Warsaw, IN, USA), USD10,000 to USD100,000 from Globus Medical, Inc, less than USD10,000 from K2 M, Inc (Leesburg, VA, USA), less than USD10,000 from Medtronic, Inc. (Memphis, TN, USA).

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request. Each author certifies that his or her institution approved or waived approval for the reporting of this case and that all investigations were conducted in conformity with ethical principles of research. This work was performed at Washington University in St Louis, St Louis, MO, USA.

A. Mesfin
Department of Orthopaedic Surgery, University of Rochester,
Rochester, NY, USA

J. M. Buchowski (✉), J. Xu
Department of Orthopaedic Surgery, Washington University in
St Louis, 660 S Euclid Avenue, Campus Box 8233, St Louis,
MO 63110, USA
e-mail: buchowskij@wustl.edu

M. Mehrad
Department of Pathology and Immunology,
Washington University in St Louis,
St Louis, MO, USA

Fig. 1A–B (A) An AP view of the cervical spine shows loss of height of the C6 vertebral body, and (B) the lateral view shows a pathologic fracture of C6 (arrow).

Fig. 2A–B (A) A T2-weighted sagittal MR image shows a C6 pathologic fracture. There is 4-mm retropulsion of C6 into the central canal, resulting in severe central stenosis and cord compression without intramedullary T2 hyperintensity. (B) On short tau inversion recovery MRI, there is high T2 signal in C6 and the adjacent C5–C6 and C6–C7 disc spaces.

Imaging Interpretation

An AP view (Fig. 1A) of the cervical spine showed loss of height of the C6 vertebral body, and the lateral view (Fig. 1B) showed a pathologic fracture of C6. The intervertebral disc spaces were intact. On T2-weighted sagittal MRI (Fig. 2A), there was a C6 pathologic fracture with widening of the C6 vertebral body in the AP dimension, with greater than 60% loss of height centrally. There was 4-mm retropulsion of C6 into the central canal resulting in severe central stenosis and cord compression without intramedullary T2 hyperintensity. There was increased T2 signal of the C6 vertebral body, the left pedicle, articular facet, both lateral columns, and into the bone forming the bilateral transverse foramen to surround the vertebral

arteries. There was extradural extension of soft tissue around the C6 vertebral body into the anterior perivertebral space. On short tau inversion recovery MRI (Fig. 2B), there was high T2 signal within C6 and the adjacent C5–C6 and C6–C7 disc spaces.

Differential Diagnosis

- Giant cell tumor
- Aneurysmal bone cyst
- Langerhans cell histiocytosis
- Ewing's sarcoma
- Chordoma
- Bacterial infection

Fig. 3A–C (A) Langerhans cells (LCs) with lobulations and/or indentations of the nuclear membrane (blue arrow) are seen. Osteoclastlike giant cells (thin arrow) and eosinophils (thick arrow) are present (Stain, hematoxylin & eosin; original magnification, 9400). (B) Cells that are immunoreactive with vimentin, an

intermediate filament marker, are stained brown (arrows) (Stain, immunohistochemistry with hematoxylin counterstain; original magnification, 9400). (C) Cell membrane staining of the LCs by CD1a, a histiocyte marker, is shown (arrows) (Stain, immunohistochemistry with hematoxylin counterstain; original magnification, 9400).

To help establish the diagnosis, the patient underwent a percutaneous CT-guided biopsy of the C6 vertebral body preoperatively and the specimens were evaluated histologically (Fig. 3).

Histology Interpretation

On microscopic evaluation, sections of the C6 vertebral body showed focal osteonecrosis with associated marrow fibrosis and scattered osteoclastlike giant cells (Fig. 3A). A sheet and clusterlike proliferation of Langerhans cells (LCs) also was identified (Fig. 3A). An inflammatory cell infiltrate that primarily consisted of eosinophils accompanied the LCs. Other inflammatory cells were present, including neutrophils, plasma cells, and lymphocytes (Fig. 3A). The LCs were strongly immunoreactive with vimentin (Fig. 3B) and CD1a (Fig. 3C).

Based on the history, physical examination, laboratory studies, imaging studies, and histologic picture, what is the diagnosis and how should the patient be treated?

Diagnosis

Langerhans cell histiocytosis (LCH) leading to pathologic C6 vertebral burst fracture

Discussion and Treatment

Based on the results of the imaging and biopsy, our patient was diagnosed with LCH. A common radiographic characteristic of LCH is vertebra plana, or flattening of the vertebral body [2, 7, 10, 11, 24], although this imaging appearance is not unique to LCH. This is caused by the proliferation of

histiocytes and subsequent destruction of the vertebral body [2, 7, 10, 11, 24]. The diagnosis of LCH was confirmed by immunohistochemistry. LCs are diffusely reactive with S100 protein [1] and CD1a [19]. The definitive diagnosis for LCH is determined with histologic analysis since other conditions can mimic the imaging and clinical presentations.

Giant cell tumors (GCTs) of the spine usually are localized to the sacrum and are rare in the cervical spine [24]. GCTs are benign yet aggressive lesions with a high recurrence rate after resection [4, 12, 17, 24]. On histologic analysis, sheets of giant cells are seen [17], in contrast to the occasional giant cells present in our patient's histologic analysis. Aneurysmal bone cysts (ABCs) of the spine can be solitary or secondary to other tumors such as GCTs and osteblastomas. ABCs occur in younger patients (first to third decade) similar to our patient [24]. ABCs of the spine frequently are encountered in the posterior elements, but involvement of the vertebral body has been reported [5, 18, 20]. On MRI, one of the common findings of ABCs is fluid-fluid levels and these were absent from our patient's MRI [24]. Histologically, the lesion consists of hemorrhagic cystic spaces separated by fibrous septae and sometimes by bone. Ewing's sarcoma is found in the mobile spine in 5% of cases [3, 16, 25]. On radiographs, Ewing's sarcoma can present with vertebra plana similar to LCH. Histologically though, Ewing's sarcoma has the characteristic sheet of small round blue cells. Chromosomal translocations also are characteristic of Ewing's sarcoma. Cervical chordomas are rare accounting for only 5% of all chordoma cases [28]. Histologically, chordomas have groups of cells with characteristic physaliferous or bubbly cytoplasm [27]. The biomarker brachyury has been noted to have 98% sensitivity and 100% specificity for the detection of chordomas [22]. Although there was a slight elevation of the white blood count and inflammatory factors, the diagnosis in our patient was not a bacterial

Fig. 4A–C (A) We used the Smith-Robinson approach and encountered the tumor in the soft tissue plane of the prevertebral fascia. (B) Corpectomy of C6 was performed and (C) a titanium cage system was used for reconstruction.

Fig. 5A–B (A) AP and (B) lateral views show the principles of intralesional resection performed via corpectomy of C6 and reconstruction and stabilization used in this patient.

infection because of the involvement of the vertebral body only rather than concurrent involvement of the disc space as seen in infections. Infections of the cervical spine are relatively rare accounting for 10% of spine infections [9, 26]. Histologic analysis of infections also would show a predominance of polymorphonuclear cells in contrast to the sheets of LCs and some eosinophils seen in our patient.

LCH (previously called eosinophilic granuloma) is a benign tumor commonly found in patients younger than 20 years. The reported incidence of LCH is one per 1.5 million [21]. In a series of 214 LCH cases, 6.5% were located in the spine [6]. A study of 30 children with localized LCH noted a 40% incidence of LCH in the spine [10]. Huang et al. [11] recently reported on 30 adults with LCH of the spine and found 21 (70%) of the lesions to be localized to the cervical spine. Bertram et al. [2] performed a meta-analysis of LCH of the cervical spine in 2002 and only found 53

cervical spine cases. The natural history of LCH of the spine is not well defined. In a series of 15 patients with LCH of the spine, two did not receive any type of intervention and at an average of 3 to 11 years followup, no recurrence were noted [14]. Four of seven pediatric patients with cervical LCH managed with observation and bracing were noted to have resolution of the LCH without recurrence [8]. Kamimura et al. reported on two pediatric patients with spine LCH with neurologic manifestations who were treated with immobilization [13]. These patients experienced subsequent improvement in neurologic function and no recurrence at 5 years followup [13]. A long-term followup of 23 pediatric patients with LCH found nonoperative treatment consisting of either chemotherapy, radiation, or observation to be curative in the majority of cases [10]. However, two of the 23 patients required surgical intervention owing to deformity associated with the LCH afflicted vertebral body.

LCH is a clonal proliferation of LCs occurring as an isolated lesion or as part of a systemic process [29]. The LCs represent a cellular component of the dendritic cell system rather than tissue macrophages (histiocytes) and therefore the designation of Langerhans cell (eosinophilic) granulomatosis was suggested by Lieberman et al. [15]. Histologically, LCH is characterized by proliferation of LCs, which consist of large, ovoid, mononuclear cells, with a folded nucleus, centrally located basophilic nucleolus, and a moderate amount of eosinophilic cytoplasm. An inflammatory cell infiltrate primarily consisting of eosinophils, and scattered polymorphonuclear leukocytes, plasma cells, and lymphocytes, is present in the background. The diagnosis of LCH is confirmed by immunohistochemistry.

Treatment options for LCH include cervical orthoses and observation [10], CT-guided corticosteroid injection [23], and surgical treatment with and without postoperative radiation therapy [11].

We elected to perform open treatment of the LCH-affected C6 vertebral body owing to the patient's presentation of motor weakness, radiculopathy, and sensory deficits. The soft tissue extension of the tumor was encountered in the prevertebral fascia (Fig. 4A). A corpectomy of C6 (Fig. 4B) was performed and a titanium cage system (Pyramesh®; Medtronic, Memphis, TN, USA) was used for reconstruction (Fig. 4C). We harvested anterior cancellous iliac crest autograft for use in the cage followed by placing an anterior titanium plate bridging the corpectomy site (Aviator™; Stryker, Mahwah, NJ, USA). We elected to stabilize the posterior elements by performing an instrumented C5–C7 fusion. To prevent recurrence, 6 weeks after the operation, the patient was treated with conventional external-beam radiation consisting of a total dose of 2000 cGy. At last followup, 12 months after the operation, the patient denied pain and his left upper-extremity strength and sensation had returned to normal. Radiographs (Fig. 5) showed the instrumentation had maintained its position.

References

1. Azumi N, Sheibani K, Swartz WG, Stroup RM, Rappaport H. Antigenic phenotype of Langerhans cell histiocytosis: an immunohistochemical study demonstrating the value of LN-2, LN-3, and vimentin. *Hum Pathol*. 1988;19:1376–1382.
2. Bertram C, Madert J, Eggers C. Eosinophilic granuloma of the cervical spine. *Spine (Phila Pa 1976)*. 2002;27:1408–1413.
3. Boriani S, Amendola L, Corghi A, Cappuccio M, Bandiera S, Ferrari S, Picci R, Difiore M, Gasbarrini A. Ewing's sarcoma of the mobile spine. *Eur Rev Med Pharmacol Sci*. 2011;15:831–839.
4. Boriani S, Bandiera S, Casadei R, Boriani L, Donthineni R, Gasbarrini A, Pignotti E, Biagini R, Schwab JH. Giant cell tumor of the mobile spine: a review of 49 cases. *Spine (Phila Pa 1976)*. 2012;37:E37–E45.
5. Boriani S, De Iure F, Campanacci L, Gasbarrini A, Bandiera S, Biagini R, Bertoni F, Picci P. Aneurysmal bone cyst of the mobile spine: report on 41 cases. *Spine (Phila Pa 1976)*. 2001;26:27–35.
6. Bunch WH. Orthopedic and rehabilitation aspects of eosinophilic granuloma. *Am J Pediatr Hematol Oncol*. 1981;3:151–156.
7. Calhoun JD, Thompson SB. Vertebra plana in children produced by xanthomatous disease. *Am J Roentgenol Radium Ther Nucl Med*. 1959;82:482–489.
8. Denaro L, Longo UG, Papalia R, Di Martino A, Maffulli N, Denaro V. Eosinophilic granuloma of the pediatric cervical spine. *Spine (Phila Pa 1976)*. 2008;33:E936–E941.
9. DeSanto J, Ross JS. Spine infection/inflammation. *Radiol Clin North Am*. 2011;49:105–127.
10. Garg S, Mehta S, Dormans JP. Langerhans cell histiocytosis of the spine in children: long-term follow-up. *J Bone Joint Surg Am*. 2004;86:1740–1750.
11. Huang W, Yang X, Cao D, Xiao J, Yang M, Feng D, Huang Q, Wu Z, Zheng W, Jia L, Wu S. Eosinophilic granuloma of spine in adults: a report of 30 cases and outcome. *Acta Neurochir*. 2010;152:1129–1137.
12. Junming M, Cheng Y, Dong C, Jianru X, Xinghai Y, Quan H, Wei Z, Mesong Y, Dapeng F, Wen Y, Bin N, Lianshun J, Huimin L. Giant cell tumor of the cervical spine: a series of 22 cases and outcomes. *Spine (Phila Pa 1976)*. 2008;33:280–288.
13. Kamimura M, Kinoshita T, Itoh H, Yuzawa Y, Takahashi J, Ohtsuka K. Eosinophilic granuloma of the spine: early spontaneous disappearance of tumor detected on magnetic resonance imaging. Case report. *J Neurosurg*. 2000;93(2 suppl):312–316.
14. Levine SE, Dormans JP, Meyer JS, Corcoran TA. Langerhans' cell histiocytosis of the spine in children. *Clin Orthop Relat Res*. 1996;323:288–293.
15. Lieberman PH, Jones CR, Steinman RM, Erlandson RA, Smith J, Gee T, Huvos A, Garin-Chesa P, Filippa DA, Urmacher C, Gangi MD, Sperber M. Langerhans cell (eosinophilic) granulomatosis: a clinicopathologic study encompassing 50 years. *Am J Surg Pathol*. 1996;20:519–552.
16. Marco RA, Gentry JB, Rhines LD, Lewis VO, Wolinski JP, Jaffe N, Gokaslan ZL. Ewing's sarcoma of the mobile spine. *Spine (Phila Pa 1976)*. 2005;30:769–773.
17. Martin C, McCarthy EF. Giant cell tumor of the sacrum and spine: series of 23 cases and a review of the literature. *Iowa Orthop J*. 2010;30:69–75.
18. Mesfin A, McCarthy EF, Kebaish KM. Surgical treatment of aneurysmal bone cysts of the spine. *Iowa Orthop J*. 2012;32:40–45.
19. Mills SE. *Sternberg's Diagnostic Surgical Pathology*. Vol I. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:940–941.
20. Novais EN, Rose PS, Yaszemski MJ, Sim FH. Aneurysmal bone cyst of the cervical spine in children. *J Bone Joint Surg Am*. 2011;93:1534–1543.
21. Nyholm K. Eosinophilic xanthomatous granulomatosis and Letterer Siwe's disease. *Acta Pathol Microbiol Scand Suppl*. 1971;216(suppl):1–10.
22. Oakley GJ, Fuhrer K, Seethala RR. Brachyury, SOX-9, and podoplanin, new markers in the skull base chordoma vs chondrosarcoma differential: a tissue microarray-based comparative analysis. *Mod Pathol*. 2008;21:1461–1469.
23. Rimondi E, Mavrogenis AF, Rossi G, Ussia G, Angelini A, Ruggieri P. CT-guided corticosteroid injection for solitary eosinophilic granuloma of the spine. *Skeletal Radiol*. 2011;40:757–764.

24. Ropper AE, Cahill KS, Hanna JW, McCarthy EF, Gokaslan ZL, Chi JH. Primary vertebral tumors: a review of epidemiologic, histological, and imaging findings. Part I: benign tumors. *Neurosurgery*. 2011;69:1171–1180.
25. Sciubba DM, Okuno SH, Dekutoski MB, Gokaslan ZL. Ewing and osteogenic sarcoma: evidence for multidisciplinary management. *Spine (Phila Pa 1976)*. 2009;34(22 suppl):S58–S68.
26. Tay BK, Deckey J, Hu SS. Spinal infections. *J Am Acad Orthop Surg*. 2002;10:188–197.
27. Walcott BP, Nahed BV, Mohyeldin A, Coumans JV, Kahle KT, Ferreira MJ. Chordoma: current concepts, management, and future directions. *Lancet Oncol*. 2012;13:e69–e76.
28. Wang Y, Xiao J, Wu Z, Huang Q, Huang W, Zhu Q, Lin Z, Wang L. Primary chordomas of the cervical spine: a consecutive series of 14 surgically managed cases. *J Neurosurg Spine*. 2012;19:292–299.
29. Willman CL. Detection of clonal histiocytes in Langerhans cell histiocytosis: biology and clinical significance. *Br J Cancer Suppl*. 1994;23:S29–S33.