Primary Malignant Tumors of the Cervical Spine

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Educational Objectives

As a result of reading this article, physicians should be able to:

1. Describe the clinical features of primary malignant tumors of the cervical spine.
2. Define the imaging characteristics of these tumors.
3. Discuss work-up, biopsy, and staging in these patients.
4. Determine the appropriate treatment of patients with primary malignant tumors of the cervical spine including new operative techniques for tumor resection.

Primary malignant tumors of the cervical spine are rare but challenging because of the spine’s unique structure and proximity to vital structures. A thorough clinical and imaging investigation is necessary for the oncological and surgical staging of these lesions. New operative techniques for aggressive en bloc resection of these tumors through combined anterior and posterior approaches and reconstruction of the spinal column have improved the oncological outcome with low local recurrence rates and increased patient survival.

Epidemiology

Malignant bone tumors are rare, accounting for 0.4%-1% of all tumors. Only 10% of these affect the spine, with 4.2%-6.3% affecting the mobile spine above the sacrum. In children and adolescents, malignant tumors account for <30% of all spine tumors, whereas in adults, approximately 75% of spine tumors are malignant. The male to female ratio is 2:1, with an even distribution among all spine levels. Multilevel involvement may be noted, and at diagnosis, the tumor may extend to the paravertebral soft tissues.

Myeloma and solitary plasmacytoma are the most common primary malignant tumors of the adult spine, accounting for approximately 30% of all primary malignant spine tumors. In the Mayo Clinic Registry, only 3% of all myeloma cases affected the cervical spine. Solitary plasmacytomas are diagnosed in approximately 3% of myelomas, with 50% occurring in middle-aged men (mean age 50 years). Non-plasma cell lymphomas account for approximately 10% of primary malignant lesions. In the Mayo Clinic Registry, only 0.8% of all lymphoma cases affected the cervical spine. Non-plasma cell lymphomas are associated with epidural, rather than bony manifestations.

Chordomas of the spine are the second most common solid spine tumors, accounting for 33% of the primary malignant tumors of the spine. Eighty-five percent of all chordomas occur in the sacrum or the clivus. In the Mayo Clinic Registry, only 6% of all chordoma cases affected the cervical spine. These tumors are thought to arise from notochordal remnants in the vertebral disks. They are considered low-grade, slow-growing, locally invasive, indolent malignancies, that behave aggressively in the region of their origin and metastasize late in their course.

Chondrosarcomas are the second most common solid tumors, accounting for approximately 10% of primary malignant tumors of the cervical spine.
spine tumors. In the Mayo Clinic Registry, only 1.5% of all chondrosarcomas affected the cervical spine. Most chondrosarcomas are relatively indolent and tend to recur locally before distant spreading occurs. Various low to highly malignant histologic subtypes of chondrosarcomas have been reported. Osteosarcomas and Ewing’s sarcomas are highly malignant bone lesions, accounting for 10% of malignant primary tumors of the spine. Osteosarcomas occur in the spine in <3% of any other skeletal location. In the Mayo Clinic Registry, only 0.5% of all osteosarcomas and only 0.4% of all Ewing’s sarcomas affected the cervical spine. Ewing’s tumors occur primarily in children. Osteosarcomas may rise primarily in the spine (usually seen in adults), or they may occur secondarily in areas previously irradiated or in patients with Paget’s disease (usually seen after age 60 years).

**CLINICAL PRESENTATION**

Primary malignant tumors of the cervical spine usually manifest pain as the primary symptom. However, they may be diagnosed incidentally on plain radiographs or physical examination. Severe night pain preventing sleep or waking the patient is a common symptom. Spasm, scoliosis, or torticollis; neck stiffness and tenderness, and dysphagia due to compression of the esophagus may be associated symptoms. General symptoms such as weight loss and anorexia can also occur. Neurological deficits are common; however, the incidence of neurological deficits at diagnosis is reported to be <10%. Aggressive tumors produce cord or root compression more rapidly than indolent neoplasms.

In upper cervical spine tumors, pain usually is the initial symptom. Neurologic deficits in these patients are less frequent and occur late in the disease process because of the wide spinal canal at this level. More likely, neurologic symptoms result from spine instability rather than direct compression from the tumor. In lower cervical spine tumors, an insidious onset of cervical pain, usually is the initial symptom. Radicular pain is most common in cases with soft-tissue or bony encroachment on the foramina and may be associated with hypesthesia and muscle weakness.

**IMAGING**

Plain radiographs remain the first imaging tool in the diagnosis and evaluation of malignant tumors of the cervical spine. Standard imaging features include a radiolucent and destructive lesion or severe osteopenia of one or more vertebrae, often associated with pathologic fracture (Figure 1A). Other findings include the loss of a pedicle on an anteroposterior (AP) view, an osteoblastic lesion, the destruction of one or more vertebrae with preservation of the disks, or a paraspinal soft-tissue mass, with or without calcification. Collapse of the vertebral body with radiographic appearance of vertebral plana has been reported. Secondary spine deformities, such as kyphotic or scoliotic angulation, may also be observed.

Bone scintigraphy shows increased radioisotope uptake in the majority of malignant spinal tumors (Figure 1B). The disadvantage is the low specificity due to the high rates of false-positive findings in coexisting degenerative spondylosis in older patients and pyogenic infections of the spine. In most cases, hematopoietic and lymphoproliferative tumors, such as leukemia and plasma-cell dyskrasias plasma-cell malignancies produce little, if any, osteoblastic reaction and therefore are not evident on isotope bone scan.

Computed tomography (CT) is more sensitive than plain films and more accurate than magnetic resonance imaging (MRI) in imaging bone lesions (Figure 1C). Computed tomography is most useful in oncological staging for the CT-guided needle biopsy and the surgical staging and instrumentation planning of patients with diagnosed malignant tumors of the spine. Computed tomography and MRI provide the most detailed views of the transverse and longitudinal extent of the tumors, the presence of a reactive tissue margin, or the invasion of the epidural space (Figures 1D and 1E).

Magnetic resonance imaging is most useful in the evaluation and differential diagnosis of intra- and extradural spinal lesions. Spine tumors usually are evident on MRI before canal compromise or instability develops. However, MRI may not be feasible in some cases (eg, in patients with pacemakers or other metallic implants and clausrophobia or obesity).

Angiography and selective arterial embolization can be performed for vascular tumors.

**BIOPSY**

Biopsy is the final step in the preoperative work-up for the determination of the histological type and staging of the tumor. In vascular lesions, embolization is indicated prior to biopsy. Three types of biopsy techniques are used: percutaneous needle (fine-needle aspiration or CT-guided core biopsy), open incision, and excisional biopsy.

Fine-needle aspiration provides a small amount of tissue and is associated with a high rate of false-negative results. In the cervical spine, its use is limited, and generally is performed to confirm metastatic disease, local recurrence of a known lesion, or lesions with a limited differential diagnosis.

Percutaneous CT-guided core biopsy although more difficult, has been performed successfully in the cervical spine. It is considered the best way to diagnose primary or secondary spine malignancies, with a low incidence of tumor spreading in the surrounding tissues.

Open incision biopsy should be performed in cases where sufficient tissue is required for immunohistochemical, molecular, and microbiological analyses. Open biopsy of cervical spine lesions is best obtained through an anterior approach rather than by laminectomy. This prevents contamination of the epidural space by...
violation of the pseudocapsule of the tumor. Meticulous hemostasis should be maintained. Although often impossible in the cervical spine, biopsy with an adequate margin of healthy tissue should be included, and all contaminated tissue and hematomas should be excised at the definitive surgical procedure. Excisional biopsy should be reserved for tumors of the posterior elements of the cervical spine.

It is recommended that the surgeon performing the definitive procedure also be involved in the biopsy and preoperative staging of the disease.

In few cases, biopsy can be avoided especially when imaging features are strongly consistent with a certain diagnosis such as recurrent primary tumor, metastatic disease, and in cases in which a certain diagnosis, such as multiple myeloma, can be provided.

STAGING

The purpose of staging is to identify the location and local or systemic extent of the lesion and to confirm whether it is a primary or metastatic, benign or malignant tumor.

Oncologic Staging

The principles of the Enneking staging system divides benign bone tumors into three stages: stage 1, also called latent or inactive; stage 2, active; and stage 3, aggressive (Figures 2A-2C). Stage 3 tumors generally do not have a true capsule, or the capsule is thin and discontinuous, and the tumor extends outside of the vertebral compartment of origin. Because of the high rate of local recurrences and probable malignant degeneration, treatment should focus on an aggressive surgical approach, with a safe, wide margin surgi-

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Figure 1: Chordoma of C2 vertebra in a 68-year-old woman. Lateral radiograph shows a destructive osteolytic lesion of the C2 vertebra (A). Bone scintigram shows increased radioisotope uptake (B), CT shows osteolysis of the C2 vertebral body (C), and T-1 (D) and T-2 (E) weighted MRI show anterior and posterior tumor soft-tissue extension.
cal excision of the lesion, in addition to adjuvant therapy as indicated.43-46

According to the same system, malignant tumors are staged as low grade (stage I), high grade (stage II), or any grade tumor with distant metastases (stage III) (Figures 2D-2G). Low-grade, stage I malignant tumors are further subdivided into stage IA (tumors remaining inside the vertebra) and stage IB (tumors extending into the paravertebral compartments). No true capsule but a thick pseudocapsule of reactive tissue is associated with these lesions. The major difference between stage 3 primary benign and stage I malignant tumors is the potential for satellite lesions or foci of active tumor within the pseudocapsule, which often are neglected when inadequate resection is performed. The treatment of choice for these tumors is wide en bloc excision with adjuvant megavoltage irradiation.2

High-grade, stage II malignant bone tumors are also subdivided into stage IIA (intracompartamental tumors within the vertebra) and stage IIB (tumors extending outside the vertebra into the surrounding paravertebral region). Stage III includes the same lesions as stages I and II, but with distant metastases, in addition to intra- (stage IIIA) and extra-compartmental (stage IIIB) extension. Because of the rapid tumor growth, no reactive tissue

Figure 2: Stage 1 benign tumors (A). The tumor is inactive and contained within its capsule (1). Stage 2 benign tumors (B). The tumor is growing, and the capsule (1) is thin and bordered by a pseudocapsule of reactive tissue (2). Stage 3 benign tumors (C). The aggressiveness of these tumors is evident by the wide reaction of healthy tissue (2), and the capsule (1) is thin and discontinued. Stage IA malignant tumors (D). The capsule, if any, is thin (1) and the pseudocapsule (2) is wide and contains an island of tumor (3). Stage IB malignant tumors (E). The capsule, if any, is thin (1), and the pseudocapsule (2) is wide and contains an island of tumor (3). The tumoral mass is growing outside the compartment of occurrence. Stage IIA malignant tumors (F). The pseudocapsule (2) is infiltrated by tumor (3), and the island of tumor can be found far from the main tumoral mass (skip metastasis, 4). Stage IIB malignant tumors (G). The pseudocapsule (2) is infiltrated by tumor (3), which is growing outside the vertebra. An island of tumor can be found far from the main tumoral mass (skip metastasis, 4). (Reprinted with permission from Boriani S et al. Primary bone tumors of the spine. Terminology and surgical staging. Spine. 1997; 22:1036-1044. Copyright © 1997. Lippincott Williams and Wilkins.)
layer is formed and continuous seeding of tumor nodules (satellite nodules) and nodules at some distance from the main lesion (skip metastases) are observed. Extension can also occur into the epidural space.

Surgical Staging

Surgical staging is the final step in the preoperative work-up of the patient. The unique anatomy of the vertebra and the difficulty of spine tumor resection led to the first surgical classification system proposed by Weinstein, Boriani, and Biagini (WBB staging system), which has been further modified and tested.2,3,42,44 In the WBB staging system, the vertebra in the transaxial plane is divided into 12 radiating zones (numbered 1 to 12 in a clockwise order) and 5 concentric layers (A to E, from the paravertebral extrarosseous compartments to the dural involvement). The longitudinal extent of the tumor is recorded according to the levels involved. (Reprinted with permission from Boriani S et al. Primary bone tumors of the spine. Terminology and surgical staging. Spine. 1997; 22:1036-1044. Copyright © 1997. Lippincott Williams & Wilkins.)

A modification of the Enneking oncologic staging system was proposed by Tomita et al.,11 who incorporated a description of the affected anatomic site and extent of the tumor. This system has been reported in relation to the thoracolumbar spine; however, it is relevant to the cervical spine as well. According to this classification system, the vertebral body is divided into five anatomic sites: the body (1), the pedicle (2), the lamina and spinous process (3), the epidural canal (4), and the paravertebral area (5), with the numbers reflecting the common sequence of tumor progression (Figure 4). Intra-compartmental lesions are in sites (1), (2), and (3), and extracompartmental lesions in sites (4), (5), and (6). A type (7) lesion is one with multiple lesions or “skip” metastases (Figure 5). The purpose of this surgical system is to further define the lesions that can be excised en bloc. This can be attempted in lesions (2) to (5) and with a relative indication in lesions (1) and (6). According to the author, wide en bloc surgical resection is not recommended in lesions type (7).

TREATMENT

Management of primary malignant tumors of the cervical spine is challenging. Complete excision of the tumor is the goal of treatment. Until recently, because of the unique anatomic structure of the cervical vertebra, the proximity to major vessels and the spinal cord, and the difficulty attaining wide excision of the spinal tumor, most surgical procedures included curettage and piecemeal intralesional tumor resection. As a result, incomplete tumor excision, tumor cell contamination of the surrounding tissues, and high rates of local recurrences and distal metastases were reported.11,47,48

Lymphoproliferative and plasma cell neoplasms usually are radiosensitive even in response to low doses of conventional radiation. Systemic chemotherapy is also frequently indicated. Surgery is rarely necessary. Indications include progressive neurologic deficits, due to spinal instability, spinal cord pressure or nerve entrapment by tumor mass, or pathologic fracture, or recurrent lesions after maximum dose irradiation.13,17 The prognosis for solitary plasmacytoma is better than multiple myeloma, with a higher mean survival rate.16

The goal of treatment for chordomas of the cervical spine is en bloc surgical resection (Figure 6).18,49 However, in most cases, only marginal or intrasosseal resection is feasible.42,49 Intrasosseal excision is associated with high recurrence rates.13,49 Chordoma is not sensitive to chemotherapy and only high-dose radiation therapy seems to slow the evolution of the disease.13

Chondrosarcomas are usually low-grade tumors and are resistant to irradiation and chemotherapy.16 The treatment of choice is wide surgical resection with wide surgical margins, which in some instances requires total en bloc spondylectomy.21 These tumors tend to recur locally with prolonged disease-free periods before distant metastases occur.

The natural course of osteosarcomas...
usually is rapid and a poor prognosis is anticipated.\textsuperscript{13,22} To improve survival, wide tumor resection is recommended with safe margins.\textsuperscript{13} Although adjuvant radiotherapy has been reported when wide resection is not feasible, osteosarcomas are not radiosensitive. Total en bloc spondylectomy is the treatment of choice for osteosarcomas of the spine, in addition to neoadjuvant and postoperative chemotherapy.\textsuperscript{8,10,13,22,50}

Multi-agent chemotherapy followed by wide tumor resection is the mainstay of treatment for Ewing's sarcoma.\textsuperscript{13} In cases of neurologic deterioration, spinal decompression may precede chemotheraphy. High-dose radiation therapy and chemotherapy may be used as adjuvant to surgical treatment or alone when operative treatment is not feasible.\textsuperscript{24,39}

**Surgical Considerations**

Several studies describing the surgical excision of primary malignant or aggressive benign spine tumors using combined anterior and posterior surgical approaches have been reported.\textsuperscript{4,8,11,21,22,50-52} However, the combined anteroposterior procedures may be more extensive and traumatic than the single posterior or anterior approach and may increase the chance of contamination by tumor cells and subsequent local tumor recurrence.\textsuperscript{11}

Total en bloc spondylectomy has been described for complete tumor resection and oncologic management of primary malignant vertebral tumors of the thoracic spine.\textsuperscript{11,12} The procedure is performed in two steps, consisting of en bloc laminectomy after bilateral pediculotomy using a stainless-steel threadwire saw (step I), and en bloc corpectomy followed by anterior fusion with instrumentation and spacer grafting and posterior spinal instrumentation (step II).\textsuperscript{10,47,48,51}

The major risks in total en bloc spondylectomy are mechanical damage to adjacent neural structures during the excision of the pedicles, possibility of tumor cell contamination during pediculotomy, injury of major vessels during dissection of the anterior aspect of the vertebral body, blood perfusion disturbance of the spinal cord at the level of surgery, and excessive bleeding from the internal vertebral and epidural venous plexus.\textsuperscript{11}

The use of the threadwire saw is believed to minimize tumor cell contamination of the surrounding tissues or the surgical incision.\textsuperscript{9} No major complications such as mechanical damage, dural tears or leakage of cerebrospinal fluid, damage to the nerve roots, neurological complications, or signs of aseptic necrosis, such as bone absorption or collapse and sclerotic changes, have been reported with the use of threadwire saw.\textsuperscript{9,50,53-56}

In the cervical spine, wide surgical resections have been attempted using techniques similar to total “en bloc” spondylectomy. In a recent case report by Fujita et al.,\textsuperscript{18} a chordoma was located on one side of the C5 vertebral body (Figure 6). A special modification was made to allow the threadwire saw to be hooked inside the pedicle. This modification involved ligating the left vertebral artery followed by making troughs in the vertebral body and endplates of C6 and C4. However, the use of the threadwire saw resulted in an intralesional margin on the dura mater near the insertion of the left C6 root because the tumor had invaded the neural foramen at that level.

Cohen et al\textsuperscript{52} described a technique for total spondylectomy for osteosarcoma involving the cervical spine. The method involved separately staged posterior and anterior approaches (Figure 7). However, the resection described in this case was by definition intraslesional.

Ligation of a vertebral artery may sometimes be inevitable to avoid massive hemorrhage during tumor resection surgery. Although several reports\textsuperscript{18,57-59} on this approach exist, because of its vital blood supply and the possibility of other coexisting occlusive disease that might affect the contralateral vertebral artery later in the future, the vertebral artery should be preserved whenever possible.

In a recent study,\textsuperscript{57} the vertebral artery was unilaterally ligated with no postoperative signs of spinal cord, brain stem, or cerebellum ischemic dysfunction. Ligation of a vertebral artery should be performed for safe margin tumor resection, only when the tumor is located on the side of the minor or equal diameter of vertebral artery, which should always be confirmed with preoperative angiography.

For the treatment of chordomas originating at the cranio-cervical junction, the lateral transfacetal retrovascular approach has been reported avoiding neuraxis.
Figure 5: Schematic diagram of the surgical classification of vertebral tumors. (Reprinted with permission from Tomita K et al. Total en bloc spondylectomy: a new surgical technique for primary malignant vertebral tumors. Spine. 1997; 22:324-333. Copyright © 1997. Lippincott Williams & Wilkins.)

Figure 6: CT showing a lytic lesion in the left C5 vertebral body, sclerotic borders, and widening of the left C5-C6 foramen (A). CT showing an osteolytic lesion with lobular pattern accompanied by soft tissue extension (white arrow) in the vertebral body of C5 (B). T1-weighted MRI showing a slight increase in intensity in the lateral side of C5 with soft tissue extension (C). Schematic illustrating the technique used for cutting the left pedicle of C5 using the threadwire saw (D). Postoperative lateral radiograph showing anterior interbody fusion of C5 to C7 with the plate (E). (Reprinted with permission from Fujita T et al. Chordoma in the cervical spine managed with en bloc excision. Spine. 1999; 24:1848-1851. Copyright © 1999. Lippincott Williams & Wilkins.)
Figure 7: Total cervical spondylectomy for osteosarcoma of the C6 vertebra. Illustrations showing the posterior approach for resection of the posterior elements of C5 to C7, exposure of the nerve roots and vertebal arteries bilaterally, transpedicular C6 partial vertebrectomy, placement of a temporary spacer in the vertebrectomy defect, segmental instrumentation and fusion using lateral mass screws (C3 to C5), pedicle screws (T1 to T3) and cross-links. (A) Illustrations showing the anterior approach for bilateral exposure of the vertebral arteries and nerve roots, and en bloc resection from C5 to C7 vertebral bodies including the C5-C6 and C6-C7 intervertebral disks, and reconstruction with a titanium cage filled with allograft and cervical plate from C4 to T1 (B). (Reprinted with permission from Cohen ZR et al. Total cervical spondylectomy for primary osteogenic sarcoma. Case report and description of operative technique. J Neurosurg Spine. 2002; 97:386-392. Copyright © 2002. American Association of Neurological Surgeons.)
retraction.60 This procedure is considered an indication for anterior located vertebral body tumors with lateral extension and vertebral artery invasion, with or without an intradural mass. It allows for spinal cord decompression, C2 corpectomy without C1 or C2 hemilaminectomy, and anterolateral reconstruction and posterior instrumentation. It is considered restrictive when a spacious cephalad exposure is necessary, as in clivus chordomas.60

In the cervicothoracic junction, tumor resection often is troublesome because of the thoracic cage and adjacent neurovascular structures. A combined cervicothoracic surgical approach of anterior cervical access, median sternotomy, and anterior thoracotomy has been reported,61 resulting in gross tumor resection, with maintenance of the sternoclavicular joint and sparing of the uninvolved neurovascular structures.

Wide excision or total en bloc cervical spondylectomy usually results in spinal instability, thus spine reconstruction is necessary, as in the level of the resection. Autografts (eg, iliac crest, fibula, or ribs), allografts, and artificial spacers have all been used to achieve anterior spine fusion in reconstructive surgery.52,53,62,63 Recently, structural titanium mesh cages have been designed with varying available diameters and heights, and great resistance and maintenance of spinal alignment for anterior vertebral body structural support.53,64,65 Inside these cages, autograft or allograft can be inserted for bone fusion.

Preoperative selective arterial embolization after spinal angiography and adjuvant radiation therapy or chemotherapy can be performed as indicated from the preoperative oncological and surgical staging of the disease.3,9

Postoperative adjuvant chemotherapy has been shown to be effective in decreasing local recurrence and improving oncological outcome and survival of patients with osteosarcoma or Ewing’s sarcoma of the cervical spine. Wound
lavage with a cis-platinum solution has been reported after resection of osteosarcoma, although the merit of this practice is unproven.9,66

**CONCLUSION**

Primary malignant tumors of the cervical spine are rare. Neck or radicular pain is the most common initial symptom. Appropriate clinical and radiographic evaluation of the patient, biopsy, oncologic and surgical staging, and adequate operative techniques and adjuvant therapies can improve clinical, oncologic, and functional outcome. Preoperative angiography and selective arterial embolization, adjuvant radiation therapy, or chemotherapy can be performed as indicated. Surgery is the main treatment for most cervical spine malignant tumors. En bloc resection with a wide surgical margin results in a better prognosis. Total en bloc spondylectomy is a new, promising surgical technique to allow complete tumor resection with low rates of local tumor recurrence. Adjuvant irradiation or chemotherapy is indicated for certain tumor histologies.66

**REFERENCES**

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