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Chordoma of the Spinal Column

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Chordomas account for 2% to 4% of primary malignant bone tumors and arise from notochordal remnants in spinal segments from the clivus through the coccyx. Although they are considered slow-growing sarcomas with a low initial propensity for metastasis, they are often associated with significant local bone destruction and neural compression. Unfortunately, such lesions show poor response to standard ionizing radiation and chemotherapy, and intralesional surgical resection leads to a high likelihood of local recurrence. Current treatment paradigms include radical en bloc resections as initial management when possible and use of high-energy photon or proton beam radiation for recurrent or residual disease. Because up to 50% of such lesions are in the sacrum, patients undergoing aggressive surgical resection often benefit from a multidisciplinary team approach involving neurosurgery, general surgery, plastic surgery, medical and radiation oncology, and rehabilitation services.

Epidemiology

Chordomas are rare tumors that occur with an overall incidence of less than 1 in 1,000,000 persons [1]. Interestingly, however, they still represent the most common primary malignant bone tumor of the sacrum [2] and the most common primary malignant tumor of the mobile spine [3]. In terms of anatomic distribution, it is generally accepted that sacrococcygeal location is the most common (45%–50%), followed by spheno-occipital location (35%–40%) and then location in the mobile spine vertebral bodies (10%–15%) [1]. A large National Cancer Institute epidemiologic study of 400 cases found an almost equal frequency at the skull base, mobile spine, and sacrum, however [1]. Within the mobile spine, cervical location is the most common (nearly 50%), followed by lumbar and then thoracic locations [3]. Chordomas can occur at any age, even in extremely young children, but they usually appear in middle age. The median age at diagnosis is 58.5 years, and only roughly 20% occur in patients who are younger than 40 years of age [1]. They occur almost twice as frequently in men compared with women, and the incidence in people of black African descent is extremely rare [4].

Pathophysiology

During embryonic development, the notochord runs the entire length of the spine. Although the nucleus pulposus is the only anatomic derivative of the notochord in the developed spine, chordomas do not originate from this structure but, instead, arise from the vertebral body. Nonneoplastic remnants of the notochord, called ecchordosis physaliphora, are thought to exist in the vertebral body and occasionally form small symptomatic masses [5]. Chordomas are low-grade malignant tumors that are believed to

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arise from these remnants. Consequently, they are limited to the axial skeleton and may involve the skull base, mobile spine, or sacrum. The midline location of these tumors also relates to this proposed etiology.

On histologic preparations, the physaliphorous (from the Greek word for "bubble-bearing") cells that constitute chordomas contain abundant vacuolated cytoplasm. Not uncommonly, foci of bland/benign hyaline cartilage are prominent in chordoma sections, denoting the subtype chondroid chordoma. Immunohistochemically, a distinct profile exists for chordomas allowing differentiation from the two most commonly confused entities, chondrosarcomas and mucinous adenocarcinomas. Specifically, chordomas are immunoreactive for S-100 and epithelial membrane antigen (EMA) [5].

Chordomas are generally considered "slow-growing" but are locally aggressive. They arise in the vertebral body and may grow posteriorly to compress the spinal cord or nerves, or they can extend anteriorly into paraspinal soft tissues. Although metastases are infrequent initially, roughly 30% of sacrococcygeal chordomas eventually metastasize [6]. In the sacral region, chordomas usually involve the fourth and fifth sacral vertebrae and protrude anteriorly into the pelvis [7]. They usually do not invade pelvic structures because of limited growth through the presacral fascia but spread insidiously along the surfaces and interstices of local bone. Poor prognostic factors include large size, subtotal resection, microscopic necrosis, and Ki-67 index greater than 5% [8]. Current series suggest that 5-year survival is 50% to 68% and 10-year survival is 28% to 40% [1,9–11].

Evaluation of patients

History and physical examination

The most common signs and symptoms of chordoma are location dependent, with any combination of pain, weakness, sensory abnormalities, or bowel/bladder/sexual dysfunction. Because most of these tumors are slow growing, they are often associated with the insidious onset of pain for many months to years before definitive diagnosis [3,9]. The mean duration of symptoms in one review ranged from 4 to 24 months (mean of 14 months) [12].

In the sacral region, the capacity of the spinal canal and pelvis to accommodate regional expansion allows tumors to attain enormous dimensions by the time of clinical detection. In these cases, the most common presenting symptom is pain in the lower back or sciatic region, followed by constipation (from rectal compression), neurologic compromise (attributable to sacral plexus involvement), and presence of a sacral or gluteal mass. In the mobile spine, neurologic deficit occurs with increased frequency compared with sacrococcygeal tumors, approaching 50% in one series [9,11]. Chordomas in the cervical spine may also present with airway obstruction or dysphagia or as an oropharyngeal mass because of the extensive soft tissue component of the tumor.

Imaging

The usual appearance on CT consists of lytic bone destruction in addition to a disproportionately large soft tissue mass (Fig. 1). Calcification is present in 30% to 70% of cases [13]. Like giant cell tumors, but unlike other tumors of the vertebral column, chordomas often infiltrate the intervertebral disc space as they spread to adjacent vertebral bodies. On T1-weighted MRI, chordomas appear iso- or slightly hypointense compared with muscle, and on T2-weighted images, they are hyperintense to muscle (Fig. 2) [13]. They enhance with gadolinium and often have foci of low signal attenuation in the areas of calcification. Unlike most bone tumors, chordomas may show reduced uptake or normal distribution of isotope on bone scan [14].

Special tests

All patients referred for resection of chordomas should be assessed completely for evidence of local and systemic spread. This may require CT of the chest, abdomen, and pelvis and a bone scan. In addition, although imaging may appear quite characteristic for the diagnosis of chordoma, tissue-proved diagnosis is still of paramount importance because it may dictate the degree of surgical aggressiveness and the type of adjuvant therapy. Of note, there is a marked tendency of chordomas to recur along a biopsy tract [8]. For this reason, biopsy needles should not transgress other body cavities (eg, oral cavity, rectum) and the biopsy tract should be clearly marked on the skin, such that subsequent surgical resection of the tumor involves this potential site of recurrence.

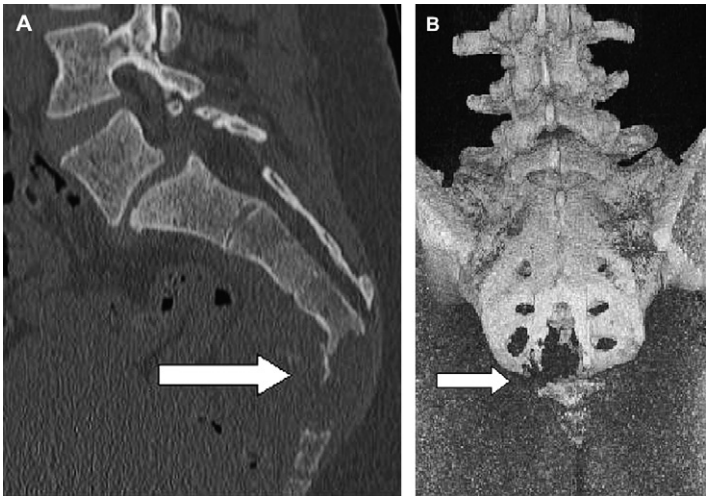

Fig. 1. CT of sacral chordoma shows lytic destruction on two-dimensional sagittal reconstruction (*A*) and three-dimensional reconstruction (*B*) (*arrows*).

Treatment

Goals

Low-grade malignancies, such as chordoma, require a radical en bloc resection, including a circumferential margin of uninvolved tissue, to effect cure [6]. The extent of surgical resection has been found to play a major role in determining the length of disease-free survival (Fig. 3) [6,12,15,16]. Although a distinct capsule is often seen within soft tissues, a wide margin of tissue should be resected to reduce the risk for local recurrence [17]. Furthermore, the margins within bone are often indistinct. Thus, in the sacrum, where the intervertebral discs have been replaced with bone by adulthood, surgical resection should extend at least one whole sacral segment beyond the area of gross disease if the advancing edge is to be included in an en bloc resection.

Surgery

Sacral tumors

Because of the complex anatomy of the sacral region, aggressive resections are technically

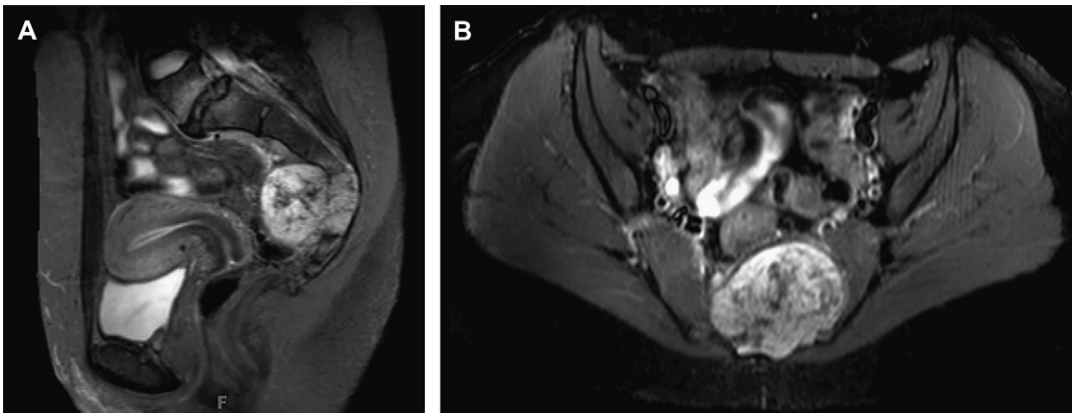

Fig. 2. T2-weighted MRI of a distal sacral chordoma shows a hyperintense expansile mass in the sagittal (*A*) and axial (*B*) planes.

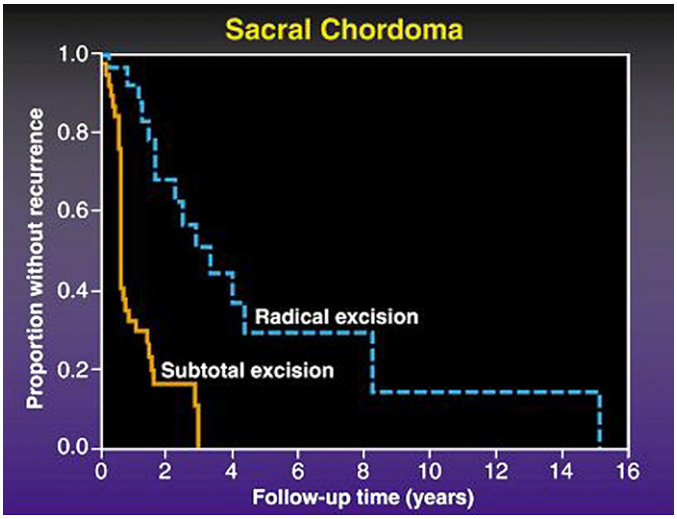

Fig. 3. Kaplan-Meier estimates of time to recurrence for patients undergoing surgery for treatment of sacral chordomas, with radical resection in 21 patients and subtotal resection in 33 patients. (*Data from* York JE, Kaczaraj A, Abi-Said D, et al. Sacral chordoma: 40-year experience at a major cancer center. Neurosurgery 1999;44(1):74–9 [discussion: 79–80].)

demanding procedures that often require the expertise of multiple surgical specialties, including surgical oncology, neurosurgery, orthopedic surgery, vascular surgery, and plastic surgery. Appropriate preoperative planning requires a firm anatomic understanding, familiarity with the advantages and limitations of the different exposures, and a clear sense of the surgical objective. Because of large tumor size and complicated regional anatomy, standard unidirectional approaches (eg, anterior, posterior, perineal, lateral) are frequently combined to obtain adequate exposure. Combined approaches may be performed simultaneously, performed consecutively under the same anesthetic, or staged.

Neurologically speaking, wide resections may necessitate the intentional sacrifice of sacral roots, resulting in the loss of bowel, bladder, and sexual functions. The resulting clinical deficits depend on the level and number of sacral nerve roots that are sacrificed. Sacral amputations can be divided into low (S3 and below), middle (S2–S3), and high

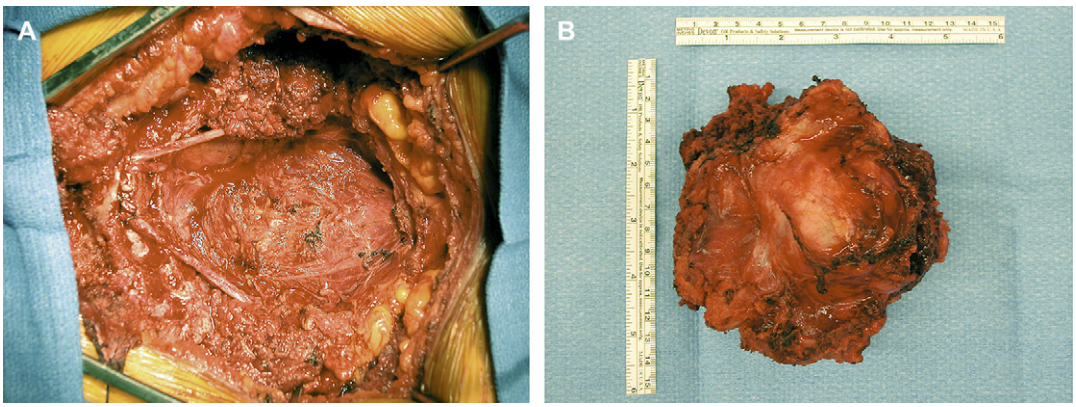

Fig. 4. Intraoperative images after high sacrectomy for chordoma resection show operative field (*A*) and a specimen removed en bloc (*B*).

(S1–S2) resection and total sacrectomy (above S1) (Fig. 4) [18]. Additional resection of the unilateral pelves may also occur, a hemipelvectomy. In patients with amputations distal to S3 (with removal of the distal sacral roots and the coccygeal plexus), deficits are usually limited, with preservation of sphincter function in most and possible reduction in perineal sensation and sexual ability [18]. Transverse resections involving S2 to S3 (including removal of one to all four roots of S2–S3) involve the highest variability in functional results. There is seldom any relevant motor deficit; however, many patients have saddle anesthesia and significant reduction in sphincter control [19]. It has been reported that that functional urinary and fecal continence is generally achievable if at least one S2 nerve root can be preserved [18,20]. Not surprisingly, section of the S1 nerve roots or levels proximal to S1 results in clinically relevant motor deficits, such as walking with external support, and loss of sphincter control and sexual ability. Removal of sacral roots (S1–S5) on only one side (S1–S5) results in expected ipsilateral deficits in strength and sensation; however, sphincter control may be only partially compromised [20].

Additional considerations of radical sacral chordoma resections include infection, blood loss, soft tissue reconstruction, and spinopelvic stabilization. The lower extent of posterior sacral incisions is located near the anus; thus, wound contamination is of great concern. In addition, there is risk for inadvertently entering the bowel during the procedure. Because of large soft tissue defects created by radical resection, involvement

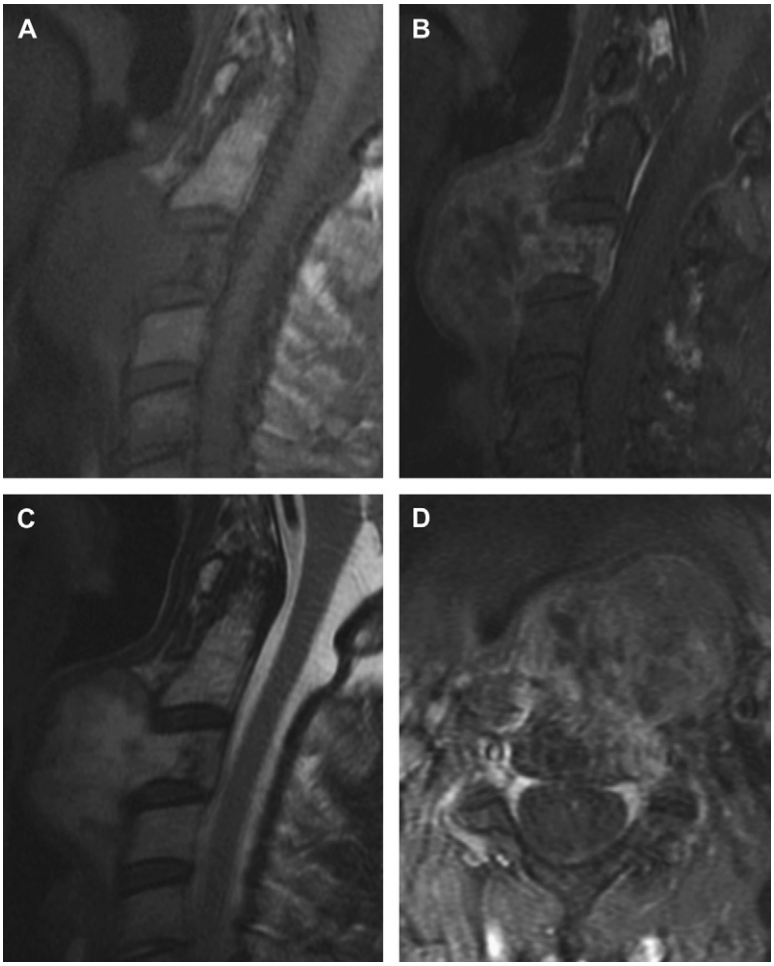

Fig. 5. MRI demonstrates extensive retropharyngeal extension of a C3 chordoma. Sagittal T1 (*A*), sagittal T1 with gadolinium (*B*), sagittal T1 (*C*), and axial T2 (*D*) images are shown.

of plastic surgery is recommended. Rotational gluteal flaps or transpelvic vertical rectus abdominis myocutaneous (VRAM) flaps can be used to obliterate dead space and improve wound healing. Finally, high sacral amputation can disrupt spinopelvic stability, requiring advanced instrumentation techniques to reconstruct the continuity of the pelvic ring and spinal column [21]. Multiple instrumented fixation procedures have been described to allow the patients earlier mobilization [21–23].

Tumors of the mobile spine

Spondylectomy, the term used to describe complete vertebral segment removal, is best suited for well-demarcated primary spinal neoplasms that involve all vertebral elements circumferentially, have not metastasized, and have not invaded intradurally. Recent advances in imaging techniques may play a role in improving the prognosis of chordoma by discovering small tumors [24–27], which can be treated more easily with an en bloc resection. Unfortunately, inadequate tumor margin is the main factor negatively affecting prognosis [8] and seeding of the tumor [28]; thus, large chordomas may not be amenable to oncologically adequate resection [29]. As shown by Boriani and colleagues [3], the rate of local recurrence after intralesional excision of mobile spine chordomas, even if associated with conventional radiation therapy, is consistently higher and earlier (8 of 12 cases at an average of 37 months).

The most common location for chordoma of the mobile spine is the cervical vertebrae, followed by lumbar and thoracic regions in descending order. The C2 and C3 vertebrae are the most commonly involved, and tumors here can have significant extraspinal extension into the retropharyngeal space and epidural spread with spinal cord compression (Fig. 5). Rarely, lesions at separate vertebral levels may be seen and may represent benign notochordal rests. Multifocal chordoma is extremely rare. Surgery for chordoma of the upper cervical spine requires special planning with multidisciplinary teams, including ear, nose, and throat (ENT) and plastic surgeons assisting in access and closure. For anterior approaches after posterior osteotomy and stabilization, transoral approaches are usually not sufficient to complete en bloc resection. Transglossal and transmandibular approaches are often used to provide adequate visualization and working room to prevent tumor capsule violation during surgery (Fig. 6). Complications from en bloc resection in the upper cervical spine can be common and significant and include instrumentation failure (because of inadequate instrumentation at the clival-cervical junction), swallowing difficulties, hoarseness, Horner's syndrome, and hypoglossal nerve injury, among others. Tracheostomy is usually required and is done in

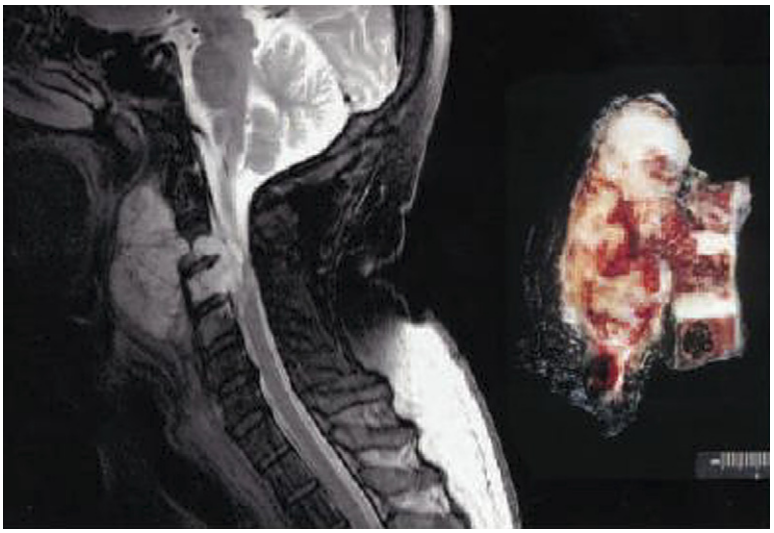

Fig. 6. (*Left*) Sagittal T2-weighted MRI shows a chordoma of the subaxial cervical spine. (*Right*) Sagittal cross-section of the specimen after en bloc resection is also shown. (*From* Rhines LD, Fourney DR, Siadati A, et al. En bloc resection of multilevel cervical chordoma with C-2 involvement. Case report and description of operative technique. J Neurosurg Spine 2005;2(2):199–205.)

prophylactic fashion, as is long-term feeding tube/percutaneous endoscopic gastrostomy (PEG) placement.

Intralesional extracapsular excision is a reasonable choice when en bloc resection is not feasible or the possibility of local contamination by tumor is high [3]. This option is especially relevant in the cervical spine, where en bloc resection is rarely possible and is highly morbid and the margin is usually intralesional [30,31]. Furthermore, the morbidity associated with dural resection must be anticipated [3]. In general, resection of chordoma in the mobile spine should be attempted when feasible by removing the complete vertebra and surrounding the pseudocapsule with "extracapsular" excision, followed by referral to radiation oncology (Fig. 7). This procedure guarantees an excellent rate of long-term local control [3]. In cases in which gross or microscopic residual tumor is likely or in cases of recurrent tumor growth, the combination of palliative or debulking surgery with high-energy radiation seems promising [11,32].

Adjuvant therapy

Radiation therapy

Chordomas are considered to be relatively radiation resistant, requiring high doses for successful control [33]. Many reports have failed to show any significant benefit from conventional or hyperfractionated radiation therapy after subtotal tumor excision [16,34,35]; however, others have found that subtotal excision plus radiotherapy was superior to subtotal excision alone in lengthening disease-free survival [6,36]. In general, between 60 and 65 Gy is considered a minimum useful dose, but ensuing collateral damage is not uncommon [37,38]. It has been difficult to assess the optimal radiation dose because the available data often have variation in the degree of surgical resection; because of the multiplicity of surgical procedures; and because of the postoperative policy used for the timing, delivery, and quality of the radiotherapy [35,39]. In recent years, however, significant advances have been made in the delivery of radiotherapy with photons, specifically using the technique of intensity-modulated radiotherapy (IMRT) [32,40]. IMRT allows greater conformal delivery, thus achieving higher doses to the target and lower doses to surrounding tissues.

Delivery of radiotherapy using protons also seems to be promising. Protons permit improved sparing of critical organs because of the particular ballistics of protons, in which dose deposition is limited mainly to the so-called "Bragg peak" [41]. Thus, the integral dose is low, and the treatment is extremely conformal to the target volume [42]. Interestingly, a planning exercise comparing photon and proton beams showed that both treatments achieve equally homogeneous coverage of the target volume but that the dose administered to critical organs was lower using protons [43], allowing 15% to 30% greater delivery of radiation dose with the possibility of improved local control or survival [40]. As a result, the use of proton therapy for such radioresistant tumors located near highly radiosensitive critical organs may prove beneficial.

Chemotherapy

Likely because of their low malignancy grade, chordomas have not been shown to be sensitive to chemotherapy. Recently, the use of imatinib mesylate (Gleevec [Glivec]; Novartis Pharma AG, Basel, Switzerland), an inhibitor of platelet-derived growth factor receptor-β (PDGFRβ), was used on six patients with advanced disease [44]. Interestingly, it was found to have antitumor activity in these patients. Larger clinical trials are currently underway.

Summary

A large proportion of patients who have chordoma (approximately 50%–70%) are not cured of their disease and ultimately die [1]. Current series suggest that survival at 5 years is 50% to 68% and survival at 10 years is 28% to 40% [1,9–11]. Chordomas have been shown to metastasize to the lungs, bone, skin, brain, and viscera in up to 5% of cases at the time of diagnosis and in up to 65% of cases late in the disease course [11,45–49]. Despite such metastatic potential, survival seems to be affected more by local progression of disease [9]. Because of the frequent large size at the time of diagnosis, locally invasive nature, and challenges of obtaining tumor-free margins around the spine, inadequate surgical treatment is frequent [15,50]. Unfortunately, despite the use of radiotherapy as an adjuvant therapy, local recurrence is common after subtotal resection [9,11]. Thus, although there are anecdotal reports of successful long-term control using radiotherapy regimens, it is generally agreed that

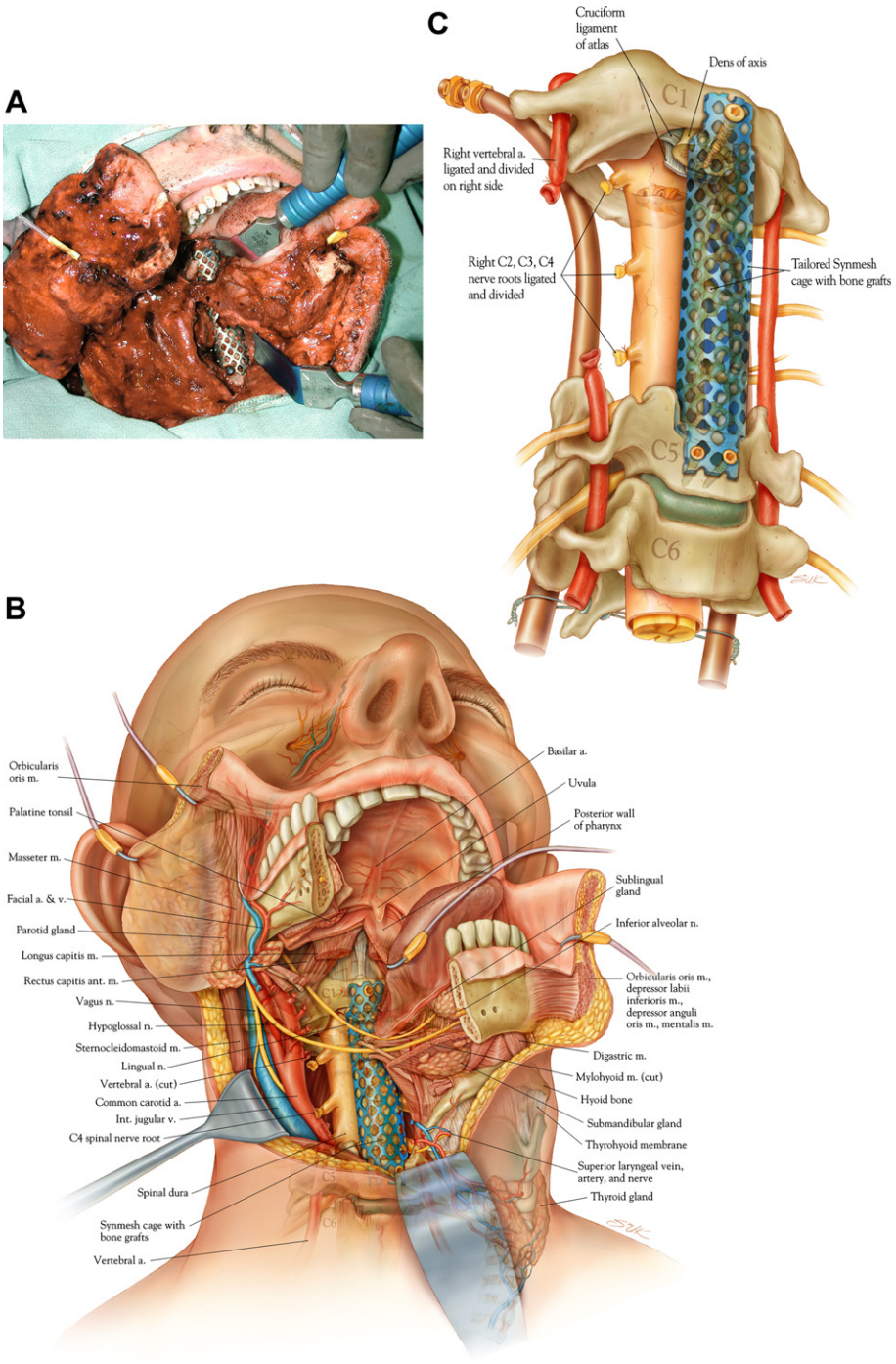

Fig. 7. Series of images shows approach and final construct after radical resection of cervical chordoma. (*A*) Intraoperative photograph of exposure. (*B*) Artist's depiction shows the complete exposure with transmandibular access and cage reconstruction in situ. (*C*) Illustration of the final construct. (*D*) Postoperative axial CT images with bone windows and sagittal reconstructed images reveal the position of the screws, cage, and posterior rods. (*From* Rhines LD, Fourney DR, Siadati A, et al. En bloc resection of multilevel cervical chordoma with C-2 involvement. Case report and description of operative technique. J Neurosurg Spine 2005;2(2):199–205.)

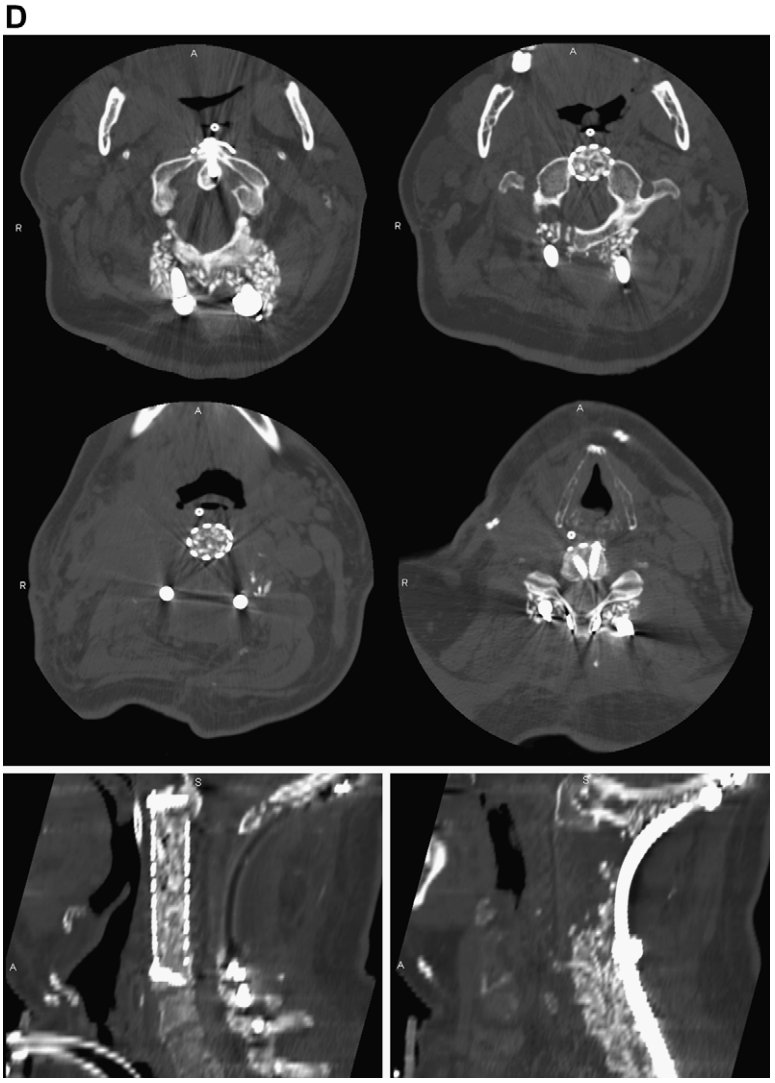

Fig. 7 (*continued*)

aggressive en bloc surgical resection is the treatment of choice when technically feasible [6,9,11].

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