Eur Spine J (2009) 18:293–300
DOI 10.1007/s00586-009-0907-y

GRAND ROUNDS

Upper cervical spine chordoma of C2–C3

Liang Jiang · Zhong Jun Liu · Xiao Guang Liu · Qing Jun Ma · Feng Wei · Yang Lv · Geng Ting Dang

Published online: 17 February 2009

Abstract

Chordoma is a rare low-grade malignant neoplasm derived from the remnants of the embryonic notochord. This locally invasive neoplasm is subject to recurrence after treatment. The median survival time is estimated to be 6.3 years. Various treatment approaches have been attempted, including radical excision, radiotherapy and chemotherapy. Treatment outcome is significantly influenced by the size and site of the chordoma. Recently, Imatinib, a molecular-targeted agent, has been shown to have antitumor activity in chordoma. Proton radiotherapy, stereotactic radiotherapy and intensity-modulated radiotherapy have also been used. Surgical treatment is still the primary choice for chordoma. It has become more aggressive in recent years, evolving from intralesional or partial excision to *en bloc* resection. However, upper cervical localizations make such en bloc resection in most cases not possible. We present and discuss the therapeutic challenges of a young female with large retropharyngeal chordoma who presented to our institution after conventional photon beam radiotherapy. This C2/3 tumor was classified IB according to the Enneking classification. It distributed to layers A–D and sectors 1–6 according to the Weinstein Boriani Biagini Classification. The left vertebral artery (VA) was encapsulated and displaced. One stage intralesional extracapsular tumor excision and reconstruction was achieved by combined bilateral high anterior cervical approaches and posterior approach. No recurrence or metastasis was observed 3 years after the operation. She returned to her previous occupation as office worker.

Keywords Chordoma · Atlantoaxial spine · Surgery

Case presentation

A 26-year-old female presented to our institution after a transoral biopsy of a large retropharyngeal tumor, which was diagnosed as a chordoma. She had dysphagia and neck pain 9 months ago. The retropharyngeal mass was noticed by otolaryngologist. After transoral biopsy, she had conventional photon beam radiotherapy with 40 Gy and then her symptoms totally disappeared. Since there was no reduction of tumor volume 6 months after radiotherapy, she was referred to our department. She had no other significant medical history and she did not exhibit any neurological deficit.

L. Jiang · Z. J. Liu (✉) · X. G. Liu · Q. J. Ma · F. Wei · Y. Lv · G. T. Dang
Orthopaedic Department, Peking University Third Hospital, No 49. North Garden Street, HaiDian District, 100191 Beijing, China
e-mail: zjliu@bjmu.edu.cn

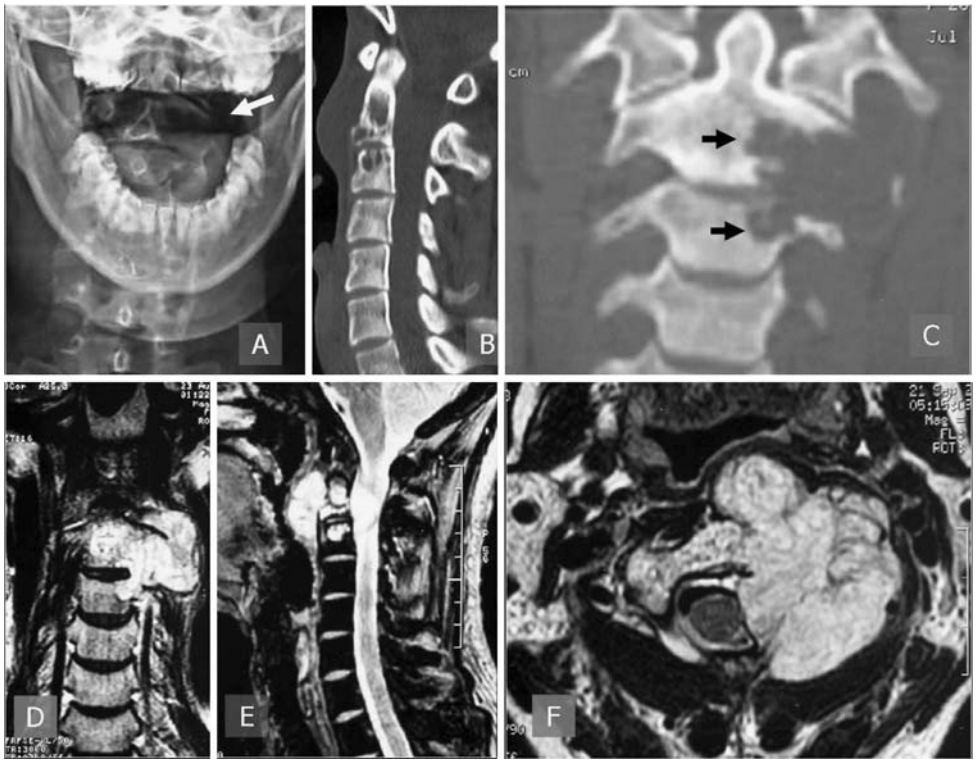

Fig. 1 X-rays, CT and MRI of the C2–3 retropharyngeal mass

Diagnostic imaging section

Plain radiographs showed a poorly demarcated lesion of the left C2 vertebral body on the open mouth view (Fig. 1a arrow). A computed tomography (CT) scan showed an erosive lesion of C2 and C3 (Fig. 1b, c). Magnetic resonance imaging (MRI) showed that the tumor extended from the bottom of the odontoid to C3 vertebra in the sagittal and coronal plane. In the axial plane, it compressed the dura and the left internal carotid artery. The left vertebral artery (VA) was encapsulated and displaced. The spinal cord was displaced to the right by the tumor. This C2/3 chordoma distributed to layers A–D (Fig. 2), sectors 1–6 according to the Weinstein Boriani Classification [2], therefore should be classified IB (malignant extracompartmental) according to the Enneking classification.

Diagnostic, epidemiology

Chordoma is a relatively rare low-grade malignant neoplasm deriving from remnants of the notochord, constituting between 1 and 4% of malignant bone tumors. It predominantly arises from the axial skeleton, while extra-axial chordoma has also been reported. Its incidence has been estimated to be one per one million inhabitants per year. It can affect patients from all ages with a predilection for men with a ratio of 1.6–1 (10). The frequently reported anatomic distribution of chordoma, sacral ~50%, spheno-occipital ~35%, spinal ~15%, was based primarily on 262 patients from the Mayo Clinic experience. Based on more recent 400 cases from the United States [10], 32% of cases were presented at cranial sites, 33%

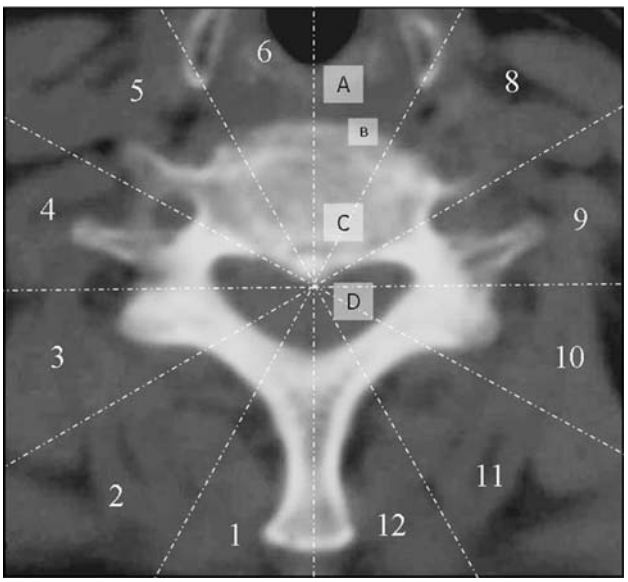

Fig. 2 Layers (*A–D*) and Quadrants involvement according to Weinstein Boriani Classification (normal cervical vertebra represented)

spinal and 29% sacral. Median age is around 60 years, but skull-base presentations affect a younger age, and may even occur in children and adolescents.

Chordoma is characteristically slow-growing, locally invasive neoplasm. In most cases, the Enneking stage is IB—low grade malignant, extracompartmental. Additionally, they can be difficult to distinguish radiographically and pathologically from chondrosarcoma. Sometimes, chordoma has dumbbell shape which could be diagnosed as neuromas. Spine chordomas have also been diagnosed as tuberculosis and hemangioma. The mainstay to achieve appropriate diagnosis is a biopsy performed by trocar under CT scan control with the biopsy track that can be excised during the surgical excision.

Metastases are rare and occur to the lung or to the spine, exceptionally they can occur in other sites of the musculoskeletal system or even in the skin, brain, and other organs. The survival rate appears to be affected more by local tumor progression than by metastasis. The life expectancy from diagnosis is 6 months to 2 years in the untreated skull base chordoma patient. Median survival was 6.3 years in the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute, looking at a 22 years database record. In the United States the 5- and 10-year relative survival rates were 67.6 and 39.9%, respectively. There were no significant differences in survival although median survival was slightly lower in spinal chordomas (5.9 years) compared to cranial (6.9 years) and sacral (6.5 years) presentations.

Because of their location, behavior, and the confusing diagnostic picture, chordomas can be difficult to manage. Treatment outcome is significantly influenced by the size and site of the chordoma. In general, cervical chordomas are so uncommon that articles have reported long-term follow-up evaluation of such tumors on a case-by-case basis only.

Atlantoaxial chordoma is extremely difficult to treat mainly because of its location close to vital structures. Since there is a large dural space at the C1–C2 location, the tumor usually gets quite large before the patient has some clinical manifestation. Compression of neural tissues and invasion of the brainstem or spinal canal may result in serious neurologic complications. It often encapsulates and/or displaces the vertebral artery and nerve roots.

Rationale for treatment and evidence based literature

Various treatment approaches have been attempted, including isolated radiotherapy, combined radiation and surgical excision, and surgical excision alone. Surgery remains the treatment mainstay of chordoma. Excellent team work is needed for aggressive and successful surgical treatment in most cases. These factors plead for early referral to a tertiary care center with advanced surgical capabilities and availability of newer modalities of radiation therapy.

Medical treatment

Chemotherapy has long been known to be inactive in chordoma. It alone might be an option for supportive care once the disease extends and progresses. Cisplatin could be used locally after tumor resection, if marginal tumor contamination is suspected. Recently, Imatinib, a protein-tyrosine kinase inhibitor and a molecular-targeted agent, has been shown to have antitumor activity in chordoma [9]. The mechanism is poorly understood, although blockade of platelet-derived growth factor (PDGF) signaling has been proposed as the cause of tumor control.

Radiotherapy

Chordomas were traditionally recognized as radioresistant. The tolerance dose of the spinal cord is lower than the curative dose, which should at least be in the 70 Gy range [3]. But radiation is valuable, especially for incomplete excision. In conventional photon radiotherapy a dose of less than 45–50 Gy is well within the radiation tolerance, given less than a 5% probability of myelopathy within 5 years. However, with the advent of new radiation modalities (i.e. the proton beam, charged carbon ions, stereotactic radiotherapy and intensity-modulated radiotherapy), it is possible to deliver high doses of radiation while protecting vital structures. Adjuvant radiation is now warranted and has offered improved clinical outcomes. There is extensive experience in the management of chordomas with proton beam therapy, and favorable results have been demonstrated [6]. For the radiation oncologist it is easier to identify the tumor margin before the surgery, but such preoperative radiotherapy might lead to higher operative and post operative complication rates. Postoperative radiation is more common in clinical practice, but the tumor margin is more difficult to identify and the metal implants might disturb the radiation efficacy. Radiation ports also need to be configured to treat the surgical route and the tumor bed in order to reduce the risk of surgical seeding. The cost-effectiveness ratio for carbon radiotherapy is 2,539 € per 1% increase in survival, or 7,692 € per additional life year [7].

Most authors suggest that maximal tumor excision surgery followed by high-dose radiotherapy should be the standard of care for these patients, while Boriani have demonstrated that margin-free en-bloc resection alone is enough.

Surgical treatment

Chordomas are characterized by frequent recurrences after incomplete surgical resection, usually within 2–3 years. Boriani, states that "Prognosis is heavily affected by the appropriateness of the first surgical treatment; once recurred, further treatments are always unsuccessful at midterm." Others may prefer incomplete surgical excision to preserve initially the neurologic function, despite the risk of increased recurrence that will lead to further palliative surgery.

Surgical treatment has become more aggressive in recent years, evolving from intralesional or partial excision to *en bloc* resection. In 1997, Weinstein, Boriani et al. described their Classification system for surgical staging for spine tumors. Such system is based on dividing the vertebra in 12 quadrants and different layers of tumor involvement from A to D. Tomita described total *en bloc* spondyloectomy (TES) using a threadwire T-saw for malignant vertebral tumors in the thoracolumbar spine. To achieve a wide resection margin, Boriani and his colleagues even removed the dura infiltrated by tumor and reconstructed the dura defect with dural patch.

In 2006, Boriani and his colleagues [1] published a retrospective study of 52 chordomas cases of the mobile spine in a 50-year period. Twelve of 16 cases having intralesional extracapsular excision with radiation had recurrence at average 30 months, while 12 of 18 patients having en bloc resection are continuously disease-free (CDF) at average 8 years. They noted that the only treatment protocol associated with CDF at follow-up longer than 5 years is margin-free en bloc resection. Major complications include vertebral artery injury, cerebrospinal fluid (CSF) leak, nerve palsies and paralysis. The mortality rate for skull base tumors is frequently quoted at 5%, and this number is 7.7% in Boriani's spine series.

In his series no differentiation in the type of radiotherapy used was mentioned. They also did not discuss the difference between cervical and thoracolumbar chordoma. Cervical tumor excision, especially in the atlantoaxial region, might mandate more sophisticated surgical technique. In the cervical spine few cases have been reported of *en bloc* excision, due to anatomical constraints. Even less radical resection case has ever been reported for atlantoaxial chordoma [11]. The peculiar anatomical complexity of the cervical region includes the dens, the vertebral arteries, the transverse processes around and the nerve roots. Since most chordomas are stage IB at diagnosis, margin free excision means resection of paravertebral muscle, nerve root, vertebral artery, even dura or retropharyngeal mucosa. These seem impossible for most cases.

In 1999, Tomita et al. [5] first described TES for cervical chordoma (IB) through a single anterior approach with T-saw. Unfortunately, after the C5 vertebral body had been removed with a T-saw the residual tumor along the C6 root and dura mater had to be removed in a piecemeal fashion. The tumor bed was irrigated by distilled water and cisplatin solution and then underwent adjunctive radiotherapy. Unfortunately, the chordoma recurred 9 years later in the soft tissue (Tomita personal communication). In 2007, Boriani et al. [8] reported en bloc excision for a C4 chordoma (IA) with combined posterior and anterior approach. He concluded that TES is feasible in the midcervical spine by double approaches, provided the tumor involves only layers B and C, with a maximum extension to sectors 5–8. Currier et al. [4] has a similar case with 9 years follow-up.

There are three major anterior approaches for atlantoaxial chordoma. The experience and abilities of the surgical team dictates the surgical procedure used. (1) Bilateral high anterior cervical approach can provide clear visualization of C2 vertebral body and bilateral transverse processes, while the dens is not appropriately exposed [13]. (2) The anterior midline transoral with/without transpalatine approach is for spinal lesion located from the midclivus down to the level of C3 and laterally within 2 cm to either side of the midline. However, the tumor cannot be radically excised by this approach, if it extends laterally outside the transverse process. Menezes reported transpalatopharyngeal approach for 18 clivus-craniocervical chordoma cases in 2001. He used piecemeal excision with judicious use of curet and a diamond bur for occipital condyles or atlantal lateral mass tumor involvement. The author did not provide radiotherapy and follow-up information in detail; at least one patient had no tumor progression for 10 years. (3) Transmandible approach combined with anterior cervical approach could provide ideal exposure from clivus to lower cervical spine. This approach is more aggressive and often requires a free flap for the posterior pharyngeal wall reconstruction. Rhines et al. [12] reported the most aggressive TES for C2–4 chordoma (IB) in 2005. They used a right lateral neck dissection and a transmandiblar, circumglossal, retropharyngeal exposure.

Procedure (surgery, intervention)

The tumor was classified as IB, TES seemed not feasible. Because of its large volume and its extent in the soft tissue and in the spine canal it was removed by intralesional spondylectomy through a single stage combined anterior and posterior approach. The most important step

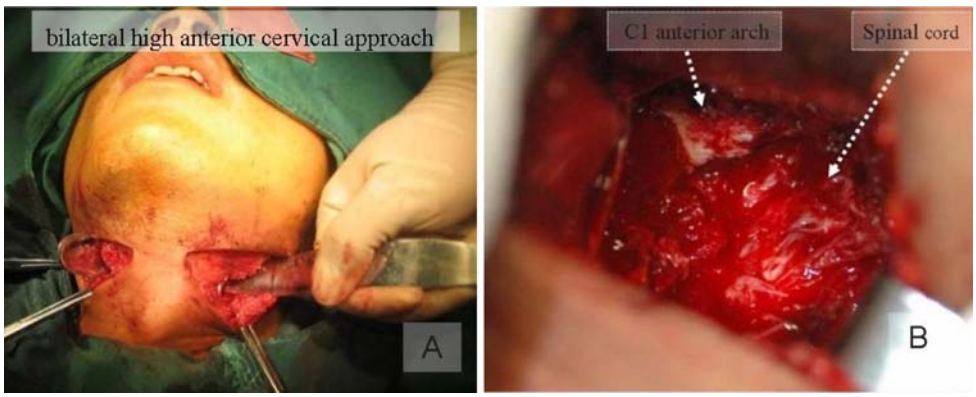

Fig. 3 Procedure imaging section

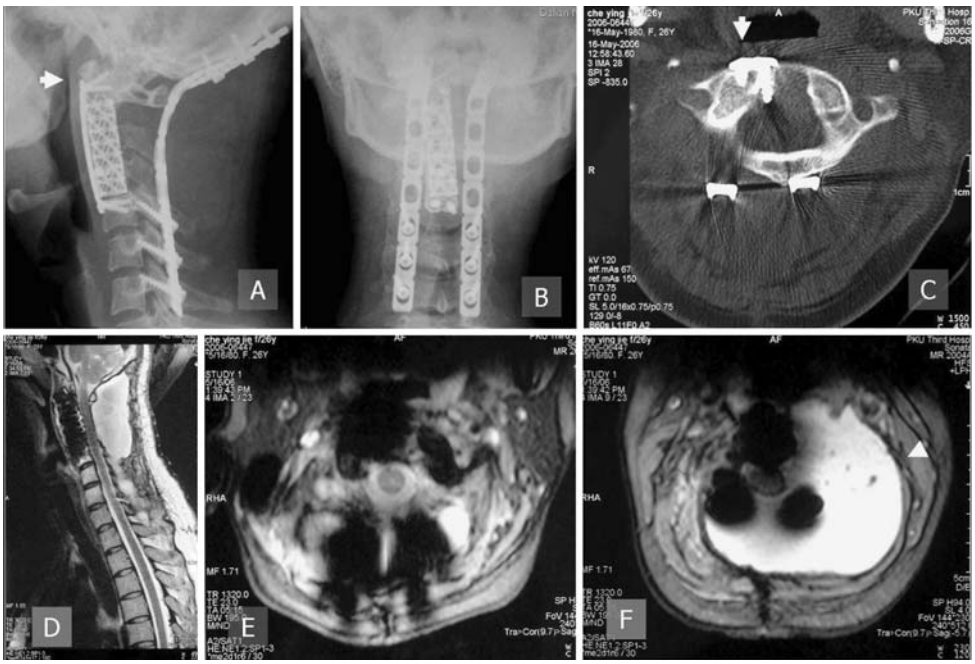

Fig. 4 Postopreative image at 3 year follow-up. **a**, **b** X-rays, **c** axial CT of C1, **d** sagittal MRI, **e**, **f** axial MRI of C2 and C3

was that the tumor capsule was carefully kept intact until its edges clearly exposed.

Bilateral high anterior cervical approaches were performed. The tumor capsule was clearly exposed and both vertebral arteries (VAs) were skeletonized from their transverse process. After tumor mass removal, the tip of the dens was resected with a Kerrison rongeur. The tumor bed was irrigated with distilled water, and then covered by gelfoam. Titanium cage filed with iliac crest graft was inserted. Anterior cervical plate was then placed between C1 lateral mass (Fig. 3, arrow) and C4.

Then in the same setting through a posterior middle line approach the posterior part of the tumor was resected removing the left C2–3 lamina and facet were removed. The left VA and C3 nerve root were ligated and resected. Occipitocervical fixation was performed with occipital screw and cervical lateral mass screws.

Outcome

The neurological function was intact after the operation. The patient had a meningocele (Fig. 4, arrow head) that remained asymptomatic. No recurrence or metastasis was observed 3 years after the operation. She returned to her previous occupation as office worker. Patient is to continue follow up on a regular basis to rule out any sign of recurrence.

References

1. Boriani S, Bandiera S, Biagini R, Bacchini P, Boriani L, Cappuccio M, Chevalley F, Gasbarrini A, Picci P, Weinstein JN (2006) Chordoma of the mobile spine: fifty years of experience. Spine 31:493–503
2. Boriani S, Weinstein JN, Biagini R (1997) Primary bone tumors of the spine. Terminology and surgical staging. Spine 22:1036–1044
3. Casali PG, Stacchiotti S, Sangalli C, Olmi P, Gronchi A (2007) Chordoma. Curr Opin Oncol 19:367–370
4. Currier BL, Papagelopoulos PJ, Krauss WE, Unni KK, Yaszemski MJ (2007) Total en bloc spondylectomy of C5 vertebra for chordoma. Spine 32:E294–E299
5. Fujita T, Kawahara N, Matsumoto T, Tomita K (1999) Chordoma in the cervical spine managed with en bloc excision. Spine 24:1848–1851
6. Hug EB, Slater JD (2000) Proton radiation therapy for chordomas and chondrosarcomas of the skull base. Neurosurg Clin N Am 11:627–638
7. Jäkel O, Land B, Combs SE, Schulz-Ertner D, Debus J (2007) On the cost-effectiveness of Carbon ion radiation therapy for skull base chordoma. Radiother Oncol 83:133–138
8. Leitner Y, Shabat S, Boriani L, Boriani S (2007) En bloc resection of a C4 chordoma: surgical technique. Eur Spine J 16:2238–2242
9. Magenau JM, Schuetze SM (2008) New targets for therapy of sarcoma. Curr Opin Oncol 20:400–406
10. McMaster ML, Goldstein AM, Bromley CM, Ishibe N, Parry DM (2001) Chordoma: incidence and survival patterns in the United States, 1973–1995. Cancer Causes Cont 12:1–11
11. Neo M, Asato R, Honda K, Kataoka K, Fujibayashi S, Nakamura T (2007) Transmaxillary and transmandibular approach to a C1 chordoma. Spine 32:E236–E239
12. Rhines LD, Fourney DR, Siadati A, Suk I, Gokaslan ZL (2005) En bloc resection of multilevel cervical chordoma with C-2 involvement. Case report and description of operative technique. J Neurosurg Spine 2:199–205
13. Suchomel P, Buchvald P, Barsa P, Froehlich R, Choutka O, Krejzar Z, Sourkova P, Endrych L, Dzan L (2007) Single-stage total C-2 intralesional spondylectomy for chordoma with three-column reconstruction. Technical note. J Neurosurg Spine 6:611–618

Expert's comment by Stefano Boriani

Stefano Boriani, MD,
Head of Department,
Department of Orthopaedics, Traumatology and Spine Surgery,
Ospedale Maggiore-Bologna,
Largo Nigrisoli, 2,
40133 Bologna,
Italy
e-mail: stefanoboriani@gmail.com.

The importance of this article is much more relevant than the anedoctical value of a case report. Chordoma is a very difficult tumor to treat and the author exposed and discussed very well the reasons. This grand rounds case reported here is typical under many aspects: site of occurrence, evolution, symptoms. Prognosis is poor due to the extension of the lesion, the age of the patient and the highly demanding surgery required [2, 11]. Moreover, as it unfortunately happens too frequently, the patient was referred after two wrong decisions that potentially worsened the prognosis. First, the patient had been submitted to biopsy through the pharynx. According to the most elementary rule of oncologic surgery, the biopsy tract should be removed together with the tumor, otherwise it represents—for malignant tumors—a site for persisting tumor cells and a serious cause of recurrence [1]. Second, the mass had been submitted to radiation. This is ineffective on such a huge tumor and increases the morbidity of surgery, making more difficult the dissection in such a difficult area.

Before discussing the decision making process and the surgical procedure, I would like to remark some points that I feel are of some relevance when dealing with Chordomas.

In my experience, when planning the treatment the surgeon should always consider two aspects, the biological behavior and the gross pathology.

Biological behavior

Chordoma is a slow-growing tumor, with a long asymptomatic evolution, frequently discovered only after the development of huge masses. This is obviously mostly true for sacral or lumbar tumors rather than for cervical. But also the recurrence will occur late. In our series even after 94 months. This means that to evaluate the effectiveness of a treatment protocol, 5 years at least should be required. This differentiates Chordomas from other low-grade tumors, where local recurrence occurs early and the assessment of a treatment can be based on a 2 years follow-up.

The rate of Local Recurrence after en bloc resection is significantly lower compared to intralesional excision [3]. If we consider that the incidence of metastases is very low, achieving a local control has a curative meaning.

Gross pathology

Chordoma is a low vascular tumor even if some profuse bleeding sometimes occurs, possibly due to arterial encroachment rather than to intrinsic tumor vascularity. It is gelatinous like jelly. This is particularly relevant from a surgical point of view, as it can spread along the muscles and this detail is very difficult to detect on preoperative imaging. A careful MRI study is mandatory to this purpose. The sacral Chordomas typically spread along the piriformis, even into the sciatic fossa, the lumbar Chordomas spread all along the psoas like the abscesses do, the cervical chordomas invade and spread in the longus colli. All this muscular structures should be included in the resection. The fluidity of the tumor tissue provokes seeding all along the surgical field and explains the reported cases of multiple foci of local recurrence [1]. This also makes very difficult en bloc resection even if feasible, as the tumor mass can be easily broken during the surgical manipulation, spilling tumor from superficial solution of continuity even imperceptibly. This also affects the margin evaluation by the pathologist and the reported cases of recurrence after "wide margin" en bloc resection, which is substantially higher for Chordoma than for any other malignant tumor. We could state that a real wide margin for a chordoma of the spine is extremely difficult to achieve.

Even worse is the problem when the tumor expands into the epidural space. Resection of the dura [4, 7] has a role in the treatment of bone tumors of the spine, when the dura is adherent to the tumor and can represent a margin. But when the tumor spills in the canal, it becomes "extra-compartimental" and any surgery fails to be oncologically appropriate. Adjuvants to surgery are therefore required.

From this viewpoint, Chondrosarcoma is quite easier to treat, being a solid tumor, developing firm masses, easy to detect on imaging and to manage during the surgical procedure [5].

As a consequence, from a theoretical point of view, the treatment planning of a C2 should first consider an en bloc resection [6, 8, 10]. In the reported case, however, anatomical and surgical constraints prevent from the practical application of this surgical plan. The margins of the possible en bloc resection include unresectable structures; the epidural extension prevents appropriate margins, as in that region the resection is intralesional, and resection of the dura does not seem reasonable or even feasible. Further, the soft mass is predominant, making impossible to avoid breakage and consequent spilling.

The authors did perform an intralesional extracapsular excision, removing all the visible tumor piecemeal and excising carefully all the surrounding resectable structures. I think that the authors found an excellent solution, with good morbidity/effectiveness ratio. The 3 years disease-free evolution is a very good result taking into account the site, the age of the patient, the previous incorrect treatment.

A possible criticism to the technique performed first concerns the decision to perform a bilateral approach. Risk of tongue ischemia if both lingual arteries are ligated or damaged exists. Maybe a wide monolateral extensile approach is more prudent or even a trans-glosso-mandibular approach [9], which moreover could have given the possibility to resect the biopsy tract.

The role of preoperative angiography should be pointed out to detect the predominant vertebral artery and to obturate—if possible—the one encased by the tumor. This to me is very important as it makes surgery easier, both in case of en bloc resection as in case of intralesional excision.

As a conclusion, in my opinion the treatment planned and performed in this patient is correct, considering the site and the extension of the tumor. Even if en bloc resection is the treatment of choice of Spine Chordoma, the feasibility of this procedure is limited by surgical constraints. It is important to remark the attempt to perform extra-capsular intralesional excision by double approach surgery, was also reported by Suchomel et al. [12].

References

1. Arnautović KI, Al-Mefty O (2001) Surgical seeding of chordomas. Neurosurg Focus 10:E7

2. Bergh P, Kindblom LG, Gunterberg B, Remotti F, Ryd W, Meis-Kindblom JM (2000) Prognostic factors in chordoma of the sacrum and mobile spine: a study of 39 patients. Cancer 88:2122–2134
3. Biagini R, Boriani S, Bandiera S (2003) Subsitution in vertebral resection. Chir Organi Mov 88:185–191
4. Boriani S, Bandiera S, Biagini R, Bacchini P, Boriani L, Cappuccio M, Chevalley F, Gasbarrini A, Picci P, Weinstein JN (2006) Chordoma of the mobile spine: fifty years of experience. Spine 31:493–503
5. Boriani S, De Iure F, Bandiera S, Campanacci L, Biagini R, Di Fiore M, Bandello L, Picci P, Bacchini P (2000) Chondrosarcoma of the mobile spine: report on 22 cases. Spine 25:804–812
6. Kawahara N, Matsumoto T, Tomita K (1999) Chordoma in the cervical spine managed with en bloc excision. Spine 24:1848–1851
7. Keynan O, Fisher CG, Boyd MC, O'Connell JX, Dvorak MF (2005) Ligation and partial excision of the cauda equina as part of a wide resection of vertebral osteosarcoma: a case report and description of surgical technique. Spine 30:E97–E102
8. Leitner Y, Shabat S, Boriani L, Boriani S (2007) En bloc resection of a C4 chordoma: surgical technique. Eur Spine J 16:2238–2242
9. Neo M, Asato R, Honda K, Kataoka K, Fujibayashi S, Nakamura T (2007) Transmaxillary and transmandibular approach to a C1 chordoma. Spine 32:E236–E239
10. Rhines LD, Fourney DR, Siadati A, Suk I, Gokaslan ZL (2005) En bloc resection of multilevel cervical chordoma with C-2 involvement. Case report and description of operative technique. J Neurosurg Spine 2:199–205
11. Sciubba DM, Chi JH, Rhines LD, Gokaslan ZL (2008) Chordoma of the spinal column. Neurosurg Clin N Am 19:5–15
12. Suchomel P, Buchvald P, Barsa P, Froehlich R, Choutka O, Krejzar Z, Sourkova P, Endrych L, Dzan L (2007) Single-stage total C-2 intralesional spondylectomy for chordoma with three-column reconstruction. Technical note. J Neurosurg Spine 6:611–618