Case Report

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Retropharyngeal chordoma extending to the spinal cord, mimicking a neurogenic tumor: a case report and literature review

Sun Joo Lee[1], Sung Hwa Paeng[2], Mi Seon Kang[3], Soo Jin Jung[3], Shin Ae Yoon[4], Ha Young Park[3], Hye Kyoung Yoon[3], Young Il Yang[3] and Hwa Jin Cho[3]

Abstract

Chordomas are rare, locally aggressive bone malignancies with poor prognoses. However, those with minimal or no bone involvement are more easily resectable because of their well-delineated margins and thus have better prognoses. Such extraosseous chordomas of the spine are localized both intradurally and extradurally. Only a few case reports have focused on extraosseous, extradural spinal chordomas. Radiologically, this type of chordoma has a dumbbell shape; however, dumbbell-shaped spinal tumors are traditionally thought to be neurogenic tumors (i.e., schwannomas or neurofibromas). We herein report a unique case involving a woman with a dumbbell-shaped extraosseous chordoma protruding predominantly into the retropharyngeal space. A 44-year-old woman presented for evaluation of a left submandibular mass. A T2-hyperintense, gadolinium-enhancing mass was found in her cervical spinal canal, protruding through the C2/3 neural foramen into the retropharyngeal space with minimal vertebral involvement. The initial diagnosis was a neurogenic tumor, most likely a schwannoma. After subtotal removal, the pathologic diagnosis was a chordoma. Because chordomas and schwannomas have significantly different prognoses, caution is warranted when a dumbbell-shaped tumor is identified

[1]Department of Radiology, Inje University School of Medicine, Busan Paik Hospital, Busan, Republic of Korea
[2]Department of Neurosurgery, Inje University School of Medicine, Busan Paik Hospital, Busan, Republic of Korea
[3]Department of Pathology, Inje University School of Medicine, Busan Paik Hospital, Busan, Republic of Korea
[4]Department of Pediatrics, Chungbuk National University Hospital, Cheongju, Chungcheongbuk-do, Republic of Korea

Corresponding author:
Hwa Jin Cho, Department of Pathology, Inje University Busan Paik Hospital, 75 Bokji-ro, Busanjin-gu, Busan 47392, Republic of Korea.
Email: eunhasu101@hanmail.net

in the spine with minimal or no vertebral deterioration on radiology. This report also provides the first thorough review of extraosseous dumbbell-shaped intraspinal–extraspinal chordomas.

Keywords
Chordoma, dumbbell, extraosseous, neurogenic tumor, retropharyngeal space, case report

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Introduction

Chordomas are rare, slowly growing tumors with an overall incidence of 8.4 per 10 million people and high morbidity and mortality rates.[1] Their prognosis is poor, and the median survival duration is 6.29 years because of their high local aggressiveness.[1] Primary treatment typically consists of surgical resection followed by adjuvant radiotherapy.[2] One study revealed that the most significant factor affecting the prognosis of chordomas is aggressive excision on first presentation of the disease.[3] Although surgeons strive to completely remove chordomas, these locally aggressive tumors are often located in very challenging areas such as the skull base, mobile spine, or sacrococcygeal bone.[4,5]

Chordomas generally arise from anywhere in the central neural axis because they originate from the extradural vestiges of the notochord.[6] Chordomas are primarily located in the axial skeleton; i.e., the base of the skull, the vertebral bodies, and the sacrococcygeal bone.[4] Extraosseous chordomas are uncommon compared with intraosseous chordomas and occur in both axial and extra-axial locations.[7] Only 11 case series have documented the special radiologic pattern of extraosseous chordomas, which have a dumbbell appearance.[8–18] The representative dumbbell-shaped tumors of the spine are benign neurogenic tumors, usually schwannomas.[16] Dumbbell-shaped lesions responsible for neural foramina widening include meningiomas, plasmacytomas, chordomas, infectious lesions, and cysts associated with the surrounding bone and spinal cord.[16] Therefore, treatment options may differ, and the prognosis may be compromised because of partial resection of the tumor. We herein report a case involving a woman with a dumbbell-shaped extraosseous chordoma that protruded prominently into the retropharyngeal space and spinal canal.

Case report

A 44-year-old woman presented to the Ear, Nose, and Throat Department of our hospital with a 1-week history of a left submandibular mass and sore throat. On physical examination, the mass was found to be fixed and soft with no evidence of tenderness. She had a stiff neck; however, dyspnea, dysphagia, or other neurological symptoms were absent.

A neck computed tomography scan with contrast enhancement showed a 3.5-cm dumbbell-shaped mass extending into the spinal canal, left neural foramen, and left retropharyngeal space of C2/3. The mass-induced expansion of the left neural foramen of C2/3 is shown in Figure 1. Axial (Figure 2(a)) and sagittal fat-suppressed (Figure 2(b)) T2-weighted magnetic resonance imaging (MRI) showed a 3.5- × 3.1- × 4.1-cm hyperintense mass that was abutted against the left C3 nerve root and extended into the

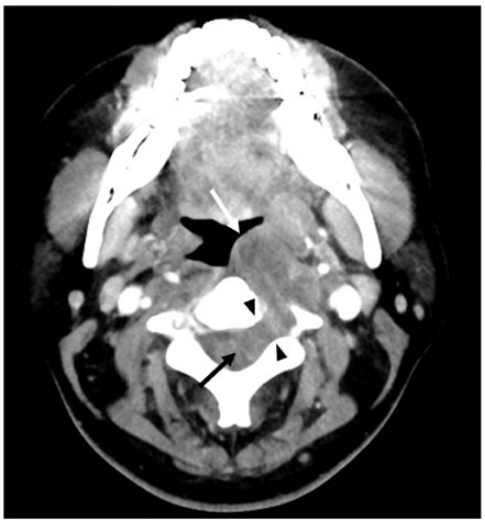

Figure 1. Neck computed tomography scan with contrast enhancement showed a 3.5-cm dumbbell-shaped mass (arrows) that extended into the spinal canal, left neural foramen, and left retropharyngeal space of C2/3. Note the widening of the left neural foramen of C2/3 by the mass (arrowheads).

left retropharyngeal space through the left neural foramen of C2/3. Minimal focal invasion of the left lateral body of C2 and widening of the left neural foramen of C2/3 by the mass were observed. Axial (Figure 2(c)) and sagittal (Figure 2(d)) gadolinium-enhanced T1-weighted fat-suppressed MRI showed heterogeneous enhancement. Neurogenic tumors, including both benign tumors (e.g., schwannomas and neurofibromas) and malignant tumors (e.g., malignant peripheral nerve sheath tumors) were considered as differential diagnoses. Transfemoral cerebral angiography revealed that the feeding artery branched from the left proximal external carotid artery (Figure 3).

The neurosurgeon planned a two-stage operation. First, a left anterior approach would be used by an ear, nose, and throat surgeon and neurosurgeon to remove the main tumor from the retropharyngeal space. Next, a posterior approach would be used to remove the tumor from its intraspinal location. The surgeon estimated that any invasive procedure before surgery may cause complications and therefore decided to perform intraoperative frozen diagnosis.

During the first operation, the left anterior cervical approach revealed an intradural extramedullary tumor at C1–3 that extended into the retropharyngeal area. The portion of the tumor located in the retropharyngeal space was flexible and relatively easy to remove, but the portion of the tumor located in the intraspinal and neural foramen of C2/3 was still present as shown on the postoperative computed tomography scan. As an acute complication of the tumor resection, a 6.1- × 2.8-cm hematoma was observed in the prevertebral space at the C2–4 level. The hematoma was removed with an intraoperatively inserted drainage catheter.

Grossly, the resected tumor was multinodular and yellow/white in color (Figure 4(a)). The cut surface showed no evidence of necrosis. The intraoperative frozen analysis ruled out a chordoma because chordomas usually consist of eosinophilic or clear, bubbly (physaliphorous) tumor cells arranged in lobules on a mucinous background (Figure 4(b)). In the permanent section, the lobules were separated by thin fibrous septa with inflammatory cells (Figure 4(c)). Tumor cells showing eosinophilic cytoplasm and intracytoplasmic vacuoles were arranged in a retiform pattern (Figure 4(d)). The nuclear-to-cytoplasmic ratio differed across cells, and nuclear atypia was frequently observed (Figure 4(e)). A few multinucleated tumor cells were found (Figure 4(e) [inset]). Immunohistochemical staining showed diffuse positivity for pan-cytokeratin (Figure 4(f)) and brachyury (Figure 4(g)), patchy positivity for epithelial membrane antigen, focal positivity for S100 (Figure 4(h)), and negativity for progesterone receptor and synaptophysin. The Ki-67 labeling index was 2% (Figure 4(i)). The final diagnosis was a conventional chordoma.

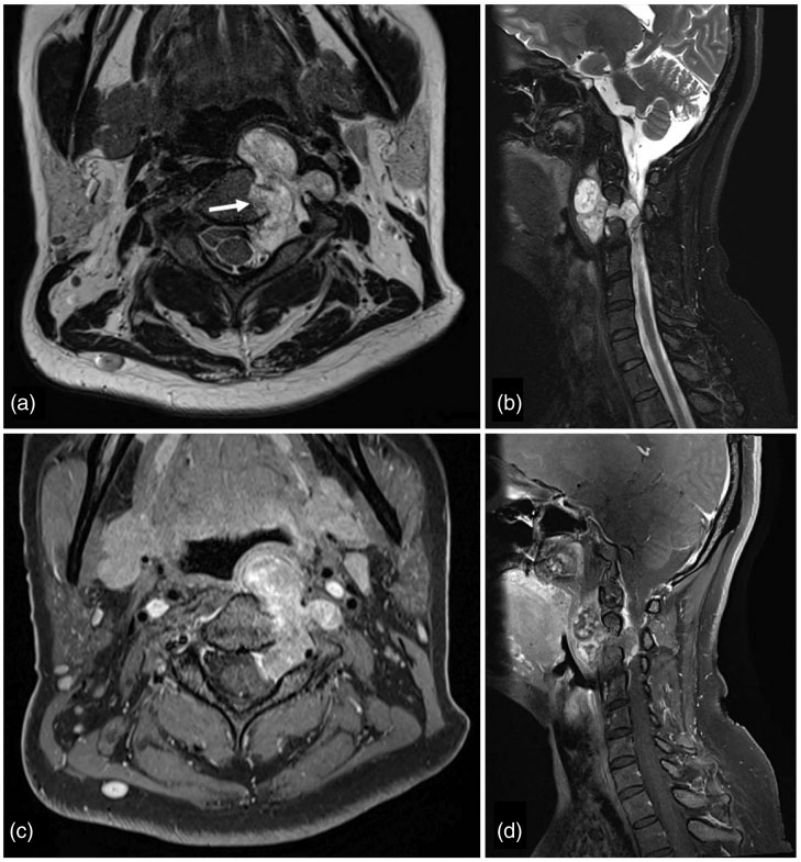

Figure 2. Axial (a, TR/TE, 4210/104) and sagittal fat-suppressed (b, TR/TE, 6040/99) T2-weighted magnetic resonance imaging showed a 3.5- × 3.1- × 4.1-cm hyperintense mass that was abutted against the left C3 nerve root and extended into the left retropharyngeal space through the left neural foramen of C2/3. Note the minimal invasion of the left lateral body of C2 (arrow) and widening of the left neural foramen of C2/3 by the mass. Axial (c, TR/TE, 835/12) and sagittal (d, TR/TE, 725/9.3) gadolinium-enhanced T1-weighted fat-suppressed magnetic resonance imaging showed heterogeneous enhancement.
TR, repetition time; TE, echo time.

On postoperative day 13, the patient refused to undergo a second operation; she was discharged and transferred to another hospital to receive proton therapy. Her follow-up was placed on hold.

Discussion

We have herein described a woman with a spinal extraosseous chordoma located intraspinally and extraspinally, presenting with a prominent mass protruding into the retropharyngeal space. The tumor was initially diagnosed as a benign neurogenic tumor because of its dumbbell shape and minimal bone involvement.

Chordomas arise in the axial skeleton. The three most common locations are the mobile spine (32.8%), skull base (32.0%), and sacrum (29.2%).[1] Chordomas originate from the notochord, which runs along the spine, pharynx, and dorsum sellae.[6]

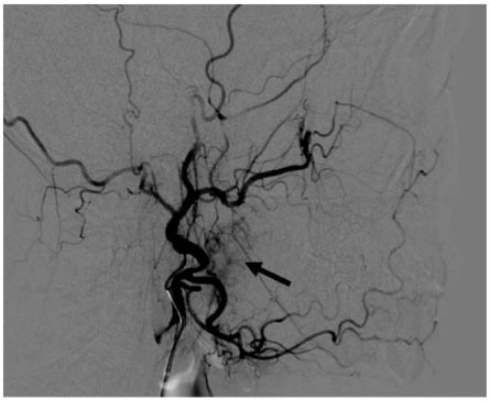

Figure 3. Transfemoral neck angiography showed the feeding artery branching from the left proximal external carotid artery (arrow).

However, extraosseous chordomas have rarely been reported.[19] Unlike osseous chordomas, extraosseous chordomas exhibit no notochordal remnants; thus, they have been suggested to be caused by a brachyury-associated molecular mechanism irrespective of whether they are sporadic or familial.[20–22]

In 1997, Jallo et al.[23] proposed the following classification system for vertebral spine chordomas: Type I, osseous extradural (the majority); Type II, extraosseous extradural; Type III, osseous intradural; and Type IV, extraosseous intradural. Extraosseous chordomas rarely involve the bone. In contrast to chordomas arising

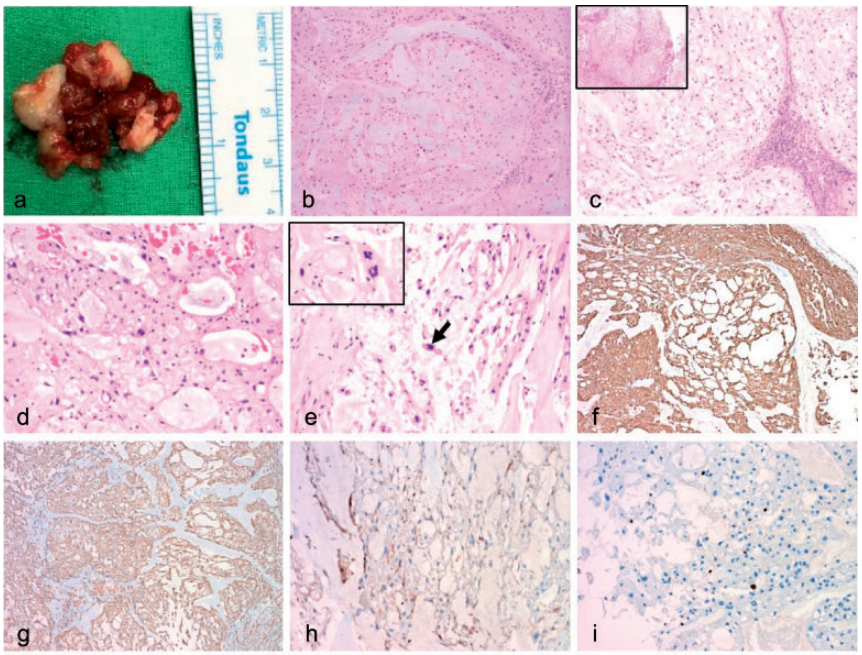

Figure 4. Gross and microscopic chordoma findings. (a) Yellow/white multinodular mass. (b) Intraoperative frozen section showing the lobular appearance with weak eosinophilic to clear cells on a mucinous background. (c) Lobules of the tumor separated by thin fibrous septa with some inflammatory cells in the septa and loosely arranged cords or nests of tumor cells on a mucinous background. (d) Retiform pattern with physaliphorous tumor cells. (e) Atypical nuclear features with evidence of mitosis (arrow). (e [inset]) Multinucleated tumor cells. (f) Diffuse pan-cytokeratin positivity. (g) Moderate to strong brachyury expression in nuclei. (h) Focal S100 positivity and patchy positivity for epithelial membrane antigen. (i) Low (2%) Ki-67 labelling index (b–e, hematoxylin–eosin stain; f, pan-cytokeratin; g, brachyury; h, S100; i, Ki-67 immunohistochemical stain; b, d, e, e [inset], h, i, ×200; c, f, g, ×100).

from bone, extraosseous Type II and IV chordomas are likely to be fully resected and have better prognoses because of their well-delineated margins.[19] In 2004, Wang et al.[24] proposed a new classification system: Type I, intraosseous extradural; Type II, intraosseous intradural; Type III, extraosseous extradural; Type IV, extraosseous intradural; and Type V, extraosseous soft tissue. Most spinal extraosseous chordomas are located in the epidural region, including intraspinal only or both intraspinal and extraspinal locations.[14] Few reports have described dumbbell-shaped tumors in an extraosseous spinal location with both intraspinal and extraspinal involvement, similar to the present case.

Dumbbell-shaped tumors in the spine are predominantly neurogenic tumors; i.e., schwannomas and neurofibromas. These may be found in patients with spinal ependymoma, meningioma, or lymphoma, or they may less commonly be metastasized.[25] Because chordomas arise from the extradural space and invade intraspinal regions, they also present as dumbbell-shaped tumors.[8–18] We reviewed previously reported spinal extraosseous dumbbell-shaped chordomas in intraspinal and extraspinal locations that were classified as having an "extraosseous extradural" pattern, as in our case (Table 1).

In addition to our case, we identified 13 cases of chordomas from 11 case reports published from 1993 to 2018. Among the 14 total cases, the tumor spinal level was predominantly cervical (10/14, 71.4%), with one case extending to the thoracic level. Others arose from the lower spine (thoracic, 2/14 [14.3%]; lumbar, 1/14 [7.1%]; sacral, 1/14 [7.1%]). The male: female ratio was 6:8, and the patients' age ranged from 5 to 81 years (mean age, 38.9 years). The patients complained of axial or one-sided spinal level sensory and/or motor symptoms. The extraspinal component of the dumbbell-shaped tumor included paraspinal soft tissue in 11 (78.6%) cases, including 1 case involving the soft tissue of the carotid triangle.[15] Other cases involved the pulmonary apex,[17] and the patient in our case had a large mass in the retropharyngeal space.

MRI revealed T1-hypointense or T1-isointense cases (9/10 cases, 90%), with only one T1-hyperintense case (1/10 case, 10%). T2-weighted images were mostly hyperintense (9/11, 81.8%), with hypointense or isointense images in two cases (2/11 cases, 18.2%). Of the seven cases in which gadolinium was applied, six (85.7%) showed evidence of enhancement.

In cases with information about bone involvement, spinal bone involvement was mostly absent (9/12 cases, 75%). Only three (25%) cases showed minimal or rare bone involvement.

Eight patients underwent total tumor resection, three underwent subtotal resection, and one underwent subtotal resection plus radiation therapy. Many patients could not be followed up for the long term, but all followed up patients showed no evidence of relapse except one suspected to have developed relapse according to radiological findings.[12] Pathologic reviews revealed that almost all tumors were conventional chordomas; the exceptions were two chondroid thoracic spine chordomas. The conventional chordomas were positive for epithelial membrane antigen, pancytokeratin, brachyury, S100, CD117 (c-kit), and platelet-derived growth factor receptors. The Ki-67 labeling index of these chordomas was low ($\leq$5%).

Extraosseous chordomas have better prognoses than intraosseous chordomas because total resection is more easily achieved.[14] Exceptions have been reported in cases of cerebral dural spread or spinal cord metastasis.[26] Unfortunately, the tumor in the present case could not be completely resected, and a hematoma associated with tumor resection remained. Therefore,

Table 1. Review of extraosseous dumbbell-shaped intraspinal–extraspinal chordomas.

No.	Author/Year	Sex/Age	Symptoms and sings	Location		Radiologic findings	Bone involvement	TX	F(m)/R	Pathology
				Spine	Extraspinal					
1	Our case	F/44	Lt. submandibular mass	C2-3	Retropharyngeal space	T1 hypo, T2 hyper, Gd enhance	Minimal	STR	1/NA	Conventional, EMA/CK/VT/S100 (+), Ki-67 2%
2	Karakida et al.[8] /1996	M/5	Neck pain and stiffness	C3-5	Paraspinal	T1 iso, T2 hyper, Gd septal enhance	No	TR	NA	Conventional
3	Gunnarsson et al.[9] /2001	M/69	Lt. hand and fingers pain	C1-2	Paraspinal	T1 hyper	No	TR	NA	S100 (+)
4	Smolders et al.[10] /2003	M/36	NA	C	Paraspinal	T1 iso, T2 hyper, Gd enhance	No	NA	NA	Not specified
5	Barrey et al.[11] /2006	F/29	Lt. C3 neuralgia, dysesthesia	C2-5	Paraspinal	T1 hypo, T2 hyper	Minimal	TR	18/-	Conventional, EMA/CK/VT (+)
6	Zhou et al.[12]	F/11	Axial pain and upper extremities pain	C2-5	Paraspinal soft tissue	T2 hyper	No	STR	8/*	Conventional, CK/S100 (+)
7	Bergmann et al.[13] /2010	M/38	Lt. neck and shoulder pain	C2-3	Paraspinal	T2 hyper	No	TR	84/-	Conventional, EMA/CK/VT/S100/CD117/PDGFR (+), Ki-67 <1%
8	Bergmann et al.[13] /2010	F/44	Rt. neck and arm pain	C2-3	Paraspinal	T1 hypo	No	TR	12/-	Conventional, EMA/VT/CK/S100/PDGFR (+), Ki-67 1%
9	Yang et al.[14] /2016	M/67	Rt. upper extremity pain, weakness in the lower extremities	C4-T2	Paraspinal	T1 hypo, T2 hyper, Gd enhance	Rare	TR	13/-	Conventional, EMA/CK/VT/S100 (+), Ki-67 5%
10	Awuor et al.[15] /2018	F/81	Shortness of breath, generalized weakness, unsteady gait	C4-7	Soft tissue of the carotid triangle	T2 hyper	No	STR	NA	Conventional, EMA/CK/S100 (+)
11	Kivrak et al.[16] /2009	F/47	Progressive hemiparesia	T9	Paraspinal	T1 hypo, T2 hyper	No	NA	NA	Chondroid
12	Fernandez et al.[17] /2010	F/31	Gait disturbance	T1-2	Pulmonary apex	T1 iso, T2 hypo, Gd enhance	NA	STR, TR	36/-	Chondroid
13	Sebag et al.[18] /1993	M/6	Rt. buttock pain, dorsolumbar spinal rigidity	L2-3	Paraspinal	T1, T2 iso, Gd no enhance	No	TR		Conventional, CK/VT/S100 (+)
14	Yang et al.[14] /2016	F/36	Sacrococcygeal region discomfort	S	NA	Gd enhance	NA	TR	58/-	NA

*, a suspicious recurrence.

CK, pan-cytokeratin; EMA, epithelial membrane antigen; F (m), follow-up (months); Gd, Gadolinium; hyper, hyperintense; hypo, hypointense; iso, isointense; Lt., left; NA, not applicable; PDGFR, plate-derived growth factor receptor; R, recurrence; Rt., right; STR, subtotal resection; TR, total resection; TX, treatment; VT, vimentin.

careful follow-up and a second operation were needed for this patient.

The present case is unique in that it presents a rare case of a chordoma involving both the intraspinal and extraspinal spaces, with the extraspinal component heavily growing into the retropharyngeal space. A few chordomas have appeared as retropharyngeal masses, but these did not have a dumbbell shape. In three cases, cervical chordomas presented as masses in the retropharyngeal space; these were osseous chordomas involving vertebral bodies.[27–29] Two other retropharyngeal chordomas that might have arisen from the posterior side of the pharyngeal wall were tightly adhered to the osseous vertebrae[30] and showed no bone involvement at all.[24]

The surgeon involved in the present case had not previously encountered an extraosseous dumbbell-shaped chordoma. He considered the tumor to be a benign neurogenic tumor (schwannoma) because the mass was lobulated, fusiform-shaped, grossly well-circumscribed, and relatively painless. The differential diagnoses were limited to dumbbell-shaped and completely extradural nerve root tumors.[16] Chordomas or ependymomas can extend through and enlarge the neural foramina. Therefore, preoperative biopsy or intraoperative frozen diagnosis of the tumor is necessary. In this case, the surgeon decided that preoperative biopsy would be too difficult for the patient; therefore, intraoperative frozen diagnosis was performed, which helped the surgeon to determine the most effective subsequent procedure.

Extraosseous and intraosseous chordomas have identical morphologies on pathological assessment[7] and express epithelial membrane antigen, cytokeratin, and S100 protein. In addition, the transcription factor brachyury is a highly specific marker for chordomas.[31] Brachyury, a notochord differentiation-associated protein, is sensitively and specifically expressed in the nuclei of chordomas. Conventional chordomas mostly consist of lobules filled with abundant myxoid matrix separated by fibrous septa. The lobules contain large cells with clear to eosinophilic cytoplasm with vacuolation, referred to as "physaliphorous cells." Nuclear atypia and pleomorphism are minimal, and necrosis is frequently observed.[5] Other subtypes of chordomas include chondroid chordomas, cellular chordomas, and dedifferentiation chordomas.[2] Pathologically, the differential diagnoses of chordomas include benign notochordal cell tumors, myxoid schwannomas, nerve sheath myxomas, chondroid meningiomas, chondrosarcomas, myoepithelioma/myoepithelial carcinomas, and metastatic carcinomas, including clear cell renal cell carcinomas or adenocarcinomas.[2,28,32]

In summary, we have presented a rare case of a dumbbell-shaped intraspinal and extraspinal extraosseous chordoma with a large retropharyngeal mass. Radiologically, a dumbbell shape is representative of a neurogenic tumor, usually a schwannoma. Because chordomas and schwannomas have very different prognoses, special caution is warranted when minimal or no vertebral destructive dumbbell-shaped tumor is seen.

Ethics

This case study was approved by the Institutional Review Board of Busan Paik Hospital (IRB No. 20-0008), which waived the requirement for informed consent. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Hwa Jin Cho https://orcid.org/0000-0002-7613-1942

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