Clinical Case Report

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An unusual case of oropharyngeal chordoma

A case report and literature review

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Abstract

Rationale: Chordomas are rare malignant neoplasms derived from incomplete regression of notochordal tissue along the cranio-coccygeal axis. Chordomas that develop in an atypical position are called ectopic chordomas, such as oropharyngeal chordomas (OCs). OCs are exceedingly rare; only 11 cases have been reported to date. Preoperative diagnosis is challenging, and an accurate diagnosis thus is based on postoperative pathologic examination findings and immunohistochemistry. Although surgical therapy and radiotherapy is performed in some patients, the 5-year survival rate is low. Increasingly more studies of chordomas have been based on molecular biology to increase the survival rate, and targeted therapy could be a new therapy in the future.

Patient concerns: The patient presented with a left oropharyngeal mass that had begun slowly enlarging 1 year previously. He reported a foreign body sensation and dysphonia during this time period.

Diagnoses: The patient was initially diagnosed with a neurogenic tumor. Routine postoperative pathology showed that the mass was consistent with a chordoma.

Intervention: Mass resection was performed.

Outcome: One year after the initial surgery, magnetic resonance imaging revealed block signal images at the left retropharyngeal space and clivus. The patient developed recurrence of the OC.

Lessons: Surgical resection is the mainstay of treatment for OC, and postoperative adjuvant radiotherapy is also important. An understanding of the unusual case described in this report may be helpful in diagnosing OC, and development of targeted therapy may help clinicians to provide novel treatment for patients with OC.

Abbreviations: CT = computed tomography, EGFR = epidermal growth factor receptor, MRI = magnetic resonance imaging, OC = oropharyngeal chordoma.

Keywords: challenging diagnosis, oropharyngeal chordoma, survival rate, targeted therapy

1. Introduction

Chordomas are rare malignant neoplasms derived from incomplete regression of notochordal tissue along the cranio-coccygeal axis. Chordomas are classified as sacrococcygeal, spheno-occipital, or vertebral according to their location. The remnant of the embryonic notochord normally inserts into the sphenoid and occipital bone after degeneration, whereas a part can become folded into the oropharyngeal wall. Cells located in the junction of the notochordal remnant and pharyngeal epithelium have the potential for rapid growth. In some circumstances, they can develop into an oropharyngeal chordoma (OC). Chordomas occurring in the oropharynx usually result in local pain, swelling, dysphagia, and dysphonia.

We herein review a case of a left OC that we followed up for 1 year.

2. Case report

A 32-year-old man presented with a left pharyngeal mass that had begun slowly enlarging 1 year previously. He reported a foreign body sensation and dysphonia during this time, but no local pain, numbness, or broken history. Enhanced computed tomography (CT) at another hospital showed a space-occupying lesion that was considered to be a neurogenic tumor.

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XL and YFW contributed equally to this work.

HYY conceived and designed the study. XL and YFW reviewed the literature, carried out the statistical analysis, and drafted the manuscript. HYY, YFW, and FW performed the surgery and follow-up. BWL and SS helped with the immunofluorescence staining. All authors read and approved the final manuscript.

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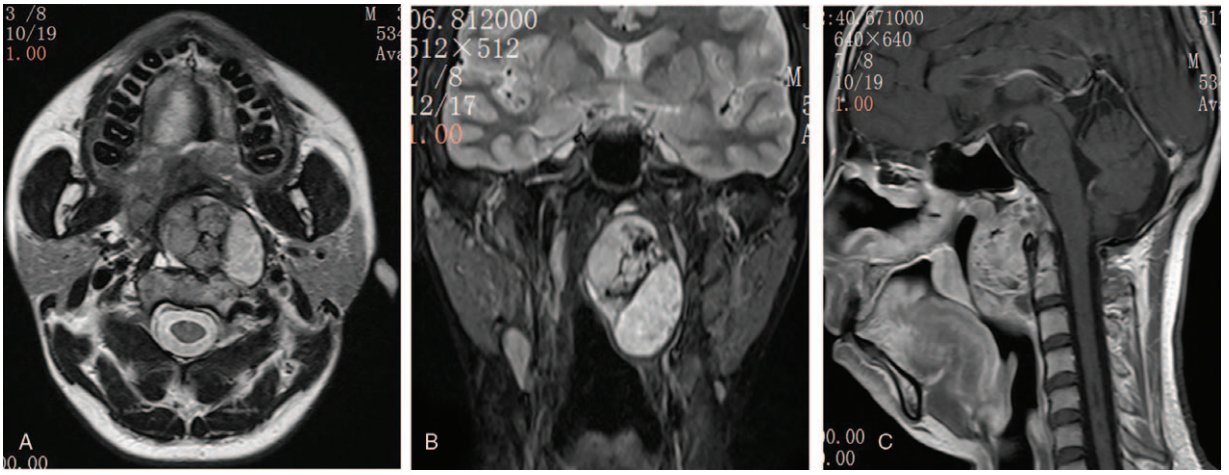

Figure 1. (A, B) Coronal and axial MRI revealed a large inhomogeneous mass causing tracheal dislodgement. (C) Sagittal MRI showed that the clivus was eroded and the left C2–3 intervertebral foramen was enlarged.

Clinical examination revealed a $4.5 \times 3.5 \times 3.0$-cm mass that could be palpated in the left oropharynx without mucosal ulceration. The mass was ill-defined, poorly mobile, firm, and nontender. The pharyngeal cavity became narrow, and the uvula was displaced toward the right. The superficial mucosa was intact. The patient had difficulty protruding his tongue and producing clear speech. Non-swollen lymph nodes were found in the submental and submandibular regions. Two porcelain-fused metal crowns were present in the lower left posterior area. The mesial and occlusal surfaces of the left mandibular third molar were decayed.

Magnetic resonance imaging (MRI) revealed a $2.9 \times 4.2 \times 5.5$-cm cystic space-occupying lesion in the left parapharyngeal space; the C2–3 intervertebral foramen was enlarged and the clivus was destroyed (Fig. 1). Panoramic radiographs showed hyperintensity at the crowns of teeth 35 and 36 and hypointensity at the mesial and occlusal surfaces of tooth 38.

The patient underwent surgery via the transoral approach. We extracted tooth 38 and sagittally split tooth 37 at the buccal alveolar bony wall. Intraoperatively, 2 lumps measuring $4.0 \times 3.5 \times 3.0$ cm and several neoplasms measuring $0.5 \times 0.5 \times 0.3$ cm were visible in the focal region. They were well circumscribed and completely resected. The intraoperative frozen section report stated "consideration of epithelial tumors."

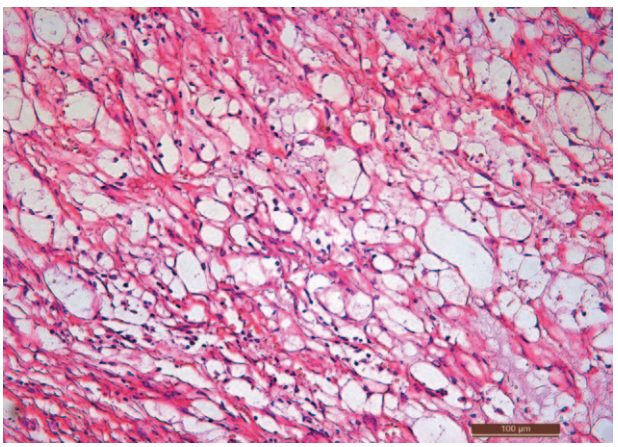

Figure 2. Histological sections of the mass displayed tumor tissue in a myxoid background and cords and lobules of vacuolated physaliphorous cells with abundant cytoplasm and a large amount of mucus. The nucleus was round or oval without definite mitosis (original magnification, ×100).

Routine postoperative pathological examination revealed tumor tissue in a myxoid background and cords and lobules of vacuolated physaliphorous cells with abundant cytoplasm and a large amount of mucus. The nucleus was round or oval without definite mitosis (Fig. 2). Immunohistochemical examination of the tumor cells revealed a strong positive reaction to cytokeratin and S-100, a scattered and weakly positive reaction to p63, and <5% positive reaction to Ki-67 in which the reaction to cytokeratin and S-100 was consistent with a chordoma (Fig. 3).

Postoperatively, the patient was followed up at our hospital. One year after the initial surgery, MRI revealed block signal images at the left retropharyngeal space and clivus, and enhanced scanning showed unequal intensification (Fig. 4). CT angiography demonstrated that the blood supply to the mass in the left retropharyngeal space arose from small vessels of the left external maxillary artery (Fig. 5). The patient developed recurrence 1 year later. Ethics approval was not required for this paper as it is a case report. Patient consent was obtained.

3. Discussion

Chordoma was first described by Luschka in Virchow's laboratory in 1857.[1] It arises from notochord tissue and occurs along the cranio-coccygeal axis. Although it is slowly growing, a chordoma is still defined as a malignant tumor because of its local aggressiveness and metastasis. About 50% of chordomas occur in the sacrococcygeal region, 35% in the spheno-occipital region, and 15% in the spine.[2] Neoplasms in the skull base can result in headache, visual disturbances, and some neurologic symptoms. Because of its deep anatomical position, the possibility of complete resection is low. Chordomas located in an atypical position are called ectopic chordomas, such as OCs. The morbidity rate associated with chordomas is approximately 0.2% of all nasopharyngeal and oropharyngeal masses,[3] and they most commonly occur in 50- to 60-year-old patients; however, Naka et al[4] reported the occurrence of chordomas in patients 4 to 80 years old with a median age of 51 years. OCs have been sporadically reported in

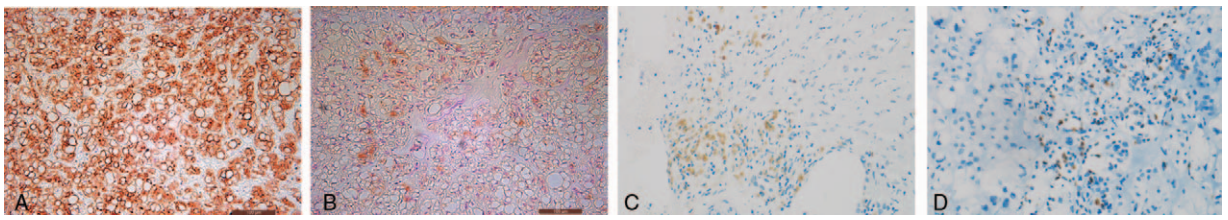

Figure 3. Immunohistochemical staining of tumor tissue showed a strong positive reaction to (A) cytokeratin and (B) S-100 (original magnification, ×100). Staining was weakly positive for (C) p63 and (D) Ki-67 (original magnification, ×400).

the literature, with the first report originating in 1959.[5] Only 11 cases of OC have since been described. A summary of the clinical features of previously reported cases of OC is presented in Table 1. The symptoms of ectopic chordomas are dependent on the tumor location and may include nasal obstruction, dysphagia, dysphonia, and even dyspnea. Despite the fact that chordomas are located submucosally, the superficial mucosa is rarely broken or bleeding. In the present case, the neoplasm measured $2.9 \times 4.2 \times 5.5$ cm on MRI and the initial presentation involved only the sensation of a lump in the throat, indicating that the tumor was slowly growing. However, no pain or neurologic deficits appeared.

Because the preoperative diagnosis of chordomas is still challenging, delayed diagnosis occurs very frequently. CT and MRI are currently used in the diagnosis of chordomas. MRI signals of the mass are commonly isointense or hypointense on T1-weighted images and hyperintense on T2-weighted images. However, several other diagnoses including neurogenic tumors and lymphoma should also be considered. In our case, the initial diagnosis was a neurilemoma. Once the clivus has become involved in such cases, a chordoma should be considered. In 2005, Köybaşioğlu et al[10] demonstrated that fine needle aspiration biopsy was helpful for preoperative diagnosis. If the tissue obtained by the biopsy is not the true lesion, negative results may be observed. Hence, immunohistochemistry is more accurate for diagnosis of a chordoma. Immunohistochemical staining of chordomas is positive for cytokeratin, epithelial membrane antigen, and S-100.

3.1. Management

The first-choice treatment of chordomas is surgical resection, and whether postoperative adjuvant radiotherapy is performed should be based on the patients' condition. Wide and complete resection is necessary because of the malignant nature of chordomas. If the capsule is inadvertently broken, the tumor will aggressively recur. However, complete excision may be difficult for those located in the upper cervical spine, such as the skull base, because of their deep anatomic location and erosion of adjacent structures. High-dose postoperative radiotherapy is usually recommended for such patients. Even when the mass is widely resected, postoperative radiotherapy should also be recommended. In the present case, the mass was well-circumscribed and completely resected. For personal reasons, however, the patient declined radiotherapy and recurrence was detected after 1 year of follow-up. However, the performance of postoperative radiotherapy to improve survival has been sporadically reported. Orecchia et al[13] found that the combination of surgical resection with prescribed doses of proton beam radiation (74 GyE) resulted in no recurrence of chordomas during a follow-up of 6 to 12 months. Despite the availability of many therapeutic methods, including transoral and transnasal surgical approaches and postoperative radiotherapy, the survival rate remains low. The 5-year survival rate is only 20%, and the median survival duration is only 4.1 years.[7] In addition, O'Connell et al[14] reported a discrepant survival rate between male and female patients; the median survival rate of male patients was twice that of female patients.

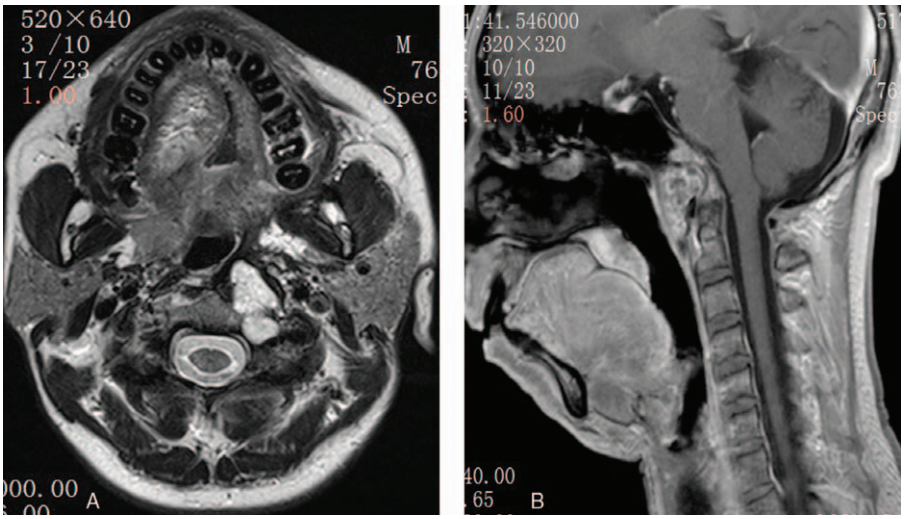

Figure 4. MRI revealed block signal images at the (A) left retropharyngeal space and (B) clivus.

Figure 5. CT angiography demonstrated that the blood supply to the mass arose from small vessels of the left external maxillary artery.

More recent studies of chordomas have been based on molecular biology to increase the survival rate. In 2007, Dobashi et al[15] observed activation of epidermal growth factor receptor (EGFR) and signal transducer and activator of transcription 3 in chordomas. These may be candidates for molecular targeted therapy and predictors of prognosis. In 2014, Zhang et al[16] found that activation of EGFR and MET promotes chordoma cell proliferation and invasion. MiR-608 and miR-34a inhibited cell proliferation and invasion and induced apoptosis of chordoma cells. MiR-34a and miR-608 were inversely correlated with MET and EGFR expression in chordoma cells. The authors therefore demonstrated that upregulation of miR-608 and miR-34a could inhibit chordoma malignancy by regulating EGFR and MET. Other authors have reported the involvement of molecules such as platelet-derived growth factor receptor-α and vascular endothelial growth factor as well as the PI3K/AKT/mTOR pathway,[17–19] all of which can be target sites for treatment of chordoma. Thus, inhibition of certain molecules and their respective pathways could be a potential therapy for chordoma.

4. Conclusion

Chordomas are uncommon neoplasms that arise from the embryonic remnants of the notochord. Although these neoplasms grow slowly, they can relentlessly erode peripheral structures. CT and MRI can help to establish the diagnosis, but more accurate diagnosis relies upon histopathological examination, which can provide characteristic indicators of chordoma. Surgical resection remains the mainstay of treatment, and postoperative adjuvant radiotherapy is also important in many cases. Increasingly more molecular biological studies are being performed to investigate chordoma, and targeted therapy may therefore be a future option for affected patients. Furthermore, because of its rarity and

Table 1

Reported cases of chordomas located in oropharyngeal region.

Study	Age/sex	Location	Size	Symptoms	Bony invasion	Treatment	Pathology	Recurrence	Follow-up
Essammaa E[5] 1959	35/M	Oropharynx	About 3.0 cm (the base)	Dysphagia	No	Surgical resection	Chordoma	No	1 y
Burge AJS[6] 1975	68/M	Posterior pharyngeal wall of the oropharynx	4.0 × 2.5 × 2.0 cm	A hard mobile "node"	No	Surgical resection with adjuvant radiation	Chordoma	No	2 y
Gladstone HB et al[7] 1998	81/M	Parapharyngeal space	8.0 cm (diameter)	Hypernasal speech, dysphagia, and right-sided otalgia	Yes	Surgical resection	Chordoma	Not described	Not described
Succo G et al[8] 2001	66/F	From the posterior oropharyngeal wall to the hypopharynx	Not described	Mucosal ulceration and a loss of weight	Yes	Surgical resection	Chordoma	No	22 mo
Wang YP et al[9] 2004	50/F	Right posterior wall of the oropharynx	5.5 cm × 3.0 cm × 2.5 cm	A sensation of a lump	No	Surgical resection	Chordoma	No	1 y
Köybaşioğlu F et al[10] 2005	50/M	Left posterior aspect of the oropharynx	5.6 cm × 4.7 cm × 2.8 cm	Dyspnea and hemoptysis	Not described	Surgical resection	Chordoma	No	1 y
Coppens JR et al[11] 2009	32/F	Nasopharynx	Not described	Nasal obstruction	No	Surgical resection	Chordoma	No	4.5 y
Coppens JR et al[11] 2009	8/F	Nasopharynx	Not described	Nasal obstruction	No	Surgical resection	Chordoma	No	14 mo
Coppens JR et al[11] 2009	5/F	Nasopharynx	Not described	Nasal Obstruction	No	Surgical resection	Chordoma	No	12 mo
Vasudevan V et al[3] 2015	73/F	Left parapharyngeal area	Not described	Hypernasal speech, dysphagia	Yes	declined treatment	Chordoma (biopsy)	Not described	Not described
Khurram SA et al[12] 2016	63/M	Right tonsillar region	5.0 cm × 5.0 cm	Neck lump, dysphagia and intermittent right otalgia	Yes	Surgical resection with adjuvant radiation	Chordoma	Yes	4 y

difficult diagnosis, a postoperative follow-up protocol should be established and more studies should be performed to fully elucidate the nature of chordoma.

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