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Abstract	Background Chordomas are histologically benign but locally aggressive tumors with
	a high propensity to recur. Our case highlights the importance of long-term vigilance in
	patients who have undergone chordoma resection.
	Case Report We report the case of a 47-year-old man with a cervical chordoma who
	developed multiple musculoskeletal ectopic recurrences in the left supraclavicular
	region, the proximal right bicep, and the left submandibular region without recurrence
	in the primary tumor site. Primary tumor resection was achieved via a combination of
	surgery, adjuvant radiation therapy, and imatinib. All recurrences were successfully
	resected and confirmed via pathology to be ectopic chordoma.
	Discussion Ectopic recurrence of cervical chordoma is rare and lung is the most
	common site of distant spread. Chordoma recurrence in skeletal muscle is particularly
	rare, with only 10 cases described in the literature. A plausible mechanism of distant
Keywords	metastatic disease in chordoma patients suggests that tumor cells escape the surgical
► chordoma	tract via a combination of cytokine release, vasodilation, and microtrauma induced
 ectopic chordoma 	during resection.
 cervical chordoma 	Conclusion Cervical chordoma with ectopic recurrence in skeletal muscle has not
 skeletal muscle 	been previously described in the literature. Skull base surgeons should be aware of the

phenomenon of chordoma ectopic recurrence in the absence of local recurrence. metastasis

Introduction

Chordomas are rare primary tumors of bone arising from notochord remnants. They predominantly involve the sacrum (50-60%), clivus (25-35%), cervical spine (10%), and rarely the thoracic spine (1%).¹⁻⁶ Chordomas have been described to have an incidence of ~0.08 per 100,000 and more commonly affect men with a peak incidence in the 50to 60-year age range.⁷ They have a low incidence in patients younger than 40 years and are rarely seen in childhood or adolescence. While histologically benign, they are usually locally aggressive with a high recurrence rate and often

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involve critical neurovascular structures. Optimal treatment includes gross total resection, en bloc if possible, followed by adjuvant radiation therapy, frequently proton beam for clival tumors.^{2–5,8,9} Despite aggressive management, the median survival based on a survival analysis using the Surveillance, Epidemiology, and End Results (SEER) database has been reported to be 6.29 years with 5, 10, and 20 years mortality rates demonstrating steep declines in survival at 67.6, 39.9, and 13.1%, respectively.⁷

Even with surgery and radiation, chordomas have a recurrence rate of ~46 to 70%.³⁻⁵ Known risk factors for recurrences are subtotal resection, absence of adjuvant radiation

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therapy, tumor location, and histologic subtype.^{3,5,9–12} Most recurrences are local, with estimates ranging from 19 to 54%; however, surgical tract dissemination and distant metastases have also been reported.^{9,12–15} The rate of metastasis varies greatly in the literature, with some estimates reported to be as low as 3 to 5% and others as high as 42%.^{3–5,11,12,16,17} Most metastases originate from primary sacrococcygeal chordomas,^{18,19} although cervical chordomas also show metastatic spread.^{9,18,20} Lung, bone, lymph nodes, and liver are among the most commonly reported metastatic sites.^{1,3,8,14,17,19} Much rarer sites include the hands, skeletal muscle, skin, and the heart.^{2,3,5,8,12,16,17,19}

Surgical approaches for chordoma are executed according to location of the tumor. For instance, the surgical strategy for spine versus clival chordomas differs significantly. Clival chordomas are resected via an endoscopic endonasal approach (EEA) or if in the lower clivus, a contralateral transmaxillary approach.²¹ In contrast, spinal chordomas are typically resected via several anterior and/or posterior approaches.²² A variety of approaches have been described for resection of cervical chordomas including anterior, posterior, combined anterior and posterior, transoral, transmandibular, transfacial, and endoscopic transnasal or transoral approaches among others.^{22,23} Of note, the excision of atlantoaxial chordomas (C1-C2) is further subdivided into three major anterior approaches¹: bilateral high anterior cervical approach for visualization of C2 vertebral body and bilateral transverse processes,² anterior midline transoral for spinal lesions located from the mid-clivus down to the C3 level, and³ transmandibular approach combined with anterior cervical approach to provide exposure from clivus to the lower cervical spine.²⁴ Patients with subaxial chordoma (C3-C7) may undergo a staged surgical approach consisting of posterior release osteotomies with tumor dissection followed by an anterior neck dissection with en bloc tumor resection on a different date.²⁵ Alternatively, patients may undergo an anterior cervical approach with longitudinal incision alone. Sacroccygeal chordomas are typically resected via a more limited set of approaches that include an anterior, posterior, or combined anterior and posterior approach.²² Furthermore, cervical chordomas are some of the least common sites among spinal column chordomas and pose significant surgical challenges.²⁶ In fact, en bloc resection of cervical chordomas has been associated with increased morbidity and mortality due to the involvement of critical neurovascular structures surrounding the cervical spine.²⁷⁻³¹

In the present article, we describe the case of a 47-yearold man with a history of cervical chordoma who developed musculoskeletal ectopic recurrences, first in the platysma and sternocleidomastoid muscles and subsequently in the biceps muscle without evidence of recurrence in the primary tumor site during either ectopic recurrence. To our knowledge, this is the only described case of a primary cervical chordoma recurring in musculoskeletal sites without recurrence at the primary tumor site. A systematic review of the literature was performed to identify cases of cervical chordomas with ectopic recurrence as well as for chordomas that recurred in musculoskeletal sites after primary tumor resection. The PubMed database was searched using the following key phrases: "metastatic cervical chordoma," "ectopic cervical chordoma," and "chordoma skeletal muscle." We excluded articles that described musculoskeletal recurrence for other tumor types and refined our inclusion criteria to chordomas limited to the cervical spine for investigation of cervical chordomas that metastasize. While the question of whether distant chordomas identified status postresection of a primary tumor are better termed distant metastases or ectopic recurrences remains unsolved, we describe our case using the term ectopic recurrence.

Case History

In December 2003, a 47-year-old man presented with neck pain and stiffness that limited his ability to turn his head to either side without any antecedent trauma. In early 2004, he noticed changes in the quality of his voice, difficulty swallowing, and began snoring in his sleep. The patient continued to have spasm-like interscapular pain that was not alleviated by muscle relaxants or nonsteroidal anti-inflammatory drugs, in addition to shortness of breath, hoarseness, and dysphagia. Due to persistent symptoms, the patient underwent back pain evaluation, prompting imaging that incidentally revealed a prevertebral/retropharyngeal mass in June 2004. Computed tomography (CT) of the neck and cranial base revealed a well-circumscribed hypoattenuating precervical mass centered on the C2 vertebral body measuring ${\sim}11.6\,cm {\times}\,4.2\,cm {\times}\,7.2\,cm$ (\blacktriangleright Fig. 1). The mass demonstrated multiple enhancing septations with involvement of both C2-C3 neural foramina, left greater than right, extending from the basion to the C6-C7 disk space. The C2 body demonstrated sclerosing and scalloping. There was mass effect evident with deformity of the left lateral spinal cord and encroachment of the mass at the left C3-C4 neural foramina. Moderate loss of disc height was noted at C4-C5 and C5-C6. C5-C6 and C6-C7 demonstrated a mild disc bulge with deformity and flattening of the cord. Based on the limited airway and the need for tissue diagnosis, a combined tracheotomy and biopsy were completed prior to resection and the pathology confirmed chordoma.

The patient underwent a left-sided anterior cervical approach in June 2004 which revealed a large, gray-colored mass with a thick capsule, displacing the trachea and esophagus ventrally and bilateral invasion the longus coli muscles. The mass dramatically compressed and displaced the patient's upper airway anteriorly, eroded the C2 vertebral body, and displaced and partially encased the adventitia of the left vertebral artery. Due to extensive extension of the tumor into the left vertebral artery, en bloc resection was not feasible. Blunt and sharp microdissection were required, but anatomy and flow of the artery were preserved. During resection, there was a remaining portion that had entered the C2–C3 foramina that could not be visualized by an anterior transcervical approach. This portion of the tumor was intentionally left to be resected in a subsequent surgical stage. The resected chordoma was tan, red, and brown with

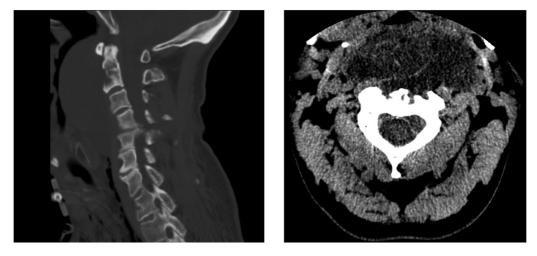


Fig. 1 Preoperative sagittal (left) CT depicting C2 chordoma within the prevertebral space extending from the basion to C6–C7 level. There is involvement of both C2 and C3 neuronal foramina, left greater than right, with expansion of the left neuronal foramen and extension into the left epidural space. Preoperative axial CT (right) details sclerosis and scalloping of the C2 vertebral body. CT, computed tomography.

myxoid features and no evidence of angiolymphatic invasion on pathology.

A postoperative magnetic resonance imaging (MRI) and CT in late July 2004 showed a residual elongated low-density cystic lesion in the retropharyngeal and vertebral space extending from C1–C5 (Fig. 2). In August 2004, the patient underwent a posterior cervical approach for C2-C3 foraminotomy, and an occipital to C3 instrumented arthrodesis. The left-sided C3 nerve root was found to be compressed inferiorly by tumor. The tumor and its capsule were resected in a piecemeal fashion until clear margins were achieved and flow of the vertebral artery was preserved. Postoperatively, the patient did well with no complications in the hospital course. However, a postoperative MRI after the second surgical procedure showed residual chordoma in the C2 vertebral segment, ventral epidural space, and surrounding the left vertebral artery in the C2-C3 level. The patient was evaluated for adjuvant proton beam therapy on May 2005; however, to improve the patient's long-term prognosis, it was recommended that the patient undergoes endoscopic



Fig. 2 Postoperative sagittal CT of C2 chordoma showing substantially smaller lesion as compared with preoperative imaging and improvement of C2–C3 neuronal foramen involvement. CT, computed tomography.

transoral approach for completion of the odontoidectomy for gross total removal of the residual chordoma prior to radiation therapy.

As a result, the patient underwent an endoscopic-assisted transoral approach for odontoidectomy and resection of the recurrent chordoma in April 2006. The resected specimen was grossly tan-red and consisted of scattered physaliphorous cells in mucoid matrix, consistent with a chordoma. MRI in September 2006 showed persistent chordoma within the original tumor bed, though the MRI could not certainly discriminate between possible residual chordoma and postoperative changes. The patient subsequently underwent proton beam and photon radiation therapy starting in March 2007 for a total of 51 days via 38 fractions for a total dose of 76.0 cobalt Gy equivalents. A follow-up MRI in October 2007 showed evidence of recurrence in the retropharyngeal region ventral to the C3 and upper C4 vertebral body as well as two to three other lesions located in the periphery of the resection site and surrounding the left-sided vertebral artery. Due to progression of the tumor, the patient started Gleevec in 2008. In both October 2008 and April 2009, follow-up surveillance MRI scans revealed that the T2 hyperintense lesions in the retropharyngeal region were stable as compared with previous imaging and were serous postoperative fluid collections.

In July 2010, the patient complained of a palpable mass in the left supraclavicular region, The mass was nontender upon palpitation. The patient reported the mass was originally pea sized and increased to about the size of a marble in 6 months. He denied any neurological changes or problems. MRI scan of the neck and cervical spine was significant for a new 2.5×0.9 cm nodular lesion beneath the skin just anterior to the sternocleidomastoid muscle, with signal characteristics slightly less dense than neighboring muscles and irregular enhancement suspicious for a chordoma. Of note, examination of the cervical spine revealed no interval change of significance. On physical examination, the mass was 1.5 to 2.0 cm in size, mobile and free of overlying skin, and irregular. A subsequent fine-needle aspiration was performed, and pathology confirmed recurrent chordoma. Direct laryngoscopy, left lower neck dissection, and excision of the ectopic chordoma were performed in August 2010. During surgical resection, the mass was located in between a previous tracheostomy scar and a left lower neck scar. The mass was found to be diffusely infiltrative of the platysma and sternocleidomastoid muscles with multiple separate small deposits of tissue encountered, all of which were all resected. There was no gross palpable or visual disease left in his neck after surgery, and no lymph node involvement was observed. The ectopic recurrence required no additional radiation of other treatments, and the primary site remained stable with no evidence of recurrence.

The patient remained clinically and radiographically stable from 2010 until 2016, when he noticed a mass in the upper bicep region of his right arm. His history of chordoma and the prior ectopic recurrence raised suspicion of another ectopic chordoma. An ultrasound demonstrated a 3.4 cm \times 2.0 cm \times 0.9 cm oval well-defined solid lesion along the superior aspect of the right biceps muscle with peripheral vascularity and small cystic components within the lesion. This new mass was resected en bloc, and pathology confirmed metastatic chordoma with diffuse and intense staining for pancytokeratin, S-100, and CD34 (**– Fig. 3**). MRI of the primary site remained stable with no evidence of residual or recurrent chordoma. After the resection of this lesion in 2016, the patient remained clinically and radiologically stable with no evidence of recurrent chordoma until 2020.

In early 2020, the patient again described a left-sided submandibular mass. He denied symptoms referable to the mass, including deep neck or jaw pain, dysphagia, and facial droop or weakness. The mass was mobile, ~ 1 cm in size, and over-layed the hyoid bone. An ultrasound of the neck mass was suggestive of chordoma. Subsequent MRI of the soft tissue of the face and neck revealed a T2 hyperintense lesion in the left neck below the mid-mandible most consistent with ectopic chordoma. The primary chordoma resection site still showed no evidence of recurrence. In March 2020, he underwent a left submandibular mass excision of the ectopic recurrence along with surrounding platysma and soft tissue. The chordoma was found in the subcutaneous plane and intertwined with the platysma. Pathology confirmed a chordoma with skeletal muscle involvement. Margins were negative for neoplasia.

The patient is currently 65 years old and remains well with no recurrence in the primary tumor site after 15 years at the time this article was written. We remain vigilant in identifying any new suspicious lesions that may represent an ectopic recurrent chordoma.

Discussion

Chordomas are a rare, low-grade subtype of bone sarcoma. In the United States, chordomas mainly originate from spinal (33%), cranial (32%), and sacral (29%) sites.³² The sacrococcygeal region is the most common site of origin

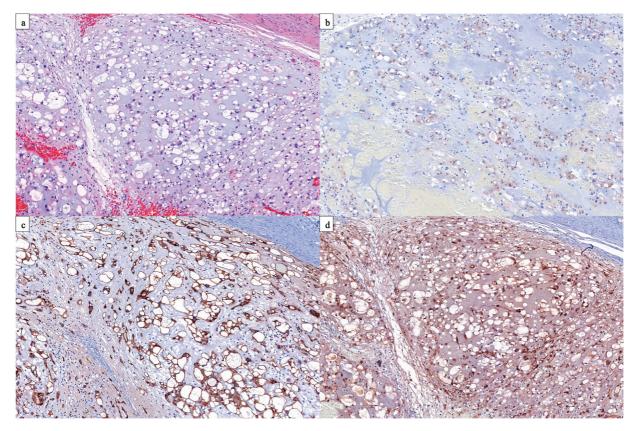


Fig. 3 Pathology for ectopic chordoma of the bicep. (a) Resected tumor with pathology consistent with a chordoma showing chords, sheets, and physaliphorous cells in a myxoid matrix. (b) Chordoma specimen staining positive for epithelial membrane antigen. (c) Chordoma specimen staining positive for S100.

	Study type	Number	Age/sex	Original location	Original treat-	Number of	Ectopic recur-	Time to	Recurrence	Treatment of
		of patients			ment	recurrences	rence loca- tion	recurrence	in primary site	recurrence
Chalmers and Coulson (1960) 44	Case report	-	49/female	Sacral	Wide local exci- sion + local radi- ation therapy	1	Triceps muscle	5 y	No	Wide local excision
Debenham (1965) ⁴⁵	Case report	1	80/male	Unknown	None—not found	2	Right gluteus maximus	N/A	Unknown	Surgical resection
Wang and James (1968) ⁴⁶	Case report		59/male	Sacrococcygeal	Surgical resection	ц	Right deltoid, axillary, infra- clavicular regions, glu- teus maximus	8 0 0 0	Yes	Multiple local partial excisions
Yarom and Horn (1970) ⁴⁷	Case report	-	57/male	Sacrococcygeal	Local radiation (telecobalt 3,500 rads) + systemic chemotherapy (nitrogen mus- tard, 0.25 mg)	-	Heart, left temporal muscle, left pectoralis ma- jor, right psoas, pelvis	2 y	Yes	Local radia- tion + chemo- therapy
Carey et al (2014) ¹⁶	Case report	F	65/male	Sacral	Wide local exci- sion with piece- meal excision	2	Widespread skeletal mus- cle metastases involving the trapezius, par- aspinal mus- culature, al mus- dinfraspinatus, triceps, glute- al muscula- ture, vastus intermedius, and tongue; liver, adrenal	3 mo	Yes	High-dose ad- juvant proton therapy + re- excision for local recur- rence; daily imatinib ther- apy subsequently
Vu and Haygood (2015) ⁵	Case report	-	50/male	Sacrococcygeal	Surgery + adju- vant radiation therapy	4	right upper thigh, gluteus maximus, oc- cipital scalp	7 y	Yes	Surgical resection
Emori et al (2014) ¹²	Case report	-	71/female	Sacral	Carbon ion radi- ation therapy	-	Thenar muscles, femur	18 mo	No	Surgical resection

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Treatment of recurrence	Palliative radi- ation therapy + neoadju- vant chemo- therapy with weekly low- dose cisplatin along with 800 mg of imatinib mesylate	lmatinib + pazopanib (800 mg/d)	Tumor remov- al with S1 and S1 joint resection	Surgical resection
Recurrence in primary site	Yes	Yes	No	No
Time to recurrence	3 y	1.5 y	34 mo	1 y
Ectopic recur- rence loca- tion	Left gluteal muscles, ischiorectal fossa	Gluteal muscles, right proximal fe- mur, posterior left humerus, right scalene muscle, inter- costal muscles adjacent to fifth rib, tongue	Right gluteal muscle	Inferior right gluteus maximus
Number of recurrences	7	m	-	-
Original treat- ment	En bloc excision	Wide surgical ex- cision, chemo- therapy, radia- tion therapy	Excision 52	Surgical resection
Original location	Pericoccygeal	Sacral	\$2/53	Sacrococcygeal
Age/sex	47/male	61/male	54/male	73/male
Number of patients	-	-	-	-
Study type	Case report	Case report	Retrospective review	Case report
Study	Rohatgi et al (2015) ⁴⁸	Biskin et al (2017) ³³	Chanplakorn et al (2020) ⁴⁹	Liu et al (2021) ⁵⁰

for spinal chordomas. Tumors originating in the cervical spine are much less common and only make up \sim 6% of all chordomas.^{2,26} Additionally, cervical chordomas can be particularly challenging due to critical surrounding neurovasculature.³¹ While most chordomas have been found to metastasize to the lung, bone, lymph nodes, and liver,^{3,8,14,17,20} chordomas have a diverse range of potential sites for metastatic growth with reports describing metastatic disease in the tongue, larvnx, breast, mandible, pleural effusions, and skeletal muscle.^{16,33-37} Cutaneous metastatic cases, also known as chordoma cutis, are quite rare with less than 20 reported cases in the literature, most originating from sacral chordomas, though origins from cervical and skull base chordomas have been documented as well.³⁸ Cardiac metastases are even rarer, with only seven reported cases originating from primary sacral and clival chordomas.¹⁸

Metastasis to skeletal muscle is quite rare, with a low incidence rate in clinical practice.³⁹ Lung cancer, gastrointestinal tumors, urologic tumors, genital tumors, and breast cancer are the most common primary malignancies that metastasize to skeletal muscle, particularly in the lower limbs.³⁹ Chordoma recurrence or distant metastasis in skeletal muscle is also rare, and in our review, we only identified 10 cases (**-Table 1**). Among the recurrent cases in skeletal muscle, primary tumors were all in the sacrococcygeal region, with exception one case that was unknown. The most common site of musculoskeletal recurrence was gluteal muscles such as the gluteus maximus. Furthermore, not only are cervical chordomas much less common but they may also have a decreased propensity to recur or metastasize to distant sites.⁴⁰ According to our review, among primary cervical chordomas that do metastasize distantly or recur ectopically, the lungs are the most common site (**-Table 2**). Another common distant site of recurrence of cervical chordomas is the skin with reports of ectopic recurrence subcutaneously in the neck, scalp, and forearm (**-Table 2**). Interestingly, one case described distant metastasis to the head of the pancreas.⁴¹

In our review of cervical chordomas with distant ectopic recurrence, we only identified one patient with recurrent disease in the anterolateral neck and muscle from a retrospective analysis (**-Table 2**), and there was no specification if recurrence had also occurred in the primary site. Another retrospective review identified a patient with metastasis to the neck with nodules in the thigh (**-Table 2**) and pelvis, but it was unclear if the metastasis was musculoskeletal in nature. To our knowledge, our case is the first description of a cervical chordoma with musculoskeletal ectopic recurrences and no evidence of recurrence in the primary tumor site.

Moreover, while the patient described in the current case has still not experienced recurrence in the primary tumor site and is doing well 16 years after surgery in the primary site and 15 years after his last radiation treatment. It is important to note that ectopic recurrence of chordoma is typically associated with a poor prognosis. In a study of 371 patients with histologically proven cervical and skull base chordoma, 13 patients developed ectopic recurrence, of which only 7 remained alive after a followup period of 29 months.⁹ In fact, ectopic recurrence is a sign of treatment failure and is often associated with a high treatment burden. In a retrospective study of five patients with ectopic recurrence, there were a total of 18 ectopic recurrences, of which 94% were related to prior surgical tracts outside of the adjuvant radiation therapy field.⁴² The patients underwent a total of 31 surgical interventions with a median of 6 interventions per patient.

A plausible mechanism of distant metastatic disease in chordoma patients has been proposed to be related to the surgical tract.⁴² It is thought that cytokine release, vasodilation, and microtrauma during surgical resection are involved in the mechanism of distant spread.⁴³ Therefore, it is possible that surgical approach for resection may be implicated in metastatic disease and surgical site seeding. A study evaluating iatrogenic seeding of skull base chordomas found that the EEA had a 1.15% incidence of seeding in comparison to a range of 2.8 to 7.3% incidence in open approaches assessed in the literature.⁴³

We propose that the mechanism of ectopic recurrence in the described case may be due to surgical tract seeding, given that the primary tumor showed significantly more mass effect on the left side, and initial surgeries of the primary tumor were open approaches. Importantly, the recurrent neck masses in 2010 and 2020 were all located on the left side. Additionally, the resected neck mass in 2010 was found to be between a previous tracheostomy and left lower neck scar. However, the ectopic recurrence in the right biceps muscle cannot be easily explained by the idea of surgical tract seeding and may have occurred due to spread via the lymphatics or vertebral venous plexus, as the vertebral venous plexus is usually a source of spread to the spinal column and not muscle.⁴² Still, there is no clear definition of surgical tract recurrence, and the mechanisms of distant metastasis or ectopic recurrence have not been clearly established. What remains of utmost importance is maintenance of a close follow-up in patients with a history or resected chordoma given the tumor's high recurrence rate and potential for ectopic spread.

Conclusion

Chordomas are rare primary bone tumors that have a propensity to recur locally, yet have the potential to recur ectopically. Cervical chordomas are rare and ectopic recurrence in skeletal muscle is even more rare. To the best of our knowledge, this is the first case describing a cervical chordoma with ectopic recurrence to skeletal muscle without recurrence in the primary tumor site. Our objective is to provide awareness of the phenomenon of chordoma ectopic recurrence even without recurrence in the primary tumor site. Finally, we attempt to highlight the importance of systemic vigilance in patients who have undergone chordoma resection.

Study	Study type	Number of patients	Age/sex	Location of cervical chordoma	Original treat- ment	Number of recurrences (local and metastatic)	Ectopic recur- rence location	Time to recur- rence in ectopic location	Recurrence in primary site	Treatment of recurrence
Bjornsson et al (1993) ⁵¹	Retrospective review	2	Unknown/ male	Cervical (unspecified)	Resection and irradiation	N/A	(1) Pleura, (2) lungs and subcu- taneous tissues	(1) 5 y, (2) 4 y (lungs), 8 y (sub- cutaneous tissues)	(1) Yes (2) No	(1) None (death), (2) none (death)
Arnautović and Al- Mefty (2001) ⁵²	Case report	-	44/female	C3-C6	Anterolateral to cervical spine ap- proach and con- ventional radia- tion therapy	-	Anterolateral neck/muscle and subcutaneous tissue	5 mo	Unknown	Unknown
Hosalkar et al (2002) ⁵³	Case report	1	8/male	2	Posterior fusion from occiput to C4, anterior transoral resec- tion of C2, proton beam radiation therapy	L	Pulmonary metastases	6 mo	No	None
Barrenechea et al (2007) ³¹	Retrospective review	1	36/male	C1-C2	Intralesional excision and proton beam radiation	-	Neck, and meta- static nodules in the thigh and pelvis	17 mo	Yes	None (death)
Vogin et al (2016)	Retrospective review	υ	(1) 58/male, (2) 49/female, (3) 25/female, (4) 50/male, (5) 53/male	Unspecified	Surgery and post- operative radiation	Unknown	 Lymphade- nopathies, lung; Jymphade- nopathies, lung metastases; (3) subcutaneous scalp and neck; subcutane- ous scalp and retroarticular; subcutane- ous R forearm 	(1) 14 mo, (2) 27 mo, (3) 17 mo, (4) 43 mo, (5) 78 mo	Unknown	 None, secondary surgery, (3) none, (4) sec- ondary sur- gery, (5) sec- ondary surgery and bifractio- nated radiation therapy
Berlucchi et al (2020) ³⁸	Case report and literature	1	55/male	C3 vertebral body	Anterior cervical approach and C3 corpectomy	3	Base of the neck cutaneous	5 y	Yes	Wide local resection
Klejnow et al (2022) ⁴¹	Case report	-	45/female	Unspecified	Cervical verte- brectomy and proton beam therapy	2	Head of pancreas	Unknown	Yes	Imatinib, radia- tion therapy

Conflict of Interest

J.J.E. received royalties from Mizuho.

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