ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXVI | No. 3 September 2022

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DOI: 10.33962/roneuro-2022-056

Romanian Neurosurgery (2022) XXXVI (3): pp. 334-341
DOI: 10.33962/roneuro-2022-056
www.journals.lapub.co.uk/index.php/roneurosurgery

Cervical Chondrosarcoma: A critical review with an illustration of a rare technically challenging case

Anil Kumar Sharma[2], Prashant Raj Singh[2], Satish Satpute[2], Nitish Nayak[2], Ashish Gupta[2], Raghavendra Kumar Sharma[1], Nitin M Nagarkar[2]

[1] A.I.I.M.S. Jodhpur, Rajasthan, INDIA
[2] A.I.I.M.S. Raipur, C.G., INDIA

ABSTRACT

Chondrosarcoma of the cervical spine is an extremely rare tumour. The indolent course and neglected behaviour of the patient often give enough time for tumour expansion. The surgical management of these types of tumours is challenging. En bloc resection is a proven ideal treatment but it is not always feasible in this region because of the proximity to vital neurovascular structures which explains the recurrence and poor prognosis of this tumour. The role of radiation and chemotherapy in these tumours is limited. We are highlighting unique huge cervical chondrosarcoma which is not mentioned in literature and its management along with a review of 34 cases, published so far.

Keywords
cervical chondrosarcoma, treatment, recurrence, prognosis

INTRODUCTION

Chondrosarcoma (CHS) comprises a heterogeneous group of cartilage matrix producing neoplasms.[1] After myeloma and osteosarcoma, chondrosarcoma is the third most common primary malignancy of bone.[2] The majority of these types of tumors are benign and metastasis occurs rarely. Incidence of CHS of the spine is 7-12% of all primary spine tumor with male predominance and usually presents at the third to fifth decade of life.[3] Most commonly it occurs in the thoracic spine (60%) followed by lumbar (20-39%) and less frequently in the cervical spine (19-20%).[4] These slow growing insidious lesions are often voluminous at the time of discovery and diagnosis is usually delayed which pose difficulty in management. Surgical treatment is ideal for these types of tumors.[5,6] However, especially in the cervical spine, due to the proximity of tumors with vitals neurovascular structures and the intricate anatomy of this region , these tumors cause great difficulty for a surgeon. We discuss a case of unique huge cervical chondrosarcoma of C3 to C5 and to the best of our knowledge, such a large tumor has not been reported in the literature. Successful complete resection of the tumor was achieved using combined posterior to anterior approach with 360 degree stablisation. We also present review of the literature of 34 cases of cervical chondrosarcomas published so far.

Corresponding author:
Raghavendra Kumar Sharma

A.I.I.M.S. Jodhpur,
Rajasthan, India

sdr.raghavendra@gmail.com

ISSN online 2344-4959
© Romanian Society of Neurosurgery

First published
September 2022 by
London Academic Publishing
www.lapub.co.uk

Case description

A 50-year-old male patient presented in our department with painless, progressive enlarging right side neck swelling for the last 5 years and weakness of all 4 limbs for the last 4 months. He was unable to walk and wheelchair-bound for the last 2 months. He also had bladder and bowel incontinence. On local examination, he had approx 8X8 cm, nontender, hard, immobile swelling over the right side of the neck,between mastoid and clavicle (Figure 1). Neurologically he had spastic quadriparesis with exaggerated deep tendon reflexes and ankle clonus . The sensation was otherwise intact. Paradoxical respiration was absent and single breath count was 15 and breath-holding time was 17 seconds. His gag reflex was intact and had no other significant neurological deficit.

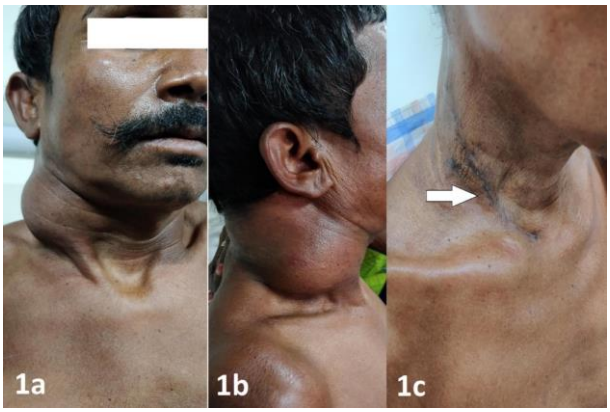

Figure 1. (a,b) Preoperative photograph of patient which shows a mass on the right side of neck; (c) postoperative photograph shows utility incision by white arrow on right side of neck with no apparent neck mass.

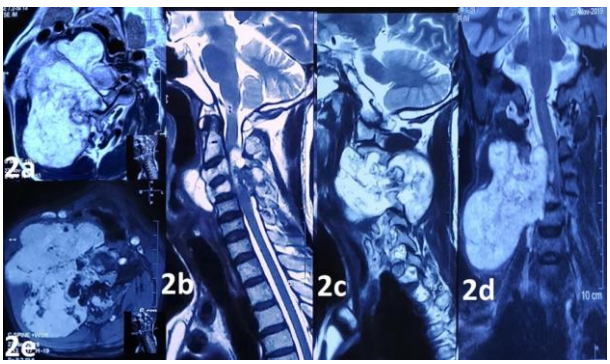

Figure 2. Preoperative magnetic resonance imaging of cervical spine (a) axial; (b,c) sagittal; (d) coronal T2 weighted images showing large hyperintense well defined lobulated predominantly exophytic lesion involving right side of vertebra with significant compressing and pushing the spinal cord on left side; (e) axial GRE sequence shows punctuate blooming foci inside the lesion.

Noncontrast computed tomography (CT) of cervical spine suggestive of the osteolytic lesion filling on the right side of the neck with C3-C5 bony destruction on the side of the tumor with irregularly mottled calcification. The vertebral artery could not be visualized on CT angiography on the right side and the internal carotid artery was pushed anteriorly (Figure 3). Magnetic resonance imaging (MRI) of the neck revealed T1 hypointense, T2 hyperintense and punctuate blooming foci on GRE sequence with large well defined lobulated predominantly exophytic lesion arising from the body and right lateral posterior arch of C3 and C4 vertebra (Figure 2). Large 8X7X7cm exophytic extramural component of the mass on right paravertebral space found which was displacing the adjacent muscles peripherally. There was Intraspinal epidural extension of tumor mass through C3-C5 neural foramina into the spinal canal and significant cord compression. A metastatic workup was done to rule out any other primary neoplastic focus or metastasis. F-18 FDG whole-body positron emission tomography with contrast-enhanced CT was performed that showed increased uptake of radiotracer on the right side of the neck with no evidence of metastasis.

Surgical technique

Because of the huge tumor and multi-compartmental involvement, combined approach with ENT specialist were planned. Due to the destruction of the C3-C4 vertebrae, the posterior cervical approach was used first then it was decided to go from anterior with the help of ENT surgeons. The patient was first placed prone and head kept in a 3-pins Mayfield fixator with the neck in the neutral position. For prolong spine surgery in a prone position, we avoid horse-shoe fixator because it may cause postoperative vision loss (POVL) .[7] A skin incision was made from inion to the C7 vertebrae. Soft-tissue dissection was done subperiosteally. Posterior vertebral elements were exposed from C1-C6 up to the lateral mass laterally but on right side lamina and lateral mass were not identified from C3-C4 due to destruction by tumor tissue. The tumor was identified with major bulk on the right side from C3-C4. The tumor was well capsulated, soft, and moderately vascular. The tumor invaded the spinous

process and right side of the lateral masses/laminae/transverse process from C3-C4.

Tumor tissue which was approached from behind was debulked in piecemeal. En-bloc excision was not possible because the tumor encased the vertebral artery and spinal cord with nerve roots. Even tiny pieces of the tumor were excised to prevent a recurrence. The cervical spinal cord which was severely compressed by the tumor was decompressed. All nerve roots were preserved and freed from surround soft tissues. Bilateral C1 lateral mass, C2 pedicle screws were inserted. Left side C3-5 and right side C5 lateral mass were placed and all metallic implants were connected with rods. The wound was closed in anatomical layers and position changed from prone to supine after placing the patient's neck on the hard cervical collar. In supine and neck neutral position, using utility neck incision [8] begins "anteriorly at the level of the cricoid and carried laterally to the posterior border of the sternocleidomastoid, continuing its gradual curve upward to end behind the prominence of mastoid process".The sternocleidomastoid muscle was divided to ease for tumor excision. ICA was identified and separated with the tumor capsule.

The major bulk of Tumor tissue along with the capsule was excised from the different compartment of the neck to create a large cavity. This anterior tumor cavity joined with the cavity made posteriorly from the previous approach. After dissecting longus colli over the C3 and C4 vertebral body, anterior tubercles were exposed. C2-3, C3-4, and C4-5 discectomy were performed and posterior longitudinal ligament was also excised. Partially destroyed vertebral bodies of C3 and C4 were excised in piece-meal fashion with the help of rongeurs. Resection was performed carefully to avoid any remnants of the tumor. After preparing endplates of C2 and C5, a corpectomy titanium mesh cage was fixed in between vertebral bodies. Artificial bone graft placed in the mesh cage to enhance the fusion. Corpectomy screws in C2 and C5 were also inserted to achieve fixation. After careful inspection of tumor residuals and bleeding spots, wound closed in anatomical layers. Just after surgery patient was neurologically the same as before, he was advised to wear a hard cervical collar. Before discharge on the fifth day, the patient developed signs of recovery in the form of a reduction in spasticity.

Histopathology

Histologically this tumor turn out to be well differentiated conventional CHS. Pathologically it is characterized by well circumscribed cartilaginous tumor with increased cellularity of chondrocytes with occasional bi to multinucleation. Moderate nuclear pleomorphism and cytoplasmic vacuolization within the chondroid matrix (Figure 5).

Follow-up

The patient was followed up clinically after 1, 3 and 6 months. The patient showed gradual improvement in his motor power of limbs. After a couple of months, he started walking and became independent after 3 months. Now the power in his upper and lower limbs is 4+/5 on MRC grade with improvement in bladder and bowel continence. As per our protocol, noncontrast computed tomography (NCCT) scan of the cervical spine was performed postoperatively to know the position of implants (Figure 4).

Table 1. Cervical Chondrosarcoma: review of 34 cases from literature

SN	Author / year	Case no	Age/sex	Level	Surgery	Grade ‡	Adjuvant radio-therapy	Follow up in months	outcome	Recurrence/duration in months
1	Arlen/1970[21]	1	56y/M	C5	STR	NS	RT	36m	death	Y/6m
		2	42y/M	NS	STR	NS	N	60m	death	Y/NS
2	Blaylock/ 1976[22]	1	43y/M	C2	GTR	Low grade	N	12m	Alive	N
3	Wronski/ 1974[23]	1	22y/M	C5-6	STR	Well diff	RT	2m	alive	N
4	Yang /2012[5]	1	29y/M	C7	STR	Low grade	N	46m	death	Y/21m

		2	32y/M	C6-7	En bloc resection	Low grade	N	140m	Alive	N
		3	42Y/M	C6	STR	Low grade	N	36m	Death	Y/24m
		4	22y/M	C7	GTR	High grade	RT	92m	Alive	N
		5	67y/M	C3	GTR	Low grade	RT	37m	alive	N
5	York / 1999[6]	1	64y/M	C4	STR	Average grade	N	7m	Death	N
		2	54y/M	C7	GTR/GTR#	Average grade	RT/N	67.2m	alive	Y/(3.7m/ 1.2m)
		3	51y/F	C7	STR/STR#	High grade	N/RT	10m	Death	Y/(4m/N)
		4	64y/F	C4	STR/STR/STR/STR†	Low grade	RT	3.5m	Death	Y/ (9/6/6/N)
6	Tessitore/ 2006[24]	1	22y/F	C7	STR	Clear cell	Proton beam therapy	12m	Alive	N
7	Ohue/ 1995[25]	1	48y/M	C5-6	GTR	Low grade	N	36m	Alive	N
8	Simsek/ 2009[16]	1	18y/m	C3	GTR	NS	N	12m	Alive	N
9	Foweraker / 2007[26]	1	43y/F	C1	STR	Well differ	RT	107m	Alive	N
10	Dejean / 1998[27]	1	64y/M	C7	STR	Average grade	N	30m	Alive	Y/24m
11	Finn / 1984[28]	1	45y/M	C7	GTR	Low grade	N	228m	Alive	N
		2	64y/M	C4	GTR	Average grade	N	8m	Death CHF	N
12	Merchant / 2014[29]	1	30y/M	C5-7	GTR	Low grade	N	12m	Alive	N
13	Boriani/ 2000[15]	1	13y/M	C7	En bloc resection	NS	N	236m	Alive	N
		2	31y/M	C5-7	En bloc resection	NS	N	40m	Alive	N
14	Strike / 2011[30]	1	60y/F	C2-4	GTR	NS	N	24m	Death due to pul mets	NS
		2	37y/ F	C4-C5	STR	NS	Proton beam therapy	48m	Death due to pul mets	NS
		3	79y/M	C5-C6	GTR	NS	N	48m	alive	N
		4	46y/M	C1-C2	GTR	NS	N	78m	alive	N
15	Sakayama/ 2004[31]	1	58y/M	C2	STR	Average grade	N	36m	alive	Y/12m
16	Gebhart/ 2008[32]	1	30y/M	C4	En bloc resection	Low grade	N	132m	Alive	N
17	Camins/ 1978[33]	1	20y/F	C5-6	GTR	Low grade	RT	1m	Alive	N
18	Shives/ 1989[10]	1	33y/F	C4	STR	Average grade	RT	14m	Death due to disease	NS

	2	58y/ M	C7	STR	Average grade	N	60m	Death due to disease	NS
	3	35y/ F	C7	STR	Low grade	RT	233m	Death due to disease	NS
	4	59y/M	C5	STR	Low grade	N	43m	Death due to disease	NS

NS- not specified; M-male, F-female; GTR- gross total resection, STR- subtotal resection; Grade: NS- not specified, RT-radiotherpay, N-no radiotherapy, m- months; recurrence (Y- yes, N-no recurrence), NS- not specified; # 2 surgical procedures in the same patient; † 4 surgical procedures in the same patient; ‡ histological grade according to Thomson and Turner-warwik11 (low, average and high grade).

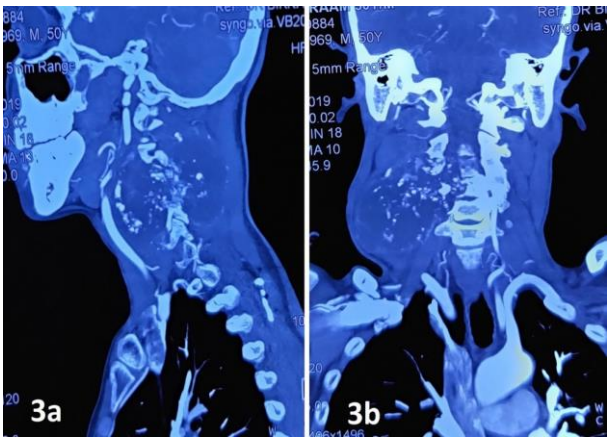

Figure 3. Preoperative computed tomography angiography (a) sagittal view shows mottled calcification within large osteolytic lesion with anteriorly displaced carotid artery; (b) coronal view shows dominant left vertebral artery without visualization of right vertebral artery with partial destruction of multiple vertebrae.

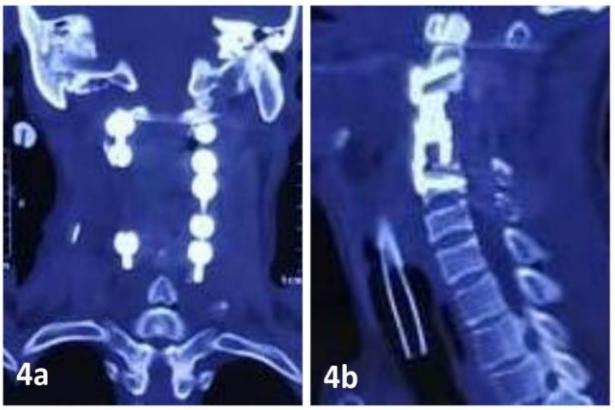

Figure 4. Postoperative computed tomography of cervical spine (a) coronal view showing metallic construct consist of bilateral C1 lateral mass and C2 pedicle screws, left side C3,5,6 and right side C6 lateral mass screws fixation with rods; (b) sagittal view showing distractable interbody cage in C2-C5 vertebral space with plate/screws.

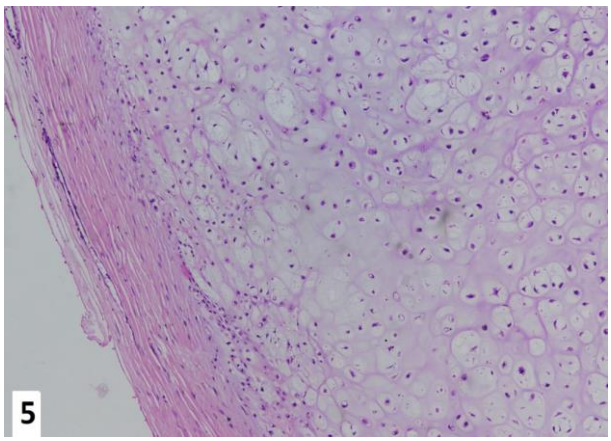

Figure 5. H&E stain 100x: shows the well circumscribed cartilaginous tumor with increased cellularity of chondrocytes with occasional bi to multinucleation, moderate nuclear pleomorphism and cytoplasmic vacuolization within the chondroid matrix.

Discussion

Spinal chondrosarcoma is a rare entity, out of the vertebral column cervical spine is the least common site affected.[3,5,6] We reviewed 34 cases of cervical chondrosarcomas in literature published by 18 authors so far (Table 1). Demographically mean age of presentation is 43.5 years and males are more commonly affected than females (25:9). Presenting feature of CHS patients showed indolent growth pattern and most common presenting symptom is local site pain.[6] Neurological features are not uncommon and present as myelopathy or radiculopathy.[9] As the tumor grows further from the vertebral body or posterior elements, it appears as a palpable mass in the neck or back. Yang et al reported in his study that the duration between the symptoms and diagnosis ranges from 3-60

months.[5] Our patient had a history of 5 years, the reason for this long-duration presentation was ignorance. The majority of tumors arise from the normal bone without any association of any benign cartilaginous pathology.[10] Various allelic losses and nonrandom genetic aberration occur in a majority of tumors (70%), Several mutations are associated with malignant degenerations of chondroma which includes amplification of c-Myc oncogene and a gain of chromosome 8. The loss of chromosome 6 and the gain of 12q12 also related to high-grade CHS. [3,4]

Yang et al reported that the tumor originated most commonly from the posterior part of the vertebral bodies (73.3%) as compared to posterior elements of the vertebra. Extraosseous paravertebral involvement also occurred in the majority of cases in his case series.[5] Our case review showed that the C5-7 vertebral region is most commonly affected by the tumor. However, no specific cervical level for common occurrence is mentioned in literature. Radiological diagnosis includes characteristics CT findings of bony destruction with irregularly mottled calcification with low attenuation of the mass lesion due to the water content of the cartilage matrix. MRI is also very useful to know the extent of soft tissue invasion.

T1-weighted images showed hypointense and T2-weighted demonstrate hyperintense images of a lesion with heterogeneous or peripheral ring type of enhancement on intravenous gadolinium injection.[3] Increased uptake of radiotracer in the region of tumors is often shown in bone scanning. Despite the lower proportion of the malignant nature of CHS, PET CT is a useful tool to diagnose the extent of disease spread. It helps in the planning of management. PET CT did not demonstrate any secondary deposition or evidence of metastasis in our patient.

Previously Thomson and Turner-Warwik classified the CHS histologically into low, average and high grade.[11] The world health organization (WHO) described CHS as nonmeningothelial, mesenchymal neoplasm.[12] Based on histologic features such as tumor cellularity, mitosis nuclear atypia, and stromal content, the grading system is used by WHO. It ranges from grade I(low grade) to grade IV (high grade). One of the most important prognostic indicators of CHS is WHO grade. In low-grade CHS, 10 years survival is 90% where it is 30-40% in high grade.[4] In our review of cases we also found 47% of cases were low grade CHS which was the most common histological type among them. Chondrosarcomas are also classified into several subtypes based on stereotypic histologic features which include conventional, mesenchymal, clear cell and dedifferentiated types.[13]

Conventional CHS is the most common subtypes (around 80%) and almost all of them are of low grade. Malignant degeneration of low-grade conventional CHS gives rise to a dedifferentiated type. Mesenchymal CHS is very much similar to dedifferentiated CHS and it has a poor prognosis with a 5-year survival rate of 50%. Finally, clear cell CHS have a better prognosis than mesenchymal or dedifferentiated subtype (McLoughlin).[3]

In tumor management, histopathological diagnosis is required. Percutaneous CT guided biopsy can be performed in this type of tumor but it requires careful interpretation. Lis et al reported 24% false-negative results in these types of sclerotic lesion.[14] Hence it was decided to undergo the excision of the tumor without a biopsy. Due to the ineffectiveness of conventional chemotherapy and radiotherapy, surgical management in the form of en-bloc resection is the only ideal method for the treatment of CHS.[5,6] Out of 34 patients in case review, en bloc resection was achieved in 4 patients. Gross total resection was associated with a better outcome as compared to STR. GTR performed in 13 and STR in 17 patients. Local recurrence is reported in 9 patients, out of which 88.9% associated with STR. Mean follow up was 58.4months. Out of 14 deaths, 12 deaths (85.7%) are recorded among those patients who underwent STR of the tumor.

Boriani et al. reported the outcome difference of en-bloc resection and intralesional excision of CHS in his study.[15] He found no local recurrence in 9 patients who were treated with en-bloc resection with wide or marginal margin whereas, there was local recurrence in all 13 patients treated with piece-meal or intralesional excision. However, due to the proximity of vital structures and technical obstacles like bleeding or spinal cord injury, it is not always possible to secure en-bloc-resection. Many case report also suggests that circumferential excision of cervical CHS could provide preserved neurological status with a long recurrence-free survival period.[16,17] Preoperative planning with a multidisciplinary approach is very essential in these

types of huge tumors. Because of the destruction of long segment vertebral column, postoperatively spinal instability would be expected as experienced by many authors, hence tumor excision along with reconstruction was decided. [16,18]

Because of huge size of tumor and restriction of neck movements, intubation itself was a challenging task. Initially we tried en-bloc resection but due to nonvisualization of vertebral artery in imaging which was untraceable even on intraoperative ultrasound and circumferential involvement of spinal cord and nerve roots, enbloc surgical decision was not feasible, hence piecemeal excision of tumor tissue along with its capsule was performed. We successful preserved all nerve roots without injury to major vessles. Follow up radiology is required to detect the local tumor recurrence or distant metastasis and it is decision making in future adjuvant therapy if possible.

Most studies reported that the adjuvant chemotherapy (CT) and radiotherapy (RT) has only limited role in CHS treatment.[5,6,15,19] Our case review also supports the limited role of RT as adjuvant therapy. RT received in 13 patients out of which 6 patients did not survive. This ineffectiveness may be due to that chemo or radiotherapy both acts on fast dividing cells and chondrosarcoma are slow growing tumors with low fractions of dividing cells. In addition to slow grade, chondrosarcomas have a rich extracellular matrix and poor vasularity, which produce hindrance of chemotherapy drug penetration.[5] Hence adjuvant therapy is not included in standard treatment recommendation.[2] Nevertheless, high dose radiotherapy or proton beam therapy may be useful to slow tumor growth and tumor recurrence but the long term results of this therapy are still unknown. Gwak et al reported that hypofractionated cyberknife stereotactic radiation therapy can potentially provide promising results in these types of radioresistant tumors.[20]

Despite the massive size of tumor and involvement of large areas of the neck and cervical spine, we successfully achieved the goal of surgery by doing complete tumor excision and restored the spine integrity by 360-degree spinal fixation. Our case is unique from all the cases reported in the literature that no case exists with so much extensive involvement of the cervical spine.

Conclusion

Huge cervical chondrosarcoma is rare and usually, these massive tumor presents with neurological deficits. Management of neglected cervical chondrosarcoma is technically challenging but adequate anatomical knowledge and detailed surgical planning in the form of a multimodality approach can prevent permanent disability and increase disease-free survival period.

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