



Fractionated Stereotactic Radiotherapy in Recurrent Clival Chordoma: A Case Report

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Abstract

Clival chordomas are a rare type of clinically malignant tumour, arising from the undifferentiated remnants of the notochord, which are slow-growing, usually radioresistant, locally aggressive and infiltrative, with high rates of recurrence and a poor prognosis. Hence, the role of radiotherapy post maximal resection in clival chordoma is undoubtedly significant, especially stereotactic radiotherapy which helps deliver higher doses with minimal dose to critical organs.

Here we are presenting the history of a 22-year-old female who had undergone multiple surgical decompressions (5 times) for recurrent clival chordoma, who presented with a history of weakness of the right upper and lower limb, difficulty of speech, and difficulty in swallowing within 6 months of last surgery. Imaging with MRI scan revealed a large, irregular lesion, arising from the superior part of the clivus, with severe mass effect on the brainstem. She was diagnosed to have a recurrence of the clival chordoma and she underwent left temporal craniotomy and decompression of lesion, immediately followed by radiation therapy with fractionated stereotactic radiotherapy to a dose of 3900cGy in 13 fractions over 3 weeks. Further dose escalation was not considered given the OARs dose constraint and the large volume of residual disease. She had neurological improvement, with 50% improvement in dysarthria and also the ability to walk with support during her last visit.

The role of radiotherapy, post maximal resection in clival chordoma is undoubtedly significant in terms of local control. It helps avoid multiple surgical interventions in the brain, like in this patient. Even a large residual tumour volume, post-surgical debulking, can be controlled with high-dose photon radiotherapy, especially when delivered by newer radiation techniques like stereotactic radiotherapy. This case study elucidates the need for use of sophisticated stereotactic fractionated radiotherapy in skull base chordomas. It also reinforces the need for adjuvant radiotherapy, for neurological and clinical improvement in large volume tumours, as it shrinks the residual tumour and also helps control local recurrence.

Keywords: *Recurrent clival chordoma, Fractionated radiotherapy, Stereotactic radiotherapy, Palliative radiotherapy, FSRT, Clival chordoma. Case report.*

Introduction

Chordomas are rare cancer types that arise from the bones of the skull base or spine. It belongs to the group of sarcomas, a type of malignant bone and soft tissue tumour. Chordomas are usually slow-growing but very difficult to treat because of the involvement of vital structures such as the brainstem, spinal cord, important nerves, and arteries. It is also shown to have a very high rate of local recurrence but a low rate of metastasis. It develops from the notochordal cells, which usually disappear when the foetus is 8 weeks old, but few cells reside within the vertebral bodies and throughout the axial skeleton.

Out of the different types of chordomas, the poorly differentiated variant, associated with deletion of SMARCB1/INI1 is common in young, more associated with skull base tumours, rare, but more aggressive, and faster growing. The prognosis of skull-base chordoma remains poor, with a mean overall survival of approximately 50% at 10 years.¹

Here, we present a case of recurrent clival chordoma, who underwent multiple surgical interventions, with significant neurological deficits who received fractionated stereotactic radiotherapy (FSRT) as an adjuvant treatment for control of local disease and to possibly avoid recurrence, who had significant neurological improvement post FSRT.

Case History

History and Presentation

We present the history of a 22-year-old female, after taking the informed consent from the patient herself and the patient's father. She presented with a history of weakness of the right upper and lower limb, difficulty of speech, and difficulty in swallowing for 1 month. No history of headache, loss of consciousness, seizures, or diminution of vision.

On examination, she was moderately built and nourished, wheelchair-bound with an ECOG (Eastern Cooperative Oncology Group) performance status of 4 and a NANO

(Neurological Assessment in Neuro-Oncology) score of 16/23. Clinically at presentation, the patient was conscious, alert, and oriented to time, place, and person, but was found to have dysarthria, left profound hearing loss, a bilateral vision of finger counting at 4 feet, left eye ptosis with corneal opacity, left lateral gaze palsy, impaired left corneal reflex, grade 4 left LMN facial palsy, impaired left side gag reflex, right side upper and lower limb power was 2/5 with MAS grade 3 spasticity, impaired sensory system (touch, pain, and temperature) on the left half of face, exaggerated deep tendon reflexes with upgoing plantar on the right side and cerebellar signs, with circumduction gait. Healthy surgical scars were present over the scalp and right upper abdomen.

Other system examinations were clinically normal. Complete laboratory evaluation and cardiac evaluation were done and found to be normal. The patient was found to have a thrombus in the left carotid artery. Pure tone audiometry showed left-sided severe sensorineural hearing loss 73db.

The patient had undergone multiple surgeries in the past including left Retromastoid Suboccipital Craniotomy and decompression (2012), left temporal craniotomy and decompression (2018), re-exploration of left temporal craniotomy and decompression (2019 - January and February (with zygomatic osteotomy and anterior petrosectomy)), left parieto-occipital craniotomy and decompression (May 2019). She did not receive any adjuvant treatment post any of these decompressions.

Radiological findings

Pre-op magnetic resonance imaging (MRI) revealed a large, irregular, lobulated, multicompartamental extra-axial lesion in the prepontine cistern, left cerebellomedullary, and cerebellopontine angle cisterns, arising from the superior part of clivus with posterior displacement of the brainstem, with severe mass effect on the brainstem, left middle cerebellar peduncle and left

cerebellar hemisphere, hyperintense on T2 and hypointense on T1 weighted images, with multiple foci of blooming and heterogeneous enhancement in post-contrast studies. The lesion was seen encasing the basilar artery, left posterior cerebral artery, right P1 segment (posterior cerebral artery), and left distal V4 segment (vertebral artery). Occlusion of the intracranial part of the left internal carotid artery was noted.

Post-op magnetic resonance imaging (MRI) showed ill-defined irregular, lobulated T2 heterogeneously hyperintense and T1 hypointense lesion measuring 4.4x3.9x3.4cm with diffusion restriction and heterogeneous post-contrast enhancement seen arising from the clivus on the left side. The lesion was seen extending up to sella

anteriorly, involving the midbrain, pons, and left cerebellar hemisphere causing effacement of the fourth ventricle posteriorly, the left temporal lobe with dilatation of temporal horn of lateral ventricle laterally, the left thalamus superiorly, till pontomedullary junction inferiorly. The lesion was seen displacing the basilar artery towards the right side and was completely encasing the left basilar artery. The posterior cerebral artery was seen with mild attenuation and there was complete occlusion of the left side internal carotid artery. Diffuse patchy meningeal enhancement was noted involving the bilateral fronto-parieto-temporal region. Left parietotemporal and suboccipital craniotomy changes were seen.

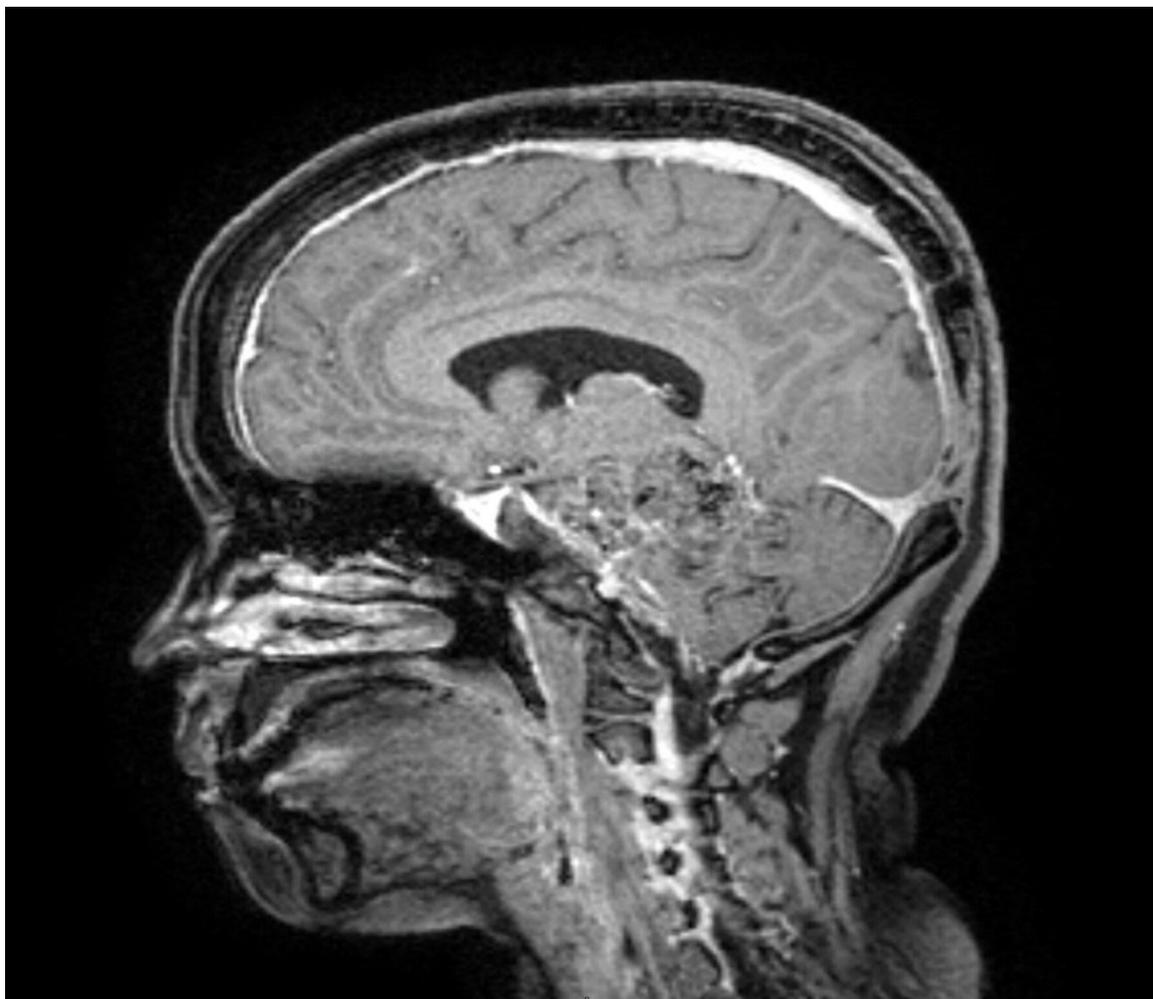


Figure 1: MRI images of the postoperative residual disease: Sagittal Image

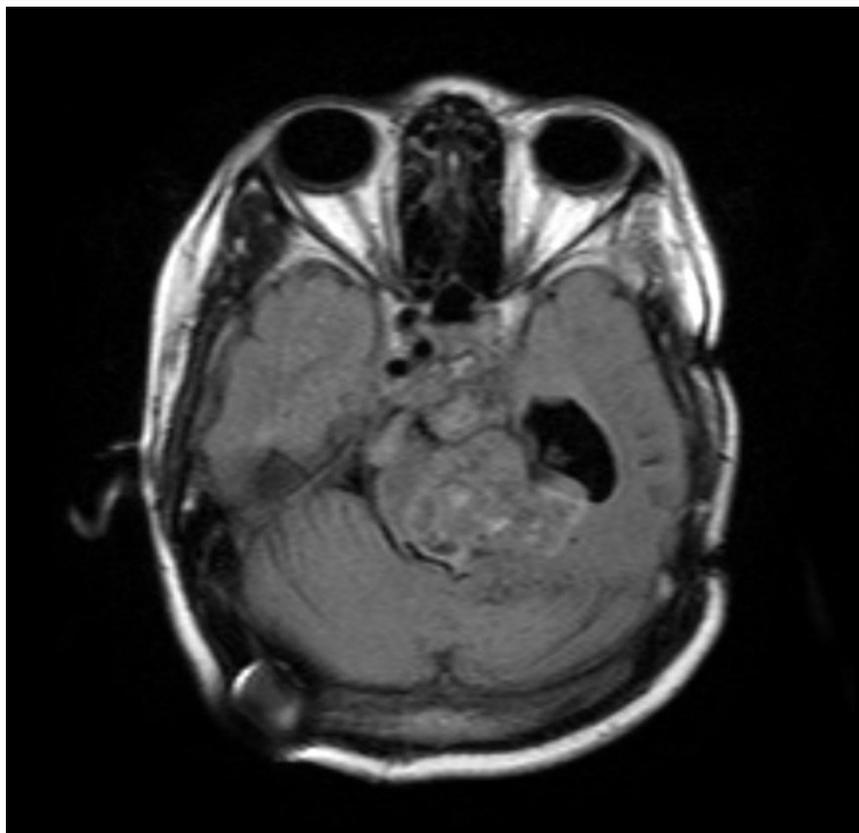


Figure 2: MRI images of the postoperative residual disease: Axial image



Figure 3: The residual disease volume as seen in CT scan images

Surgical Treatment

The patient underwent re-exploration of left temporal craniotomy and by subtemporal, transpetrosal, presigmoid, and retrosigmoid approaches, decompression of lesion (R2 resection due to extreme adhesions and ill-defined plane between tumour and brainstem) was done. Also, the patient underwent left eye tarsorrhaphy and tracheostomy. The patient tolerated the procedure well and developed no fresh deficits postoperatively. The patient developed left CSF otorrhea on post-op day 2, for which the lumbar drain was placed and removed soon after as there was no drain. The patient was started on ryles tube feeding as the patient was not tolerating a trial of oral feeds and the decannulation of tracheostomy was done after 20 days.

Immediate post-op computed tomography scan revealed subtotal decompression with frontal pneumocephalus with no operative site bleed.

Histopathology Status

Post-op histopathological examination of the tumour suggested chordoma clivus and left cerebellopontine angle. Microscopic sections showed notochordal neoplasm consisting of large lobules and sheets of polyhedral cells with distinct cell outlines with abundant clear vacuolated cytoplasm, round nuclei with fine chromatin, and conspicuous nucleoli (physaliphorous cells). Stroma showed intervening thin fibrovascular septae. Also, patchy perivascular lymphoplasmacytic infiltrate and areas of old haemorrhage were noted.

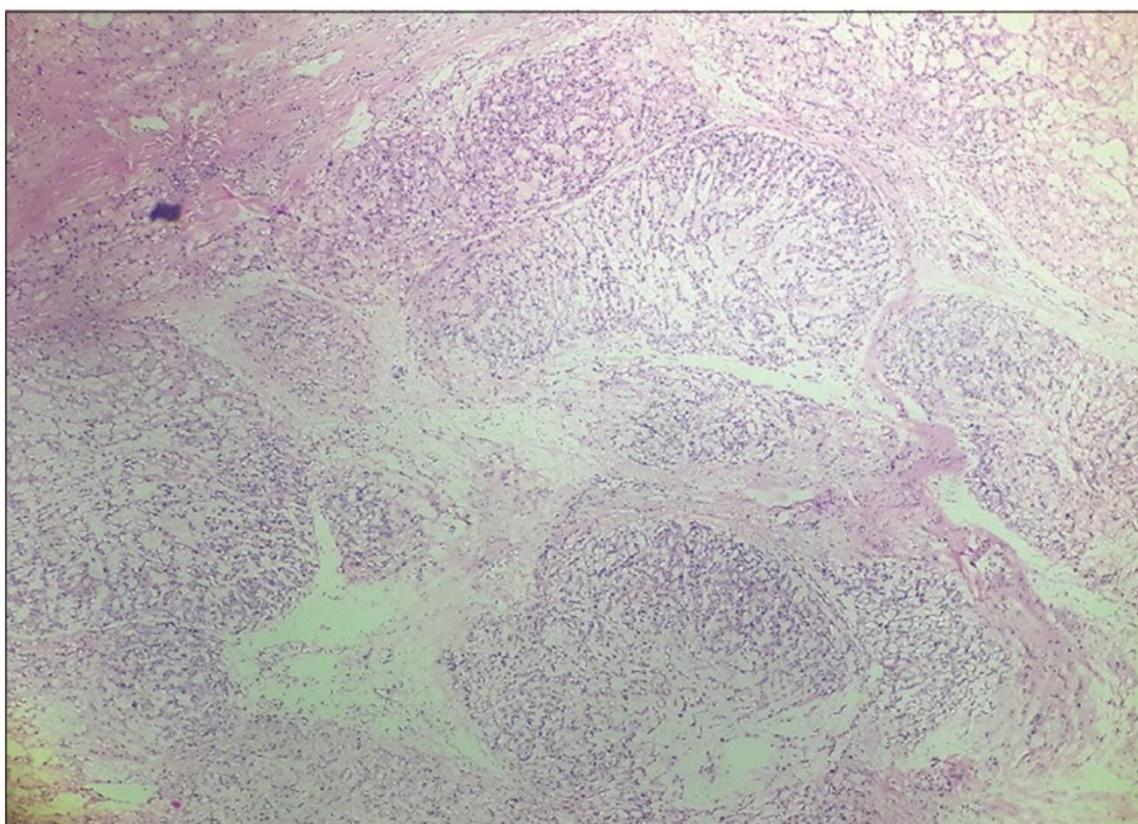


Figure 4: Lobules of physaliphorous cells separated by fibrous septa

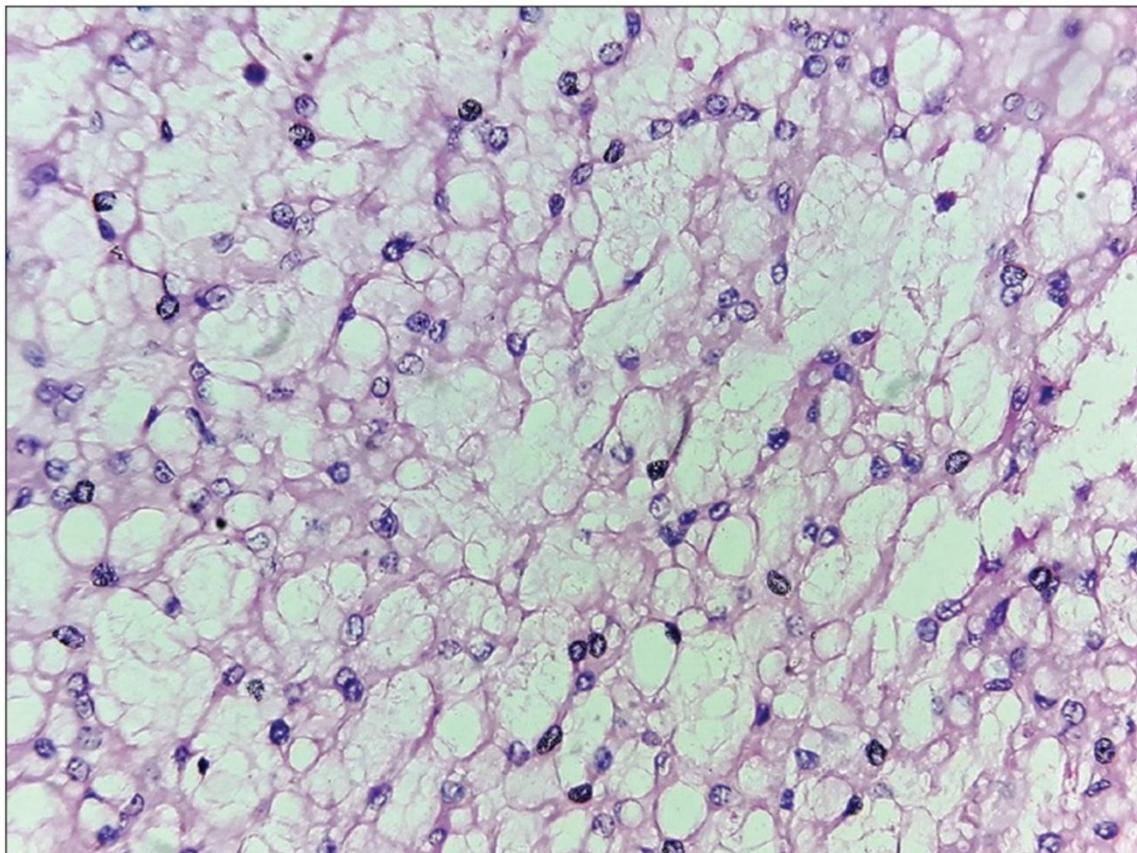


Figure 5: sheets of large cells with bubbly cytoplasm and small round nucleus.²

Radiotherapy treatment

The patient received postoperative adjuvant treatment with fractionated stereotactic radiotherapy to a dose of 3900cGy in 13 fractions over 3 weeks for the residual disease (residual volume of 53cc) (EQD2: 42.25Gy and BED 50.7Gy).

The residual disease was contoured as the CTV and 1mm margin was given to generate the PTV except near the OARs. The residual disease volume was 52.46cc and the PTV volume was 56.22cc.

Table 1 illustrates the dose to the PTV and the OAR doses.

PTV						Brain			Brain stem		Chiasma		Pituitary		Cochlea Right		Lens Left		Lens Right		Optic Nerve Left		Optic Nerve Right		Eye Left		Eye Right	
V 95 %	D mean	D mean	D 98	D 2	M U/Fr	V 10 0 %	V 95 %	V 10 5 %	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean	D mean
99.5 %	43.84g	40.9g	37.2g	42.1g	12.53	3.62 %	4.51 %	1.28 %	38.4g	31.2g	42.2g	30.7g	37.1g	32.2g	24.1g	21.5g	4.05gy	3.68gy	4.16gy	3.74gy	14.9gy	8.81gy	12.71gy	8.13gy	6.68gy	4.84gy	6.75gy	4.86gy

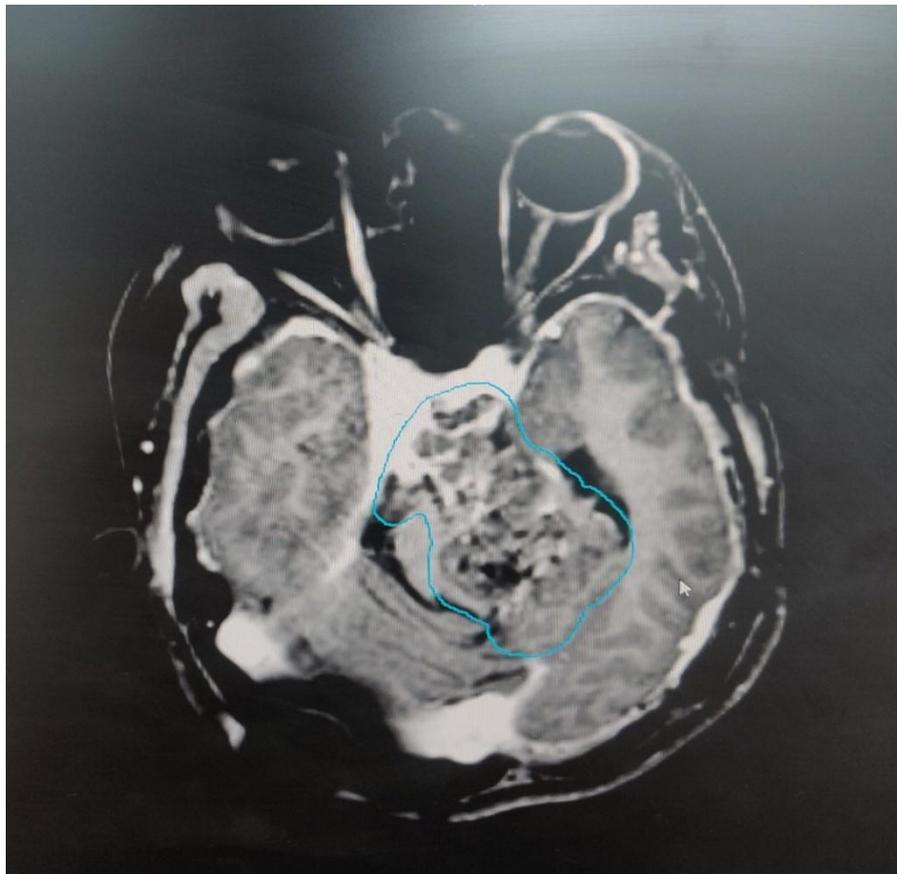


Figure 6: The PTV volume on MRI with dose colour wash.

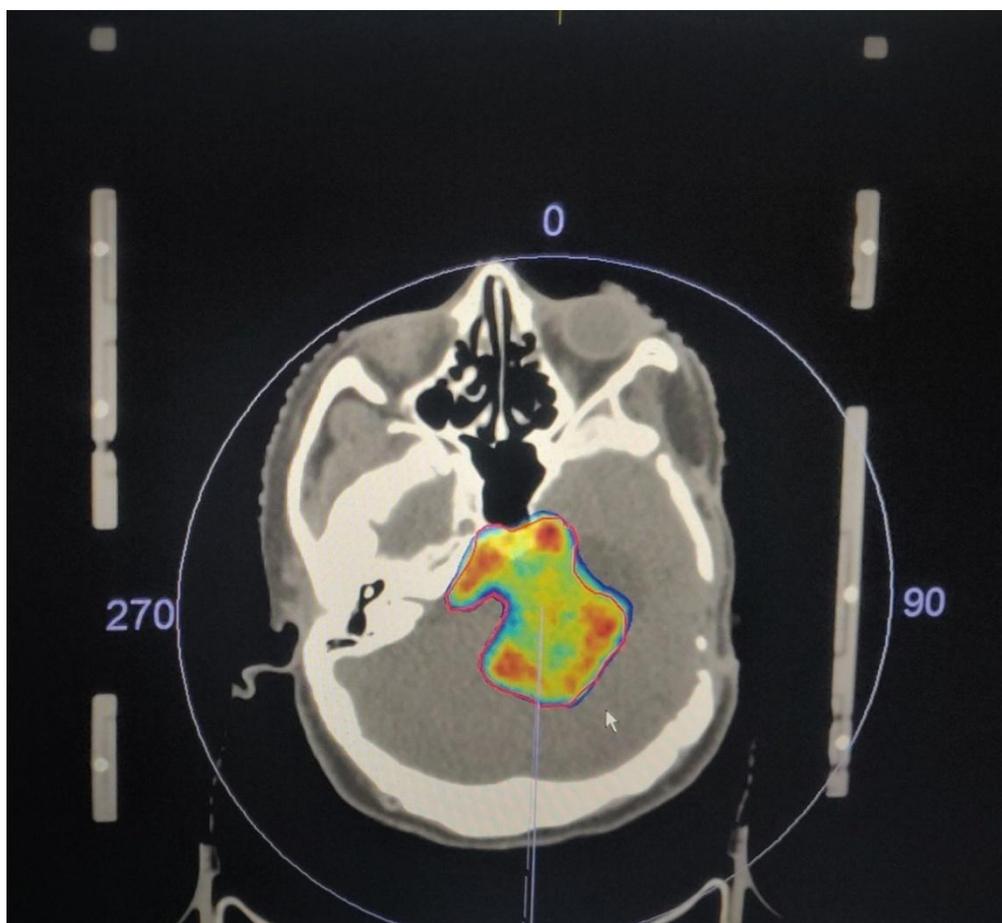


Figure 7: The PTV volume on CT with dose colour wash.

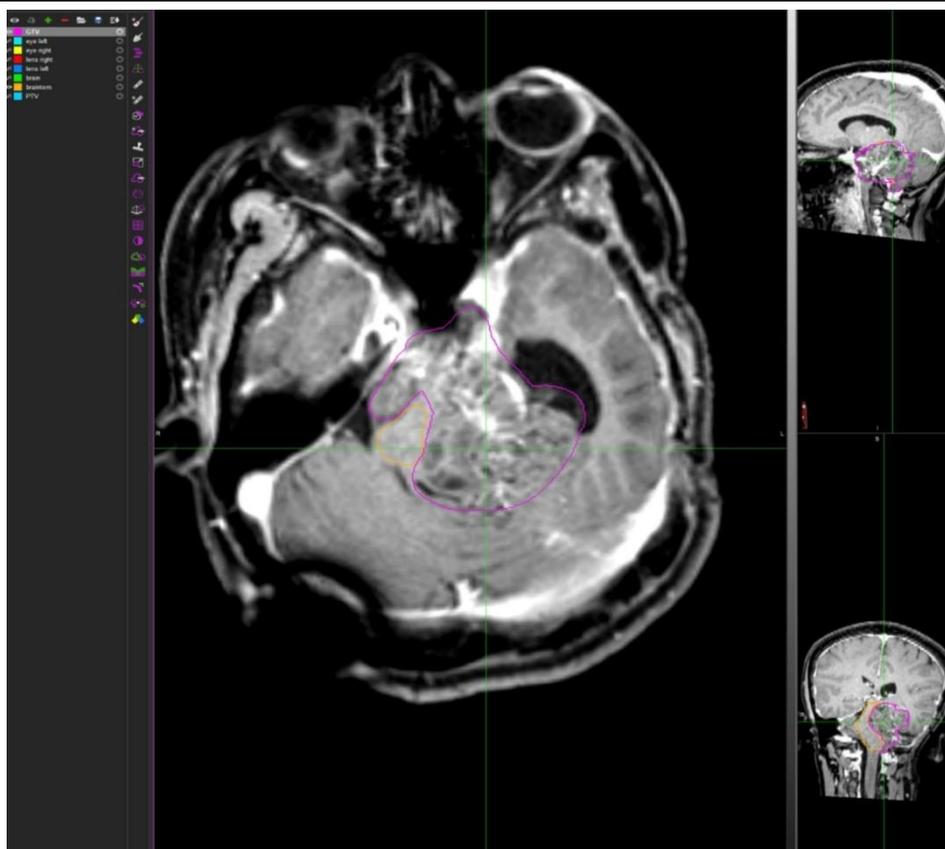


Figure 8: MRI showing PTV and the brainstem in axial, sagittal and coronal sections.

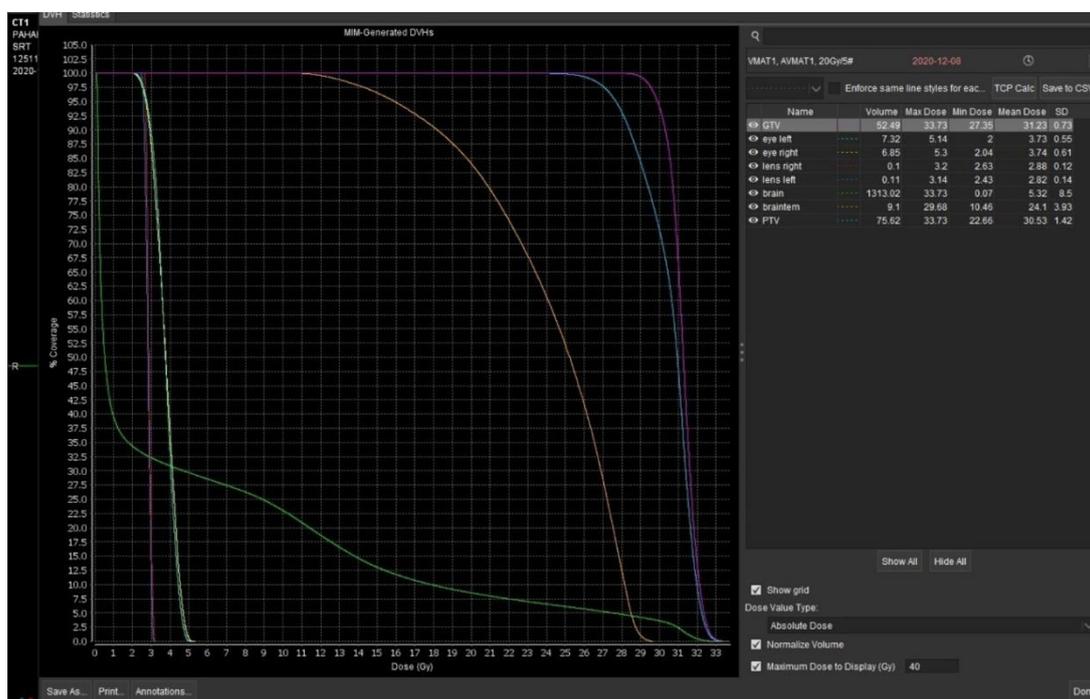


Figure 9: The DVH of the PTV and the OARs.

Discussion

Chordoma is a rare type of bone cancer accounting for only 1-4% of the total bone malignancies and about 1% of all intracranial tumours with an incidence of 0.18 to 0.84 per

million persons per year. It is locally aggressive and invasive with high rates of local recurrence and poor prognosis. It arises from notochordal remnants and has a high predilection for the axial skeleton, the most common sites being sacrum

(50%), skull base (35%), and mobile spine (15%). Its incidence has a male (10:6) predilection with peak incidence seen between 50-60 years. As per available data, the 5-year, 10-year and 20-year survival rates drop precipitously to 67.6%, 39.9%, and 13.1% respectively.³ The factors affecting prognosis adversely were found to be female sex, older age, larger tumour volume, more extensive tumour invasion, local recurrences, and dedifferentiated histology.³

Chordomas were first characterized by Virchow in 1857.⁴ The term "chordoma" was first coined by Ribbert in the 1890s. Histologically it is a low-grade neoplasm but is highly recurrent, making its clinical progression similar to that of malignant tumours. It consists of unique intracellular, bubble-like vacuoles referred to as physaliferous cells. Gene duplication in the transcription factor T gene (brachyury) is seen in familial chordomas. The current consensus goes with maximal resection followed by adjuvant radiotherapy. Conventional radiation modalities following surgery increase 5 and 10-year local control to only 36% and 23% respectively. When treated to higher doses of 79.2Gy BED with proton therapy, 10-year local control increased to 50%. But the proximity to critical structures is a dose-limiting factor. Fractionated stereotactic radiotherapy is an effective alternative in a resource-limited setting.

Although maximal resection followed by adjuvant radiation therapy is the known treatment of choice, en-bloc resection of skull base chordomas is mostly not feasible due to its proximity to vital structures.⁵ Tumour location and surgeon preference are the deciding factors for the approach and extent of the surgical resection. As invasiveness into surrounding vital structures is very common, the treatment philosophy should be to reduce neurological dysfunction. Hence, mostly the surgical excision will be subtotal or partial. This mandates the use of post-op radiotherapy as an adjuvant treatment for the postoperative residual tumour. Radiotherapy advancements like stereotactic radiosurgery (SRS) and stereotactic radiation therapy (SRT) help deliver higher doses of radiation and offer varied treatment options.⁶ Even proton beam therapy and carbon ion therapy have been applied to the treatment of skull-base chordomas and found to be effective. The dosing and timing of radiation should be strategically decided to reduce the complications due to radiation exposure to the brainstem, pituitary, optic apparatus, and other radiation-sensitive structures. It is known that radiation treatment is associated with good tumour control rates, but the rarity of the disease makes the optimal factors for radiation unknown.

Table 2: Comparison of different doses of radiation therapy used for clival chordomas in different studies. This shows that there is no proper consensus regarding the exact dose of radiation to be given.

Author	Year of study	Sample Size	RT technique	Mean RT Dose/9Gy	Mean Follow up (months)	Local control rate/OS	Number of patients with recurrence	Remark
Debus et al ⁷	2000	37	linac FSRT	66.6Gy (1.8G/fr)	27	2yr LCR 82%, 5yr LC 50%, 5yr OS 82%	11pts	1 pt. pontine ischemic lesion, hemiparesis but not mostly RT induced
Bugoci et al ⁸	2014	12	FSRT	66.6Gy (48.6-68.4Gy) in 1.8G/fr	42	5yr LCR 37.5, 5yr OS 76.4%		6 pts had progression in median TTP 17.3m
Vasudevan et al ⁹	2017	16	FSRT	37.5Gy(25-40Gy) in 5fr	28	3yr OS 94.12, 3yr LRFS 91.67%	2pts	9 pts had acute toxicity and 2 pts late toxicity
Sahgal et al ¹⁰	2014	24	IG-IMRT	76Gy in 2Gy/fr	36	5yr LC 65.3%, 5yr OS 85.6%		8 pts progressed; 8 pts had late toxicity
Jiang et al ¹¹	2013	20	CyberKnife SRS	18-50gy in 1-5fr	33	5yr LCR 52.5, 5yr OS 80%	8pts	no toxicity

This case study aims to describe the effective treatment of intracranial chordoma, use of fractionated stereotactic radiotherapy, and the adequate dose following surgical resection, keeping in view the very close proximity to vital structures and the large volume of post-op residual disease. Although conventional radiation doses of 40-60Gy was found to have a 5-year locoregional control of only 10-40%, in this case, the EQD2 was kept below 45 Gy keeping in mind the large volume of residual disease, the distorted anatomy given multiple surgical interventions and also tolerance doses of brainstem and chiasm.

Conclusion

Early diagnosis, aggressive and maximal surgical resection followed by adjuvant radiation therapy for the residual tumour is mandatory to improve the long-term outcomes. Fractionated SRT/SRS is found to be effective in getting a therapeutic response in these radioresistant tumours, with minimal toxicity to vital structures. FSRT can be taken to be a safe and cost-effective alternative to particle therapy. Higher total doses and younger age were found to be associated with improved tumour control rates. Our case study revealed that fractionated photon radiotherapy after surgery helps prevent local recurrences and also improves clinical outcomes. In this case with multiple recurrences, even the dose of less than 60 Gy delivered, respecting the OAR dose constraints and the large volume of residual disease was found to make significant neurological improvements and thus improve the quality of life of the patient. Hence, postoperative radiotherapy immediately after surgery, especially in the form of stereotactic radiotherapy, even in lower doses should be considered in cases of recurrent clival chordomas.

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