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Gamma knife surgery efficacy in controlling postoperative residual clival chordoma growth

Raef F.A. Hafez*, Osama M. Fahmy, Hamdy T. Hassan

Department of Neurosurgery and Gamma Knife Center, International Medical Center (IMC), 42km. Ismailia Desert Road, Cairo, Egypt

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ABSTRACT

Objective: This study primarily aims to evaluate the efficacy of gamma knife surgery in controlling growth progression rate of residual clival chordoma through retrospective outcome analysis of 12 consecutive patients.
Patients and methods: Data for 12 consecutive patients underwent GKS for post-operative residual histologically verified clival chordoma at our institution (IMC – Cairo- Egypt) from 2006 through end of 2017 were retrospectively reviewed and analyzed with mean follow-up period of 45 months (range12–120 months).
Results: In the last follow up MR, tumor growth control was achieved in 33.3% of patients (mean treated tumors volume was 2.7cc with mean peripheral prescription dose of 16 Gy), and 66.7% of patients reported lost tumor growth control (mean treated tumor volume was 9.2 cc with mean peripheral dose was 13.5 Gy). The overall tumor free progression with mean follow up period of 45mos was 33.3%. The Actuarial 2, 3 and 5 year tumor control rates after initial GKS was 35%, 30% and 25% respectively.
Conclusion: Without satisfactory maximum tumor reduction and sufficient high peripheral prescription radiation tumor dose, it should not be expected that GKS could efficiently control the progression of residual clival chordoma, especially for long term.

1. Introduction

Chordomas are uncommon, aggressive primary bone tumors can theoretically arise from anywhere along the notochord, however in adults, three main sites have been identified, the skull, spine and sacrum, roughly in equal distribution. The overall incidence of all chordomas is 0.08-0.5 cases per 100 000 individuals per year, and their incidence at the skull base location is 1 case per one million individuals per year, account for < 0.2%of all intracranial tumors. Patients with skull base chordoma usually presented in 4th-6th decade of life and reported to occur in patients from 3 to 95 years of age [5–9]. Clival chordoma, are benign slow growing but locally aggressive tumors. infiltrate into bone and invade nearby neurovascular structures often causing significant morbidity and mortality related to mass effect and invasion, they rarely metastasize [10–15]. The most common presenting symptom with Skull base chordomas is visual disturbances such as diplopia. Presenting symptoms may include headache and cranial nerve dysfunction, most commonly involving the third and sixth cranial nerves. Skull base chordomas can present with epistaxis and, rarely, with endocrine impairment [1,2,16].

For most clival chordoma cases, aggressive surgical resection followed by radiation therapy offers the best chance of long-term control. Routine use of postoperative radiotherapy with high-dose photon, gamma radiation or proton irradiation also plays a vital role in the management and control of chordomas. However, prognosis remains unsatisfactory, with 5-year survival rates of 54–75% [10]. Clival chordoma is associated with an increased risk of recurrence and radiation therapy is considered effective only after maximal surgery [3,6,17–21].

Still, current knowledge of chordomas forms a hermeneutic rationale for a combination of microsurgery and adjuvant radiation. The present consensus is that most specialists agree on three points: **A-** Safe maximal cytoreduction microsurgery is indicated for all skull base chordoma patients therefore a combined or a staged resection is often needed, **B-**chordomas require adjuvant treatment following initial therapy. **C-** Despite extensive surgical removal and adjuvant treatment tumor recurrence or progression is common [23,24]. Chordomas respond poorly to conventional radiotherapy and therefore Gamma knife surgery, fractionated stereotactic radiotherapy, and proton-beam radiotherapy have been used. Gamma Knife surgery (GKS) has a potential to control tumors with poor radiation sensitivity and has accordingly, reported to offer a notable effect on clival chordomas growth

Abbreviations: cc, cubic centimeter; GKS, gamma knife surgery; LTC, loss tumor growth control; TC, tumor growth control

* Corresponding author at: The International Medical Center (IMC), 42km. Ismailia Desert Road, Cairo, Egypt.
E-mail addresses: raefhafez179@hotmail.com (R.F.A. Hafez), Osama_azeem@yahoo.com (O.M. Fahmy), Hamdythabet86@gmail.com (H.T. Hassan).

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[8,24–29].

2. Aim of work

This study aims primarily to evaluate the efficacy of gamma knife surgery in controlling tumor growth progression of postoperative residual clival chordoma through retrospective outcome analysis of 12 consecutive patients treated at the Gamma Knife Center/ International Medical Centre (IMC), Cairo, Egypt, from 2006 to end of 2017.

3. Patients and methods

Data for 12 patients who consecutively underwent GKS for post-operative residual skull base histologically verified chordoma at our institution (IMC – Cairo- Egypt) from 2006 through the end of 2017 were retrospectively reviewed and analyzed. All patients completed at least 12 month follow-up with a mean follow-up period of 45 months (range12–120 months). Two patients were operated surgically in our hospital and the other 10 patients were referred for GKS after initial surgery at other hospitals. We excluded from our study 3 patients who were treated without histological diagnosis based on radiological findings and 2 who were lost follow up.

According to the obtained operative data and comparing pre-operative and pre-GKS knife MRI + contrast, the extent of microsurgery done was either, tumor biopsy in 2 patients (detected tumor residual > 90% of original volume), partial tumor removal in 8 patients (residual visible tumor approximately = > 50% of original tumor), subtotal in 2 patients (visible tumor residual < 10% of original size) and total tumor removal where there is no visible tumor residual and none of our studied cases had total tumor removal. Six patients operated via trans-sphenoidal approach, 4 patients operated via trans-cranial and two patients operated via both trans-sphenoidal and trans-cranial approach, no patients received any radiation therapy prior to GKS.

3.1. Tumor location and presenting symptoms

Treated residual post-operative clival chordoma location and extension were as follows, clivus (localized in the clivus or its axis) in 2 patients, clivus extends parasellar and cavernous sinus in 4, clivus extends to petroclival in 6, clivus extends retroclival 7 and clivus extends to cerebellopontine angle in one patient. The most common presenting symptoms was visual disturbance in form of diplopia in 11 patients (83%), abducent nerve palsy was in 9 patients, 3rd nerve palsy in 7, 4th nerve palsy in 2 and seven patients presented with headache. Other presenting symptoms included difficulty in balance in 2 patients, bulbar symptoms in 1, trigeminal parathesia in 3, hemiparesis in 1, facial nerve palsy in one and decreased hearing in one patient. The overall median Karnosky Performance Status (KPS) score was 90 (range 60–100). Table 1.

3.2. Gamma knife procedure

Elekta Leksell Gamma Knife (Models B and 4C; Elekta AB) and Gamma Plan Version 10.1 were used in this study for treatment. The standard Leksell G - stereotactic head frame is applied after local anesthesia. Target localization was obtained using high-resolution MRI (1.5–3 T), obtaining T1, T2, sequences with contrast at 1.2-mm slice thickness on zero angle without slices gap. Gamma knife Plans consisted of a mixture of shots using usually the 8 and the 14 mm helmets collimator depends on tumor volume and the radiation conformity needed. Treatment was technically feasible for all cases. After GKS treatment completion the stereotactic frame removed and all patients discharged in the same day.

3.3. Follow-up

Post-GKS, it was possible to follow up all patients every 6 months in the first year then annually afterward with surveillance neurological evaluation and MRI imaging with and without contrast. The standard GKS response classification was used to assess treatment outcomes either “Tumor control = TC” (decreased or stable in size) and “Loss of tumor control = LTC “(tumor size progression) with mean follow-up period of 45 months (range 12–120 months). The mean tumor volume upon initial GKS was 7 cc (range 2.2–16 cc), the mean peripheral prescription dose given is 14.7 Gy (range 12–18 Gy), the mean isodose curve was 35% (range 35%–40%), the mean tumor coverage was 94% (range 92–99%) and the mean maximum dose was 42 Gy (range 30–52 Gy). Table 2.

4. Results

In our study there were 7 females and 5 males, the mean age of treated patients was 45.7 year (range 13–69 years). At the last follow-up MRI, tumor control (TC) was achieved in 4 out of 12 patients (33.3%) and 8 patients (66.7%) had tumor progression with lost tumor control (LTC) after initial GKS.

Four patient achieved local tumor size control (TC) in last follow up MRI with mean follow up period of 45 months (range 12–108 months), two of them had subtotal tumor removal pre-GKS and two had partial tumor removal. Mean treated tumors volume was 2.7cc (2.2–3.2cc), mean peripheral prescription dose was 16 Gy (15–18 Gy), mean tumor coverage percentage was 98.5% (98–99%) and mean maximum dose was 46 Gy (43–52.4 Gy). Clinically three of them showed improvement in diplopia and one was clinically stable.

Eight patients showed tumor progression post-GKS and lost tumor size control (LTC) with mean follow up period 26.5 months (12–40 months), 6 of them had partial tumor removal pre-GKS and 2 had just tumor biopsy. The Mean treated tumor volume was 9.2 cc (6.2–16 cc), mean peripheral given dose was 13.5 Gy (12–15 Gy), mean tumor coverage was 92% (90–95%) and mean maximum given radiation dose was 38.5 Gy (30–43 Gy). Two of them had additional microsurgical intervention, 3 received additional fractionated radiotherapy and 2 were retreated with GKS. Figs. 1 and 2

The overall tumor free of progression with mean follow up period of 45mos after initial GKS is 33.3% (4 patients). The Actuarial 2, 3 and 5 year tumor control rates after initial GKS is 35%, 30% and 25% respectively.

According to the latest follow-up available data, for the studied 12 treated patients, 7 (58.3%) were alive and 5 (41.7%) had died and tumor progression was the main cause. No complications related to GKS reported in our studied 12 patients.

5. Discussion

Despite the increasing application of radiosurgery and radiation therapy for the treatment of chordoma, the importance of surgical resection for intracranial chordomas is currently the gold standard and unequivocal. Greater recurrence free survival has been shown to correlate with radical or subtotal removal as opposed to partial resection [6,20,23,24,30]. The preferred treatment for skull base chordoma is maximum resection followed by high-dose radiation therapy for residual and or recurrences. However, the prognosis remains unsatisfactory, with 5-year survival rates of 54–79% [C-3, 4,24]. Analysis of recurrence-free survival has shown that approximately 30% of these tumors are expected to recur as early as 1 year after surgery [10,31].

Gay et al 1995 and Al-Mefty et al 2001, reported recurrence free survival rates of 71.4 and 65%, respectively [19,21]. Samii et al. reported a similar recurrence free survival rate of 65%, but asserted that a similar control rate and less surgical morbidity could be achieved with subtotal removal and adjuvant radiosurgery [32].

Table 1
Characteristics of the GKS treated 12 patients for post-operative residual clival chordoma.

Case no	Sex	Age	Tumor location	Presentation	KPS	Pre-GKS surgical approach	Extent of tumor removal	Time of follow up	Clinical final outcome
1	M	48	Cl/Lt.para.S &petro	Headache Diplopia,3,6,5th Cr n	90	T.Cran + T.Sph	part	24	Dead
2	F	25	Cl/Retro	Diplopia,6th cr. n	100	T.Sph	ST	108	alive
3	M	55	Cl/Retro	Headache Diplopia,6th cr. n.	90	T.Cran	biopsy	36	Dead
4	M	50	Cl/Rt.para.S/CP	Headache Diplopia,6,5,7,8th cr. n	90	T.Cran	part	38	Dead
5	M	69	CL/Lt.Petro/para.S	Headache Bulbar sympt, 3th cr. n. unbalanced	70	T.Cran	biopsy	26	Dead
6	F	38	CL/para.SRetro/ Lt.Petro	Headache Diplopia,hemp,3rd Cr, unbalanced	60	T.Cran	part	40	Dead
7	F	55	Cl/petro/Retro	Diplopia,3, 6th cr. n	90	T.Sph	part	12	alive
8	F	32	CL/Retro	Diplopia,3,6th cr. n	90	T.Sph	ST	36	alive
9	F	56	CL	Diplopia, 4,6th cr. n	90	T.Sph	part	24	alive
10	F	57	Cl/Retro/Rt.Petro	HeadacheDiplopia,3rdcr. n	90	T.Sph	part	24	alive
11	F	50	CL/Retro/Petro	Diplopia,3,4,6th cr. n	90	T.Cran	part	12	alive
12	M	13	CL	Headache,6,5th cr. n	90	T.Sph	ST	12	alive

Abbreviations: CL = clival, Para.S = parasellar, Retro = retrosellar, Petro = petroclival, CP = cerebellopontine.
Cr.n = cranial nerve, KPS = karnofsky performance status, Sympt = symptoms, Hemp = hemiparesis, T.Sph = Transsphenoidal, T.cran = Transcranial.
ST = subtotal, Part = partial.

Table 2
Gamma Knife surgery treatment data.

Case no	Tumor volume. cc	Prescription dose Gy	Isodose curve	Coverage%	Maximum dose Gy	Post GKS Response	Time till TC&TCL post GKS-mos	Post GKS treatment
1	8.2	15	35	90	43	LTC	24	Microsurgery
2	3.2	18	35	98	52.4	TC	108-	–
3	9	12	35	92	34.3	LTC	36	Fractionated radiotherapy
4	8.6	14	35	92	40.2	LTC	38	Fractionated radiotherapy-
5	16	12	35	90	34.3	LTC	26	Fractionated radiotherapy
6	12	14	35	92	40.2	LTC	40	–
7	6.2	15	35	92	43	LTC	12	RGKS
8	2.3	15	35	98	43	TC	36	–
9	3	15	35	99	43	TC	24	–
10	6.4	15	35	95	43	LTC	24	Microsurgery
11	7.6	12	40	94	30	LTC	12	RGKS
12	2.2	16	35	99	45.7	TC	12	–

Abbreviations: cc = cubic centimeter, GKS = gamma knife surgery, TL = tumor growth control, LTC = loss tumor growth control,mos = months.

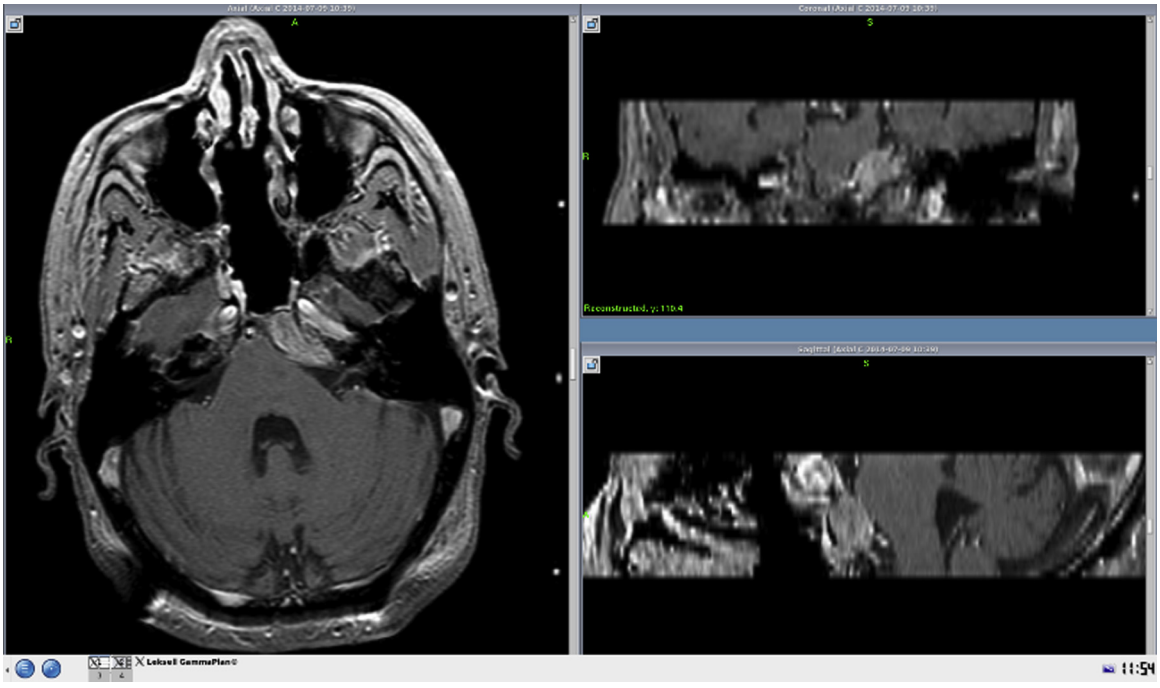

Fig. 1. Stereotactic MRI of a residual clival and left petroclival chordoma (case No.8) treated with GKS.

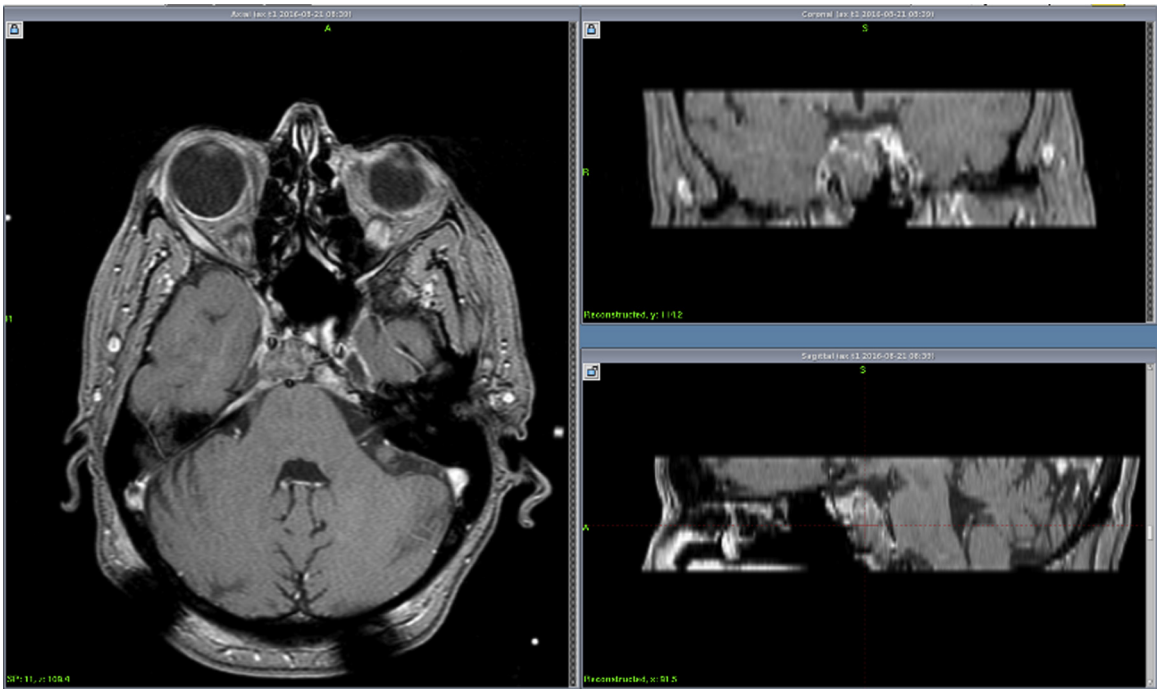

Fig. 2. Stereotactic MRI of the same case in Fig. 1, after 2 years post 1st GKS showed lost tumor control outside radiation field with progressive regrown of treated residual chordoma toward the right side that was retreated with gamma knife.

Chordomas are relatively radioresistant and require high-dose radiation to achieve control. High-dose proton irradiation is one of the most expensive therapies and has limited availability. Gamma knife radiosurgery for chordoma has been shown to offer comparable to photon-proton irradiation, with a 5-year tumor control rate of 62–76% and a 5-year survival rate of 70% [1,6].

The effectiveness of gamma knife radiosurgery for clival chordoma depends on having a small-volume tumor and a sufficient marginal dose. A tumor volume < 3.5.ml and a marginal dose > = 15 Gy improved the long-term tumor control [3,6,22].

Our results are consistent with others in that skull base chordomas are difficult to manage over the long-term. At last follow-up, tumor control (TC) was achieved in 4 out of 12 patients (33.3%) and 8 patients (66.7%) had lost tumor control (LTC) after initial GKS. In the Four patients achieved local tumor size control (TC) with mean follow up period of 45 months, the mean treated tumor volume was 2.7cc (2.2–3.2cc), mean peripheral prescription dose was 16 Gy (15–18 Gy) and mean maximum dose was 46 Gy These findings indicating that a favorable GKS outcome is expected when the treated residual clival tumor volume is < = 3.2cc and the peripheral dose is > = 15 Gy.

On the other hand the 8 patients with LTC in our study with mean follow up period of 26.5 months, the mean treated tumor was 9.2 cc, mean peripheral given dose was 13.6 Gy, mean tumor coverage was 92% and mean maximum given radiation dose was 38.5 Gy. Such data indicating that the greater the treated residual clival chordoma volume limited the peripheral given radiation dose, limited GKS conformity, and limited the maximum radiation dose with greater chance of GKS failure to tumor control growth.

Ito E, et al series 2010; over 19 residual postoperative clival chordoma patients treated with GKS reported a 5-year PFS of 47.1%. However the author indicated that long-term control of tumors is more achievable when mean tumor volume is < = 3.3 ml and mean marginal dose around > = 16 Gy, Thus Aggressive tumor removal at initial surgery contributes to the effectiveness of gamma knife radiosurgery for recurrences and residual. Furthermore, early recognition and treatment of recurrences or regrowth are required for postoperative tumor control in patients [6,27].

Patter Forander, et al 2017; reported outcomes of GKS performed in 16 postoperative recurrence/progression clival chordoma patients after the first microsurgical treatment and a median follow-up time of 34 months and mean treated tumor volume was 4.7cc, the tumor control was achieved in 50% of patients. The authors pointed that a safe maximal tumor removal is important for long-term tumor control as they noted in five patients out six who we consider disease-free after > 10-year follow-up, those patients had more aggressive surgical tumor removal [24].

Our Overall actuarial 2, 3 and 5 year tumor control rates after initial GKS is 35%, 30% and 25% respectively, these unsatisfactory outcome may be related to that 8 out of the 12 studied had larger tumor residual with mean treated volume of 9.2cc (6.2-16cc) consequently they received lower peripheral prescription dose of < = 13.5 Gy these 8 patients had lost tumor control post-GKS. with mean follow up period 26.5 months (12–40 months).

Clival chordomas are locally aggressive tumors that frequently require multi-modality treatment approaches, although maximum tumor surgical removal is essential for long term tumor control but adjuvant therapy is very essential to fulfill such goal. Clival chordoma should be viewed as a chronic progressive disease, with a continuous need to monitor and deal with potential recurrences, and progression irrespective maximum surgical removal and adjuvant radiation. Fractionated radiotherapy better to be reserved at late stage

6. Strengthens and limitations

The relative homogeneity of the studied 12 studied patients with residual postoperative clival chordoma treated with GKS strengthens the study in the face of somehow limited study size of these rare tumors.

This retrospective study represents a limitation.

The small number of cases in this study limits its interpretation; further follow-up studies and accumulation of cases are hence still required.

7. Conclusion

Without satisfactory maximum tumor reduction and sufficient peripheral tumor radiation dose, it should not be expected that GKS could efficiently control growth progression of residual clival chordoma. As concluded from our outcome results, treated postoperative residual clival chordoma volume < 3.2cc, high conformal peripheral prescription radiation dose = < 15 Gy and maximum tumor dose = > 45 Gy are important for GKS to control growth of such aggressive tumor.

Retrospective study

"For this type of study formal consent is not required, it does not contain any studies with human participants"

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Competing interests

The authors declare that they have no competing interests, and certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial in the matter or materials discussed in this manuscript. We declare that this is an original article.

References

[1] S.A. Matloob, H.A. Nasir, D. Choi, et al., Proton beam therapy in the management of skull base chordomas: systematic review of indications, outcomes, and implications for neurosurgeons, Brit. J. Neurosurg. 30 (4) (2016), https://doi.org/10.1080/02688697.2016.1181154.

[2] Maurizio Amichetti, Marco Cianchetti, Dante Amelio, et al., Proton therapy in chordoma of the base of the skull: a systematic review, Neurosurg. Rev. 403 (2009) 32.

[3] H.A. Crockard, T. Steel, N. Plowman, et al., A multidisciplinary team approach to skull base chordomas, J. Neurosurg. 95 (August (2)) (2001) 175–183.

[4] M.L. McMaster, A.M. Goldstein, C.M. Bromley, et al., Chordoma: incidence and survival patterns in the United States, 1973–1995, Cancer Causes Control 12 (2001) 1–11, https://doi.org/10.1023/A:1008947301735 PubMed CrossRefGoogle Scholar.

[5] O. Al-Mefty, L.A. Borba, Skull base chordomas: a management challenge, J. Neurosurg. 86 (1997) 182–189 PubMedCrossRef.

[6] K. Dassoulas, D. Schlesinger, C.P. Yen, J. Sheehan, The role of Gamma Knife surgery in the treatment of skull base chordomas, J. Neurooncol. 94 (September (2)) (2009) 243–248, https://doi.org/10.1007/s11060-009-9846-z.

[7] Nicola Boari, Filippo Gagliardi, Andrea Cavalli, et al., Skull base chordomas: clinical outcome in a consecutive series of 45 patients with long-term follow-up and evaluation of clinical and biological prognostic factors, J. Neurosurg. 125 (2) (2016) 450–460.

[8] J.J. Martin, A. Niranjan, D. Kondziolka, et al., Radiosurgery for chordomas and chondrosarcomas of the skull base, J. Neurosurg. 107 (2007) 758–764, https://doi.org/10.3171/JNS-07/10/0758 PubMed CrossRefGoogle Scholar.

[9] S. Krishnan, R.L. Foote, P.D. Brown, et al., Radiosurgery for cranial base chordomas and chondrosarcomas, Neurosurgery 56 (2005) 777–784, https://doi.org/10.1227/01 NEU.0000156789.10394.F5 PubMedCrossRefGoogle Scholar.

[10] E. Ito, K. Saito, T. Okada, et al., Long-term control of clival chordoma with initial aggressive surgical resection and gamma knife radiosurgery for recurrence, Acta Neurochir. (Wien) 152 (1) (2010) 57–67.

[11] M. Ammirati, A. Bernardo, Management of skull base chordoma, Crit. Rev. Neurosurg. 9 (1999) 63–69 CrossRef PubMedGoogle Schola.

[12] H. Arnold, H.D. Herrmann, Skull base chordoma with cavernous sinus involvement. Partial or radical tumour-removal? Acta Neurochir (Wien) 83 (1986) 31–37 CrossRefGoogle Scholar.

[13] J. Handa, F. Suzuki, H. Nioka, T. Koyama, Clivus chordoma in childhood, Surg. Neurol. 28 (1987) 58–62 CrossRefPubMedGoogle Scholar.

[14] K. Almefty, S. Pravdenkova, B.O. Colli, et al., Chordoma and chondrosarcoma: similar, but quite different, skull base tumors, Cancer 110 (2007) 2457–2467.

[15] K. Nishigaya, M. Kaneko, Y. Ohashi, et al., Intradural retroclival chordoma without bone involvement: no tumor regrowth 5 years after operation. Case report, J. Neurosurg. 88 (1998) 764–768 CrossRefPubMedGoogle Scholar.

[16] A.H. Menezes, Clival and craniovertebral junction chordomas, World Neurosurg. 81 (5-6) (2014) 690–692 May-Jun.

[17] M. Austin-Seymour, J. Munzenrider, R. Linggood, et al., Fractionated proton radiation therapy of cranial and intracranial tumors, Am. J. Clin. Oncol. 13 (1990) 327–330 CrossRefPubMedGoogle Scholar.

[18] A. Samii, V.M. Gerganov, C. Herold, et al., Chordomas of the skull base: surgical management and outcome, J. Neurosurg. 107 (2007) 319–324, https://doi.org/10.3171/JNS-07/08/0319.

[19] J. Debus, D. Schulz-Ertner, L. Schad, M. Essig, B. Rhein, C.O. Thillmann, M. Wannenmacher, Stereotactic fractionated radiotherapy for chordomas and chondrosarcomas of the skull base, Int. J. Radiat. Oncol. Biol. Phys. 47 (2000) 591–596 CrossRef PubMedGoogle Scholar.

[20] E. Gay, L.N. Sekhar, E. Rubinstein, et al., Chordomas and chondrosarcomas of the cranial base: results and follow-up of 60 patients, Neurosurgery 36 (1995) 887–896 CrossRefPubMedGoogle Scholar.

[21] T.A. Rich, A. Schiller, H.D. Suit, et al., Clinical and pathologic review of 48 cases of chordoma, Cancer 56 (1985) 187, https://doi.org/10.1002/1097-0142(19850701)56:1<182 PubMed CrossRefGoogle Scholar.

[22] N. Muthukumar, D. Kondziolka, L.D. Lunsford, et al., Stereotactic radiosurgery for chordoma and condrosarcoma: further experiences, Int. J. Radiat. Oncol. Biol. Phys. 41 (1998) 387–392, https://doi.org/10.1016/S0360-3016(98)00051-0 PubMedGoogle Scholar.

[23] B.O. Colli, O. Al-Mefty, Chordomas of the skull base: follow-up review and prognostic factors, Neurosurg. Focus 10 (2001) 1–11, https://doi.org/10.3171/foc.2001.10.3.2 CrossRefGoogle Scholar.

[24] Petter Förander, Jiri Bartek Jr, Tiit Mathiesen, et al., Multidisciplinary management of clival chordomas; long-term clinical outcome in a single-institution consecutive series, Acta Neurochir. (Wien) 159 (2017) 1857–1868, https://doi.org/10.1007/s00701-017-3266-1.

[25] R.G. Campbell, D.M. Prevedello, L. Ditzel Filho, et al., Contemporary management of clival chordomas, Curr. Opin. Otolaryngol. Head Neck Surg. 23 (2015) 153–161.

[26] T. Hasegawa, D. Ishii, Y. Kida, et al., Gamma knife surgery for skull base chordomas and chondrosarcomas, J. Neurosurg. 107 (2007) 752–757.

[27] E. Ito, K. Saito, T. Nagatani, et al., Intradural cranial chordoma, World Neurosurg. 73 (2010) 194–197.

[28] H. Kano, F.O. Iqbal, J. Sheehan, D. Mathieu, et al., Stereotactic radiosurgery for chordoma: a report from the north American gamma knife consortium, Neurosurgery 68 (2011) 379–389.

[29] J.H. Kim, H.H. Jung, J.H. Chang, et al., Gamma knife surgery for intracranial chordoma and chondrosarcoma: radiosurgical perspectives and treatment outcomes, J. Neurosurg. 121 (Suppl) (2014) 188–197.

[30] N. Tamaki, T. Nagashima, K. Ehara, et al., Surgical approaches and strategies for skull base chordomas, Neurosurg. Focus 10 (2001) 1–7, https://doi.org/10.3171/foc.2001.10.3.10 CrossRefGoogle Scholar.

[31] E.B. Hug, Review of skull base chordomas: prognostic factors and long-term results of proton-beam radiotherapy, Neurosurg. Focus 10 (2001) E11 CrossRefPubMedGoogle Scholar.

[32] A. Samii, V.M. Gerganov, C. Herold, M. Samii, et al., Chordomas of the skull base: surgical management and outcome, J. Neurosurg. 107 (2007) 319–324.