Role of endoscopic transnasal surgery for skull base chondrosarcoma: a retrospective analysis of 19 cases at a single institution

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OBJECTIVE Skull base chondrosarcoma is one of the most intractable tumors because of its aggressive biological behavior and involvement of the internal carotid artery and cranial nerves (CNs). One of the most accepted treatment strategies for skull base chondrosarcoma has been surgical removal of the tumor in conjunction with proactive extensive radiation therapy (RT) to the original tumor bed. However, the optimal strategy has not been determined. The goal of this study was to evaluate the early results of endoscopic transnasal surgery (ETS).

METHODS The authors retrospectively analyzed 19 consecutive patients who underwent ETS at their institution since 2010. Adjuvant stereotactic radiosurgery (SRS) was performed only for the small residual tumors that were not resected to avoid critical neurological complications. Histological confirmation and evaluation of the MIB-1 index was performed in all cases. The Kaplan-Meier method was used to determine the actuarial rate of tumor-free survival.

RESULTS The median tumor volume and maximal diameter were 14.5 cm³ (range 1.4–88.4 cm³) and 3.8 cm (range 1.5–6.7 cm), respectively. Nine patients (47%) had intradural extension of the tumor. Gross-total resection was achieved in 15 (78.9%) of the 19 patients, without any disabling complications. In 4 patients, the surgery resulted in subtotal (n = 2, 11%) or partial (n = 2, 11%) resection because the tumors involved critical structures, including the basilar artery or the lower CNs. These 4 patients were additionally treated with SRS. The median follow-up duration was 47, 28, and 27 months after the diagnosis, ETS, and SRS, respectively. In 1 patient with an anterior skull base chondrosarcoma, the tumor relapsed in the optic canal 1 year later and was treated with a second ETS. Favorable tumor control was achieved in all other patients. The actuarial tumor control rate was 93% at 5 years. At the final follow-up, all patients were alive and able to perform independent activities of daily living without continuous neurological sequelae.

CONCLUSIONS These preliminary results suggest that ETS can achieve sufficient radical tumor removal, resulting in comparative resection rates with fewer neurological complications to those in previous reports. Although the follow-up periods of these cases were relatively short, elective SRS to the small tumor remnant may be rational, achieving successful tumor control in some cases, instead of using proactive extensive RT. Thus, the addition of RT should be discussed with each patient, after due consideration of histological grading and biological behavior. To determine the efficacy of this strategy, a larger case series with a longer follow-up period is essential. However, this strategy may be able to establish evidence in the management of skull base chondrosarcoma, providing less-invasive and effective options as an initial step of treatment.

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KEY WORDS chondrosarcoma; endoscopic surgery; Gamma Knife; transsphenoidal approach; skull base tumor; stereotactic radiosurgery; oncology

SKULL base chondrosarcoma is a rare tumor comprising only 0.1% of all brain tumors, which extensively invades the petroclival regions and the anterior skull base.^{7,8,38} In addition, chondrosarcoma often involves critical anatomical structures including the internal carotid

artery (ICA) and cranial nerves (CNs), and sometimes extends into the posterior cranial fossa, penetrating the dura mater and compressing the brainstem.

Regarding the treatment strategy for chondrosarcoma, to the best of our knowledge there are only a few

ABBREVIATIONS CN = cranial nerve; EOR = extent of resection; ETS = endoscopic transnasal surgery; GKRS = Gamma Knife radiosurgery; GTR = gross-total resection; IAC = internal auditory canal; ICA = internal carotid artery; mRS = modified Rankin Scale; OpC = optic canal; PR = partial resection; RT = radiation therapy; SRS = stereotactic radiosurgery; STR = subtotal resection.

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TABLE 1. Detailed outcomes of ETS in each patient are shown

Case No.	Age (yrs), Sex	Pathology Grade	MIB-1 Index (%)	Presentation (CN)	Previous Treatment	Max Diameter/Vol (cm/cm ³)	Tumor Location
1	56, M	I	1	Abnormal olfaction (I), visual impairment (II), exophthalmos		5.5/54.1	OpC, orbit, TS, Eth, Sph, anterior cranial fossa
2	36, F	II (myxoid)	5	Diplopia (VI), tinnitus		4.2/21.1	Pet (+IAC), clivus, JF, HC, OcC
3	25, F	II	4	Diplopia (VI)	Transcranial	40/15.7	Pet, clivus, JF, HC, OcC, Pha
4	77, F	II	3	Tinnitus		3.5/11.5	Pet (+IAC), CS, clivus, JF
5	36, M	II	2	Diplopia (VI)		5.2/28.3	Pet (+IAC), bilateral CS, clivus, JF, Sph, CPA
6	29, M	II	1	Diplopia (VI)	Transcranial	3.0/9.6	CS, sella turcica, suprasellar region, clivus
7	39, M	II	3	Diplopia (VI), ataxia	Transcranial × 3	6.7/88.4	Pet (+IAC), bilateral CS, clivus, JF, Sph, pons, medulla
8	48, M	I	3	Diplopia (VI), CN XII palsy		4.6/14.5	Pet (+IAC), CS, clivus, JF, HC, OcC
9	36, F	II	1	Diplopia (III/VI), facial pain (V)	Transcranial	3.0/9.4	CS, clivus, Pet, JF, HC
10	49, F	II	5	Diplopia (VI)		3.7/11.8	Pet (+IAC), CS, clivus
11	41, M	II	1	Diplopia (VI)		3.8/21.3	CS, clivus, Pet, JF
12	32, M	II	1	Diplopia (VI)	Transcranial	4.1/16.7	Pet (+IAC), JF, CS, clivus, middle cranial fossa, CPA
13	82, F	II	3	Visual impairment (II)	Endonasal	5.0/48.3	OpC, orbit, TS, Eth, Sph, anterior cranial fossa
14	33, F	II	1	Ataxia, gait disturbance		2.6/5.2	CS, clivus, Pet (+IAC), JF, HC, middle cranial fossa, CPA
15	31, M	III	20	Epistaxis, headache	Biopsy + CyberKnife	3.7/17.0	OpC, Eth, Sph, TS, sella turcica, CS, clivus, medial temporal lobe
16	39, F	II	1	Diplopia (VI)	Transcranial	1.5/1.4	CS, clivus, Sph, Pet, middle cranial fossa, medial temporal lobe
17	30, M	II	2–3	Diplopia (VI)		4.1/8.2	CS, clivus, Pet, JF, pons
18	43, M	II	1	Diplopia (VI)		2.6/6.8	Pet, clivus, JF, CPA
19	66, F	II	1	Headache		3.1/9.4	Sph, clivus, Pet, JF, HC, pons

CPA = cerebellopontine angle; CS = cavernous sinus; Eth = ethmoid sinus; HC = hypoglossal canal; JF = jugular foramen; OcC = occipital condyle; Pet = petrous bone; Pha = pharynx; Sph = sphenoid sinus; TS = tuberculum sellae.

reports of using the transcranial approach to aim for maximum tumor resection followed by proactive extensive radiation therapy (RT), including proton-beam radiation.^{7,8,51,54} In this strategy, however, transcranial resection for the deeply seated tumor itself carries certain risks of neurological complications as well as a high degree of invasiveness even with modern skull base techniques, which proportionally increase with resection rate. Additionally, proactive high-dose RT to the original tumor bed can reduce the risk of recurrence, whereas it may simultaneously bring some undesirable adverse events.

With the recent advent of endoscopic technology in the field of neurosurgery, a wide range of skull base regions have become safely accessible.^{1,5,11,12,20,21,29,36,46} For the treatment of skull base chondrosarcoma, there are a few reports about the outcomes of endoscopic endonasal surgeries, which commonly achieved sufficient tumor resection with acceptable neurological complications.^{42,44,66} In this study, we present our recent experience of endoscopic transnasal surgery (ETS) for skull base chondrosarcoma. Based on our surgical outcomes, we discuss the efficacy of ETS and the role of stereotactic radiosurgery (SRS) in this era of state-of-the-art “less invasive” skull base surgery.

Methods

Study Population

Since 2010, 21 cases of chondrosarcomas were referred to our institution; 2 (9.5%) were treated with transcranial approaches, and 19 (90.5%) were treated with ETS. In our policy, tumors mainly extending to the lateral parts of the CNs (such as superior and lateral aspects of the optic canal [OpC] and the orbit, or the mastoid air cells outside the internal auditory canals [IACs]) are easily approached from the outside and are considered good candidates for transcranial approaches. In contrast, for tumors extensively involving the paramedian regions or the inferior portion of the petrous apex such as the clivus, sphenoid sinus, nasopharyngeal region, bilateral petrous apex, or jugular fossa, it is more reasonable to approach from inside; these are good candidates for ETS.

We retrospectively reviewed the medical records of these 19 consecutive patients who underwent ETS for chondrosarcoma. Ten patients (53%) were initially treated in our hospital, and the other 9 patients (47%) were referred to us after the failure of various treatments in previous hospitals (transcranial resection in 6 patients, transphenoidal surgery in 3, and hypofractionated RT in 1). The di-

TABLE 2. Detailed outcomes of ETS in each patient

Case No.	Pathology Grade	EOR	Time Btwn Diagnosis & ETS (mos)	Complication	Follow-Up (mos)*	GKRS (mos)*	Recurrence (mos)*	Final mRS Score
1	I	GTR	1	—	62	—	No	0
2	II (myxoid)	GTR	17	CSF leak	58	—	No	0
3	II	GTR	3	—	36	—	No	1
4	II	GTR	20	Transient abducens palsy	39	—	No	0
5	II	STR	4	—	36	Yes (3)	No	0
6	II	PR	9	—	36	Yes (5)	No	0
7	II	GTR	47	Transient abducens palsy	38	—	No	0
8	I	GTR	2	—	30	—	No	0
9	II	STR	4	—	30	Yes (8)	No	1
10	II	GTR	4	Transient abducens palsy	28	—	No	0
11	II	GTR	32	—	15	—	No	0
12	II	GTR	164	—	25	—	No	0
13	II	GTR	89	—	16	—	Yes (12)	2
14	II	GTR	8	—	19	—	No	0
15	III	GTR	54	—	15	—	No	0
16	II	GTR	55	—	16	—	No	1
17	II	PR	2	—	15	Yes (4)	No	0
18	II	GTR	8	—	7	—	No	1
19	II	GTR	4	—	7	—	No	1

* After ETS.

agnosis was histologically verified in all the patients, and the MIB-1 index was assessed.

Treatment Strategy

Since the introduction of the endoscopic approach for skull base chondrosarcomas, we have consistently applied the following strategy. First we recommend ETS, aiming for maximum resection. Second, if there is a remnant tumor component, we recommend adjuvant SRS 3–6 months after surgery. At SRS, only the residual tumor is selectively irradiated, and the patient is then followed up with periodic radiological imaging. And third, after gross-total resection (GTR), the patient is simply followed up with periodic radiological checkups. If there is a recurrence, resection or SRS is recommended depending on the tumor location. We usually recommend resection for a recurrence close to the anterior visual pathway or after high-dose RT.

Surgical Techniques

Details of our surgical approach in ETS have been described in previous publications.^{55–57} Briefly, the surgical navigation system (StealthStation Navigation, Medtronic Japan) and monitoring of CN function (electromyography of extraocular muscles, facial muscles, pharyngeal musculature with the special tracheal tube, and the tongue, as well as auditory brainstem response audiometry) were set to avoid CN injuries (Neuromaster, Nihon Kohden). Endoscopes 4 mm in diameter with 0°, 30°, and 70° lenses were used (175- to 180-mm-long rigid scopes; Karl Storz Endoscopy Japan), which were stabilized in the surgical field with a robotic holding device (Point Setter, Mitaka Kohki). The tumors were approached via the transsphenoidal

route under the 0° endoscope, and those extending laterally to the petrous apex were resected through the retrocarotid space under the angled endoscopes.⁵⁶ The tumors located in the lower clivus, the craniovertebral junction, and the nasopharynx were approached through the upper pharynx.⁵⁵ For those located in the parapharyngeal space or the pterygopalatine fossa, the transpterygoid approach or the transmaxillary approach was added as necessary. We directly approached tumors located mainly in the anterior skull base region through the ethmoidal sinus.⁵⁷ When the tumor was strongly adherent to critical anatomical regions such as the brainstem and the basilar artery or involved the adjacent CNs, resection remained maximal but judicious volume reduction and Gamma Knife radiosurgery (GKRS) was planned for the site of the residual tumors 3–6 months after surgery.

Every patient underwent endoscopic examination by an otolaryngologist at 1 week postoperatively. Patients visited our outpatient clinic at 1 month postoperatively for neurological evaluation and a second rhinological checkup.

Evaluation of Surgical Outcomes

All radiological images, including CT and MR images, were reviewed independently by 2 radiologists and 1 follow-up neurosurgeon, and the volumetric measurement was performed using GammaPlan software (Elekta Instruments, Inc.). Gross-total resection (GTR) was defined as disappearance of the tumor on postoperative MRI with contrast medium. Subtotal resection (STR) and partial resection (PR) were defined as ≥ 90% and < 90% resection, respectively.¹⁹

Follow-up MRI was performed within 3 days after

FIG. 1. Case 1. Images obtained in a 56-year-old man who presented with abnormal olfaction, impaired vision of the left eye with exophthalmos, and diplopia. MRI revealed a large mass lesion located in the anterior cranial base and nasal cavity, compressing the left orbit (**A and B**). We performed an endoscopic endonasal approach and the tumor was successfully removed. After surgery, he transiently complained of mild facial numbness, but his vision symptoms remarkably improved. The histological diagnosis was chondrosarcoma Grade I. The patient was followed up with periodic MRI without prophylactic radiation. MRI obtained at the last follow-up evaluation, 62 months after surgery, did not show any sign of recurrence (**C and D**).

surgery (short-term) to determine the extent of tumor removal, and then 3 and 6 months later. Postoperative neurological status was assessed at discharge and at 1, 3, and 6 months or later. The modified Rankin Scale (mRS) result was assessed based on the patient's condition at the final outpatient visit, and classified as excellent (mRS score of 0–1), favorable (mRS score of 2), moderately impaired (mRS score of 3), or disabled (mRS score of 4–5).⁶²

Results

The baseline characteristics of the patients and the detailed tumor locations are summarized in Table 1. Briefly, 17 patients (89%) had petroclival chondrosarcomas, and the other 2 patients (11%) had anterior skull base chondrosarcomas. Intradural extension was observed in 9 patients (47%). The median tumor volume and maximal diameter were 14.5 cm³ (range 1.4–88.4 cm³) and 3.8 cm (range 1.5–6.7 cm), respectively.

The detailed outcomes of each patient are summarized in Table 2. Among 19 tumors, 2 (10.5%) were histologically diagnosed as Grade I, 16 (84.2%) as Grade II, and 1 (5.2%) as Grade III. GTR of the tumor was achieved in 15 patients (78.9%). We abandoned attempts at GTR in 4 patients during surgery, balancing the potential risks of small but possibly serious complications with those of additional SRS. Among these 4 patients, the lower CNs were involved in calcified lesions at the jugular fossa in 2 patients (10.5%), which resulted in STR. In the other 2 patients (10.5%), solid tumor components engulfed the basilar artery or the ICA, which remained partially resected. Thus, resection rates were affected not by the intradural extension but by involvement of CNs or critical arteries in the calcified lesions.

FIG. 2. Case 5. A 36-year-old man presented with diplopia caused by bilateral abducens nerve palsy. His MRI disclosed a tumor located in the petroclival region that extended to the bilateral petrooccipital fissures and the jugular tubercle (**A and B**). At resection, the tumor was almost completely removed (**C**), but there was a small amount of residual tumor at the jugular tubercle (**D**, arrowheads). His symptoms improved after surgery, and 8 months later, he underwent GKRS for the small tumor remnant at the bilateral jugular tubercle. The yellow lines represent an 18-Gy isodose line of SRS, covering the target, and the green lines indicate 8, 10, and 14 Gy (**E**). The follow-up MRI obtained 32 months after GKRS revealed successful tumor control (**F**). Figure is available in color online only.

The 4 patients (21%) with tumor remnants underwent GKS at an interval of 3–8 months (median 5 months) after ETS. The prescribed radiosurgical dose ranged from 16 to 18 Gy (median 18 Gy) to the tumor margin and the targeting tumor volume ranged from 1.8 to 13.8 cm³ (median 6.6 cm³).

In our series, the transcranial approach and endoscopic transnasal approach were each used for the treatment of distinct types of skull base chondrosarcomas. Thus, previous transcranial surgeries did not affect the results of later ETSs. Representative cases are shown in Figs. 1–4.

Tumor Control

The patients were followed up for a median of 47 months (range 11–189 months) after the initial diagnosis and 28 months (range 7–62 months) after ETS. In 18 patients, there was no sign of recurrence on clinical follow-up examinations and radiological studies. In 1 patient (Case 13), a small tumor component rapidly recurred in the OpC 1 year after the initial ETS, and a second resection was performed without complications.

The overall actuarial tumor control rates were 92.9% at 3 and 5 years (Fig. 5), whereas tumor control was essentially achieved in all patients at the final analysis.

FIG. 3. Case 17. A 30-year-old man presented with diplopia caused by mild abducens nerve palsy. His MRI disclosed a tumor located in the petroclival region, which extended to the posterior cranial fossa, strongly compressing the brainstem with involvement of the basilar artery (BA; **A** and **B**). Notably, the tumor contained two prominent calcified (calc) parts, and one of them was embedded in the pons (**C**). A 3D computer graphics model was created for the purpose of surgical simulation (**D** and **F**). At resection, the calcified tumor component strongly adhered to the pontine surface, involving the BA (**E**). To avoid injury of the brainstem and BA, we intentionally left this calcified lesion. Postoperative MRI showed a small residual tumor in the left pons (**G**, arrowhead). His symptoms rapidly improved after surgery, and GKRS was performed for the residual tumor 4 months later. The yellow lines represent an 18-Gy isodose line of SRS, covering the target, and the green lines indicate 8, 10, and 14 Gy (**H**). Follow-up MRI obtained 12 months after GKRS revealed successful tumor control (**I**). vert ICA = vertical portion of the ICA; III = oculomotor nerve; V = trigeminal nerve. Figure is available in color online only.

Complications

In 1 patient (Case 4; 6%), transient abducens nerve palsy newly developed after ETS, which completely resolved in 2 weeks. Two patients (11%) presented with transient worsening of existing abducens nerve palsy. In these patients, the symptoms completely resolved within 3 and 6 months (Cases 10 and 7, respectively). One patient (Case 2; 6%) showed delayed CSF rhinorrhea 1 week after surgery, which required an additional surgical repair. In this case, CSF leakage had not been apparent during surgery, but suddenly occurred 1 week later. At the surgical repair, no dural defect was evident, but continuous oozing of CSF was found around the internal auditory meatus. In the 4 patients who underwent GKS, none showed radiation-induced neurological complications during follow-up. At the last follow-up periods, excellent functional outcomes were achieved in all except for 1 patient (Case 13) who had moderate impairment due to senility (mRS score of 2, unrelated to the treatment or the primary disease).

Discussion

In the present study we conducted a retrospective analysis of 19 patients with skull base chondrosarcoma to clarify the efficacy of endoscopic surgery and the role of

adjuvant radiation. This is one of the largest series of skull base chondrosarcomas treated at a single institution under a consistent therapeutic strategy. In our strategy, after initial radical treatment (GTR or STR/PR + SRS for small tumor remnants), we consistently maintained a policy of observation with periodic MRI, without proactive extensive RT covering the original tumor bed. The actuarial local tumor control rate was 93% at 5 years and all tumors were successfully controlled without any persistent neurological complications at the final analysis. Our results indicate that endoscopic skull base surgery can achieve satisfactory results, i.e., comparable rates of total or subtotal resections with fewer neurological complications compared to previous series using transcranial approaches (Table 3).^{8,10,25,51,53,54,61}

Role of ETS for Chondrosarcoma

After the introduction of endoscopic technology to the neurosurgical fields, safe surgical approaches to the paramedian skull base became feasible, and the role of surgery dramatically changed for a variety of skull base lesions.^{1,5,11–13,21,36,55,57,59,60} Recently, reports on the endoscopic approach for petrous apex lesions have been gradually increasing,^{15,22,28,33,35,36,41,47,56,59,65} whereas there are still only

FIG. 4. Case 19. A petroclival tumor was found in a 66-year-old woman with headache. Preoperative MRI and CT (A–D) disclosed a mass lesion in the petroclival area extending into the parapharyngeal space and left jugular (jug) tubercle (arrow), penetrating the clival dura mater and strongly compressing the pons (arrowhead). A 3D computer graphics model was created for the purpose of surgical simulation (E and F). The tumor was completely removed through the retro-carotid window (G and H). Postoperative MRI (I–K) showed complete removal of the tumor through an adequately wide surgical corridor (L). The arrowhead (I) and arrow (J) represent the region where the tumor had invaded before surgery and was successfully removed. cav ICA = cavernous portion of the ICA; VI = abducens nerve; VII/VIII = IAC. Figure is available in color online only.

a few reports on the outcomes of skull base chondrosarcoma, in which investigators commonly applied proactive RT regardless of the extent of resection (EOR; Table 3).^{23,42,44,66} Thus, it is difficult to definitively determine the efficacy of endoscopic surgery for skull base chondrosarcomas to date.

Compared with transcranial skull base surgery, ETS has some benefits based on the anatomical nature of chondrosarcoma. Although its histogenetic origin remains a matter of debate, it is postulated that chondrosarcoma is

a neoplasm of mesenchymal precursor cells destined to undergo chondrocytic cell differentiation,^{2,17,18} and the intracranial foci of these precursor cells are located at the synchondroses that present in the midline part of the skull base (sphenoccipital, interoccipital, petrooccipital, intersphenoidal, and sphenothmoidal synchondrosis). Indeed, almost all the skull base chondrosarcomas are located at the paramedian skull base, displacing adjacent CNs laterally. Therefore, the direct surgical approach from the nasal corridor is quite reasonable (Fig. 6). In contrast, in the transcranial approaches, significant parts of surgical procedures are performed through narrow spaces between involved CNs, and it is very difficult to balance the resection rate and the risk of neurological complications. We believe that these characteristics peculiar to the approach routes resulted in the favorable rate of GTR as well as the low rates of CN-related complications in ETS, as noted in this study and previous reports (Table 3).

However, there are some possible drawbacks to ETS. First, its surgical corridor is a long and narrow keyhole shape, which may impose some extent of difficulty on surgeons for manipulation. The second problem is the lateral limit of the surgical corridor. Basically, ETS uses the space between bilateral ICAs to approach the paramedian skull base, which means that the ICA can become an obstacle when treating tumors with extremely lateral extensions behind the ICA. To overcome these issues, we frequently used oblique-viewing endoscopes (30° or 70°), which provide an adequate surgical view for laterally extending tumors with use of variously curved surgical devices.

FIG. 5. The Kaplan-Meier curve for local tumor control (LTC) is shown.

TABLE 3. Summary of outcomes in previous reports and the present study

Authors & Year	No. of Patients	Median Volume (cm ³)	EOR (%)	Pathological Grade (%)	Follow-Up Mos (median)	Adjuvant Radiation (%)	Recurrences (%)	Time From Surgery to Recurrence (mos)	Postsurgical Deficits (%)	Final Outcomes (%)
Transcranial skull base surgery										
Sen et al., 1989	9	NA	GTR = 5 (56)	Low grade = 9 (100)	3–96 (12)	RT 60 Gy = 4 (44) for recurrent tumors	2 (22)	24 & 60	CN I = 2 (22), CN III = 1 (11), CN IV = 1 (11), CN V = 3 (33), hypopituitarism = 1 (11)	NA
Sekhar et al., 2001	22	NA	GTR = 11 (50), STR = 8 (36)	NA	NA	NA	NA	NA	CSF leak = 2 (9), CN V = 5 (23), CN VI = 4 (18), vascular injury = 3 (14)	NA
Crockard et al., 2001	17	40–50	GTR + STR = 14 (82)	Mesenchymal = 2 (12), low grade = 15 (88)	NA	RT + SRS = 4 (24) for residual tumors	NA	NA	CN deficits = 4 (24), CSF leak = 2 (12), wound breakdown = 1 (6), infection = 1 (6)	Death = 4 (24), alive = 13 (76), OS 93% at 5 yrs in low-grade tumors
Brackmann & Teufert, 2006	8	NA	GTR = 6 (75)	Low grade = 8 (100)	3–300 (135)	RT 50–56 Gy = 3 (38)	2 (25)	3 & 45	Meningitis = 1 (13), CN V = 2 (25), CN VI = 1 (13), CN VII = 2 (25), CN VIII = 5 (63), lower CN = 1 (13)	Tumor control was achieved in 5 (63); death (unrelated) = 1 (13)
Sbaihat et al., 2013	13	NA	GTR = 13 (100)	Grade I = 8 (62), Grade II = 4 (31), Grade III = 1 (8)	7–86 (mean 47)	RT = 7 (54%) for recurrent or Grade II & III tumors	2 (15)	36 & 72	CN VII = 1 (8), CN VIII = 11 (85), CN IX = 3 (23), CN X = 2 (15), CN XI = 2 (15), CN XII = 1 (8)	Alive = 13 (100)
ETS										
Mesquita Filho et al., 2014	5	NA	GTR = 2 (40), STR = 3 (60)	Grade I = 2 (40), Grade II = 2 (40), Grade III = 1 (20)	3–33 (15)	PBRT = 4 (80) or RT = 1 (20) for all cases	0 (0)	None	CN VI = 1 (20), CN VIII = 1 (20)	Alive = 5 (100)
Moussazadeh et al., 2015	8	9.8	>95% resection = 5 (63), PR = 3 (27)	NA	NA	PBRT = 8 (100) for all cases	NA	NA	CSF leak = 1 (13), fungal sinusitis = 1 (13)	Alive = 8 (100)
Present study, 2016	19	14.5	GTR = 15 (79), STR = 2 (11), PR = 2 (11)	Grade I = 2 (11), Grade II = 16 (84), Grade III = 1 (5)	11–189 (47)	GKRS = 4 (21) for residual tumors	1 (5)	12	CSF leak = 1 (5)	Tumor control was achieved in 19 (100), LTC = 93% at 5 years

LTC = local tumor control; NA = not available; OS = overall survival; PBRT = proton beam radiotherapy.

FIG. 6. A schematic of an endoscopic transnasal trajectory is shown. The tumor is located at the paramedian skull base, displacing CNs laterally. Therefore, a transnasal trajectory can directly approach the tumor between bilateral ICAs without causing interference with CNs. VI = abducens nerve; IX/X/XII = lower cranial nerves. Figure is available in color online only.

Role of Adjuvant RT

Based on our results, we insist that the routine addition of extensive RT is unnecessary in most cases of chondrosarcoma. Chondrosarcomas have frequently been reported in part of the outcomes of skull base chordoma because of their similarity to the radiographic findings and contiguity of the anatomical origin.^{13,16,23,25,40,53,54,66} In fact, both of those pathologies share several common clinical features, i.e., they are locally aggressive, destroy the deep skull base, and are resistant to conventional fractionated RT.^{27,45} Despite such similarities, their biological behaviors are largely different. Most skull base chordomas are highly proliferative, and sometimes recurrent immediately after GTR.^{16,24,50} Thus, they are often considered a malignancy, which warrants tumor resection with some extent of surgical margin as well as adjuvant extensive RT for prophylaxis.^{3,4,24,31,50}

On the other hand, the significance of adjuvant extensive RT has not yet been determined for skull base chondrosarcoma. The histological diagnosis of chondrosarcoma varies from benign to malignant, and approximately 90% of the lesions located in the skull base are classified as Grade I or II, showing relatively benign clinical courses.^{38,48} Nonetheless, according to recent clinical reports, extensive RT tended to be systematically added regardless of histological grading and EOR.^{6,31,38,44,49,63} We wonder if the automatic application of the treatment policy obtained from the experience of skull base chordoma is legitimate for the “possibly malignant” but mostly benign skull base chondrosarcoma.

Among a variety of RTs for chondrosarcoma, the efficacy of SRS has been well reported in several previous studies.^{32,34,37,39} Tumor control was excellent when a rela-

tively high radiosurgical dose (≥ 15 –16 Gy) was prescribed to the margin of small residual tumor.^{34,39} The authors of these previous studies concluded that maximal safe resection should be the primary initial management of chondrosarcoma, whereas SRS is a potent treatment option for small- to medium-sized chondrosarcomas and is associated with improvement of CN function in selected cases. In our strategy, SRS was added to limited areas only when it was considered appropriate, instead of using extensive RT. The actual rate of the patients who underwent SRS was 21%, and none suffered from radiation-induced complications. Thus, our strategy could contribute to minimizing the non-negligible risks of extensive radiation in certain patients,^{9,14,26,30,43,49,52,58,61,64} and hold promise of becoming the standard treatment strategy for skull base chondrosarcoma.

Conclusions

To definitively determine the efficacy of our strategy, further analysis based on the larger case series with a longer follow-up duration is essential. In addition, we could not determine the outcomes of aggressive subtypes (Grade III or mesenchymal type) because the current cohort included only 1 patient with such aggressive chondrosarcoma (5.3%). However, our preliminary results suggest that our treatment strategy for skull base chondrosarcoma is rational as an initial treatment policy for chondrosarcoma and may possibly help to establish evidence in the management of these intractable skull base tumors.

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Disclosures

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Conception and design: Shin, Hasegawa. Acquisition of data: Hasegawa, Kondo, Hanakita, Kin. Analysis and interpretation of data: Hasegawa. Drafting the article: Hasegawa. Critically revising the article: Shin, Saito. Reviewed submitted version of manuscript: Shin, Kondo, Hanakita, Mukasa, Kin, Saito. Approved the final version of the manuscript on behalf of all authors: Shin. Statistical analysis: Hasegawa. Administrative/technical/material support: Kin. Study supervision: Shin, Mukasa, Saito.

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