ORIGINAL ARTICLE

Complications of Skull Base Surgery: An Analysis of 30 Cases

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ABSTRACT

Objectives: To evaluate the risk factors for perioperative complications among patients undergoing craniofacial resection for the treatment of skull base tumors. Design: Retrospective analysis. Participants: The study group comprised 29 patients with skull base tumors (22 malignant and 7 benign) who underwent 30 craniofacial resections at Hokkaido University Hospital between 1989 and 2006. Of these cases, 21 had undergone prior treatment by radiation (16 cases), surgery (7 cases), or chemotherapy (1 case). Moreover, 19 needed extended resection involving the dura (11 cases), brain (5 cases), orbit (12 cases), hard palate (5 cases), skin (3 cases), or cavernous sinus (2 cases). Main outcome measures: Perioperative complications and risk factor associated with their incidence. Results: Perioperative complications occurred in 12 patients (40%; 13 cases). There was a significant difference between complication rates for cases with and without prior therapy (52.4% vs. 11.1%). The complication rate for dural resection cases was 81.8%. There was a significant difference between complication rates for cases with and without dura resection. No postoperative mortality was reported. Conclusions: Craniofacial resection is a safe and effective treatment for skull base tumors. However, additional care is required in patients with extended resection (especially dural) and those who have undergone prior therapy.

KEYWORDS: Complications, craniofacial resection, skull base surgery

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Ketcham and colleagues[1] first reported on the combined transcranial and transfacial approach for tumors of the paranasal sinuses involving the anterior skull base in 1963. Since then, improved radiological imaging techniques have allowed surgeons to evaluate the tumor extent more easily. Moreover, the use of microvascular free-flap transfer has allowed indications of craniofacial resection to be extended to patients with three-dimensional defects and wide exposure of the contents of the endocranium. However, extended resection surgery often has severe complications.

In the current study, we reviewed 30 cases of skull base surgery for tumors involving the anterior and middle cranial base. We calculated the survival and complication rates, and analyzed the risk factors associated with the incidence of perioperative complications.

PATIENTS AND METHODS

Patients

Between 1989 and 2006, a total of 30 skull base surgeries were performed in 29 patients with tumors involving the anterior and/or middle cranial fossa at the Hokkaido University Hospital, Sapporo, Japan (Table 1). This group comprised 22 males and 7 females, with a median age of 60 years (range, 26 to 71 yrs). In total, 22 of the patients had malignant tumors (squamous cell carcinoma in 11 cases, olfactory neuroblastoma in 5 cases, adenoid cystic carcinoma in 3 cases, adenosquamous cell carcinoma in 2 cases, and rhabdomyosarcoma in 1 case). The remaining seven patients had benign tumors (hemangioma in one case, trigeminal nerve neurinoma in one case, frontal sinus cyst in one case, giant cell tumor in one case, fibrous dysplasia in one case, inverted papilloma in one case, and pigmented villonodular synovitis in one case). The patient with hemangioma underwent skull base surgery twice. In total, 21 of the cases had undergone prior therapy.

Table 1 Patient Demographics

Characteristic	*n*
Total	29
Age group (yrs)	
20–39	4 (13.8%)
40–49	5 (17.2%)
50–59	4 (13.8%)
60–69	15 (51.7%)
70+	1 (3.4%)
Gender	
Male	22 (75.9%)
Female	7 (24.1%)
Medical comorbidity	
Present	5 (17.2%)
Absent	24 (82.8%)
Pathology	
Adenoid cystic carcinoma	3 (10.3%)
Olfactory neuroblastoma	5 (17.2%)
Squamous cell carcinoma	11 (37.9%)
Adenosquamous cell carcinoma	2 (6.9%)
Rhabdomyosarcoma	1 (3.4%)
Benign	7 (24.1%)
Prior therapy*	
Present	21 (70%)
Surgery alone	4 (13.3%)
Radiation alone	13 (43.3%)
Surgery + radiation	3 (10%)
Chemotherapy alone	1 (3.3%)
Absent	9 (30%)

*Based on 30 cases of skull base surgery.

Among the patients with malignant tumors, 16 cases had undergone prior radiotherapy (30 to 65 Gy), 5 cases had undergone previous surgery, and 1 case with olfactory neuroblastoma had undergone prior chemotherapy (cisplatin). Among the patients with benign tumors, two cases had undergone previous surgery, one case had recurrence of inverted papilloma, and one case had recurrence of hemangioma in the middle cranial fossa with facial nerve paralysis.

Methods

In total, 25 cases (83.3%) were treated by the anterior fossa approach with a lateral rhinotomy skin incision and/or a coronal arch-shaped skin

Table 2 Details of Skull Base Surgery*

Feature	*n*
Type of approach	
Anterior fossa	25 (83.3%)
Middle fossa	5 (16.7%)
Extent of resection	
Orbit	12 (40%)
Hard palate	5 (16.7%)
Dura	13 (43.3%)
Brain	5 (16.7%)
Skin	3 (10%)
Cavernous sinus	2 (6.7%)
Reconstruction	
RAMC free flap	9 (30%)
FA free flap	3 (10%)
Locoregional flap alone	18 (60%)

*Based on 30 cases of skull base surgery.
RAMC, rectus abdominis myocutaneous; FA, forearm.

incision (Table 2). A total of five cases of benign tumor received middle cranial resection with a temporal skin incision. All of the cases underwent skull base reconstruction. We used 3 forearm (FA) free flaps with microvascular anastomosis, 9 rectus abdominis myocutaneous (RAMC) free flaps with microvascular anastomosis, and 18 locoregional flaps.

In total, 19 of these cases needed extended resection involving the dura (11 cases), brain (5 cases), orbital content (12 cases), hard palate (5 cases), skin (3 cases), or cavernous sinus (2 cases). All of the cases that required extended resection had malignant tumors.

The clinical histories of the patients were ascertained from their medical records retrospectively. The follow-up period ranged from 9 to 210 months (median, 44 mos). We estimated the medical comorbidity using the Adult Comorbidity Evaluation (ACE)-27 index system; this was derived from the original Kaplan-Feinstein Index (KFI), which was developed to assess comorbidity in diabetes mellitus,[2] and has subsequently been modified and validated by Piccirillo[3] to include terms relevant to cancer. We classified five patients (17.2%) who were judged to be grade 2 or 3 according to the ACE-27 index as having medical comorbidities; four of these patients had cardiovascular system complications (hypertension in two, ischemic heart disease in one, and arteriosclerosis obliterans in one), and the remaining patient had respiratory system complications (pulmonary emphysema).

The survival rates were calculated, after the initial visit to our hospital, using the Kaplan-Meier method, and were compared using the log-rank test. A p value < 0.05 was considered statistically significant. Risk factors for perioperative complications were compared using Fisher's test.

RESULTS

The average operation time was 10.4 hours (range, 4.5 to 18 hrs). The figure for patients who underwent free-flap reconstruction was 13.9 hours, whereas that for patients who underwent other types of reconstruction was 7.8 hours. The average operation time for resection with free-flap reconstruction was significantly longer ($p < 0.01$). Otherwise, the figure for malignant cases was 12.1 hours and that for benign cases was 6.1 hours. The average operation time for malignant cases was significantly longer than that for benign cases ($p < 0.01$).

The average blood loss during operation was 1208 mL (range, 20 to 8360 mL). The figure for malignant cases was 1482 mL whereas that for benign cases was 388 mL. The malignant cases experienced significantly higher blood loss than the benign cases ($p < 0.01$).

Among all of the cases, the overall 5-year survival rate was 63.7%. In the 22 patients with malignant tumors, the figure was 51.3%. Table 3 shows comparative data on the overall 5-year survival rate among patients with malignant tumors. There were no significant differences in survival rate associated with age or with brain or dural resection. However, there was a significant difference in survival rate between cases with and without medical comorbidity ($p < 0.005$).

In total, 13 perioperative complications were reported in 12 of the cases (40%); these comprised

Table 3 Overall Survival Rate among Patients with Malignant Tumors

Variable	5-Year Survival Rate	*p* Value
Total ($n=22$)	51.3%	
Age		
<60 years ($n=9$)	77.8%	
≥ 60 years ($n=13$)	31.0%	0.09
Medical comorbidity		
Present ($n=5$)	0.0%	
Absent ($n=7$)	67.0%	0.0002
Brain resection		
Present ($n=5$)	20.0%	
Absent ($n=17$)	62.0%	0.15
Dural resection		
Present ($n=13$)	51.3%	
Absent ($n=9$)	50.0%	0.97

6 wound complications, 4 central nervous system complications, 1 systemic complication, and 2 other types of complication (Table 4). The wound complications were four local infections, one hematoma, and one bleed. The central nervous system complications were four cases of meningitis. The systemic complication was one case of deep vein thrombosis. The other types of complication were two donor-site complications of the RAMC flap (herniation and abscess).

Table 4 Perioperative Complications*

Type of Complication	*n*
Complications	
Present	12 (40%)
Absent	18 (60%)
Wound complications	
Local infection	4 (13.3%)
Hematoma	1 (3.3%)
Bleeding (intraoperative)	1 (3.3%)
Central nervous system complication	
Meningitis	4 (13.3%)
Systemic complication	
Deep vein thrombosis	1 (3.3%)
Others	
RAMC donor site herniation	1 (3.3%)
RAMC donor site abscess	1 (3.3%)
Perioperative mortality	0 (0%)

*Based on 30 cases of skull base surgery.
RAMC, rectus abdominis myocutaneous.

Table 5 Factors Associated with the Incidence of Perioperative Complications*

Variable	Complication Rate	*p* Value
Age		
<60 years	6/14 (42.9%)	
≥ 60 years	6/16 (37.5%)	0.94
Medical comorbidity		
Present	2/5 (40%)	
Absent	10/25 (40%)	
Pathology		
Malignant	11/22 (50%)	
Benign	1/8 (12.5%)	0.09
Prior therapy		
Present	11/21 (52.4%)	0.049
Absent	1/9 (11.1%)	
Dural resection		
Present	9/11 (81.8%)	0.0012
Absent	3/19 (15.8%)	
Brain resection		
Present	3/5 (60%)	0.36
Absent	9/25 (36%)	
Orbital resection		
Present	6/12 (50%)	0.59
Absent	6/18 (33.3%)	
Hard palate resection		
Present	2/5 (40%)	
Absent	10/25 (40%)	
Free flap reconstruction		
Present	4/12 (33.3%)	0.82
Absent	8/18 (44.4%)	

*Based on 30 cases of skull base surgery.

Among the malignant tumor patients, 11 of the 22 cases (50%) had complications (Table 5). Among the benign tumor patients, only one of the eight cases (12.5%) had a complication (bacterial meningitis). There was no significant difference between the complication rates of patients with malignant and benign tumors.

In the group without prior therapy, one of the eight cases (11%) had complications. In the group with prior therapy (including surgery, radiation, and chemotherapy), 11 of the 21 cases (52.4%) had complications. There was a significant difference between the complication rates of the groups with and without prior therapy ($p < 0.05$).

Table 5 shows the factors that were associated with the incidence of perioperative complications.

In total, 9 of the 11 (81.8%) dural resection cases had some complications: of them, 5 (45.5%) had local problems (infection, development of abscess, and bleeding), 2 (18.2%) had meningitis, 1 (9.1%) had deep vein thrombosis, and 1 (9.1%) had RAMC donor-site herniation. There was a significant difference between the complication rates of the groups with and without dural resection. However, there was no significant difference between the complication rates of the groups with and without the other types of extended resection. Moreover, there was no significant difference between the complication rates of the groups with and without medical comorbidities.

DISCUSSION

Since Ketcham and colleagues[1] reported the combined transcranial and transfacial approach for the resection of paranasal sinus tumor involving the anterior cranial fossa more than 40 years ago, skull base surgery has been put into practice throughout the world and has improved in safety. However, skull base surgery still requires a relatively long operation time, and the damage to patients can sometimes be severe. Particular attention must be paid to the complications, some of which can cause postoperative death. Here we analyzed the outcomes and perioperative complications of skull base surgery cases in our hospital, and described their characteristics.

Recent reports have shown the complication rate of skull base surgery to be 33 to 54.7%.[4–10] In our current series, the complication rate was 40%, which was comparable with these reports.

It has been unclear from previous studies whether prior therapy and the extent of resection are associated with the incidence of perioperative complications. In a collaborative study, Ganly and associates[9] reported that dural and/or brain invasion cases had significantly higher complication rates than cases without invasion; they also reported a significant difference in complication rates between cases with and without prior radiation (44% versus 34%; $p = 0.001$). However, Deschler and colleagues[11] reported no significant difference between the complication rates for patients with previous craniotomy, radiation therapy, or chemotherapy compared with those without prior therapy ($p > 0.5$). In addition, Kraus et al[5] reported no significant difference between the complication rates for patients with and without previous therapy ($p = 0.21$), or between patients with invasion (of the palate, orbit, dura, and brain) and those without invasion. In our current series, we found that prior therapy and dural resection were risk factors for perioperative complications. These discrepancies could be caused by differences in patient characteristics and surgical techniques between institutions. We predicted that prior therapy could be a risk factor for the incidence of perioperative complications. Moreover, in dural resection cases, there were many instances of local complications (45.5%) and meningitis (18.2%). It is therefore important to employ preoperative and/or postoperative antibiotict therapy for patients with dural invasive tumors.

Recent studies have reported postoperative death rates of 2 to 7.6%.[4–9,11] In our current series, there was no postoperative death. We therefore concluded that our indications for skull base surgery were appropriate.

For patients with malignant tumors, the overall 5-year survival rate for cases with skull base surgery has been reported as 52 to 56%.[4–6,12] In our current series, the overall 5-year survival rate for patients with malignant tumors ($n = 22$) was 51.3%. Shah and colleagues[7] reported that the survival rate was significantly better for patients whose tumors could be excised with limited resection compared with those requiring an extended procedure. Our current data showed that the 5-year survival rates for patients with and without brain resection were 20% and 62%, respectively. However, we were unable to find a statistically significant difference between patients who underwent limited and extended resection. Furthermore, none of the patients with medical comorbidities survived for more than 5 years. All of these cases

had disease-specific death. We therefore concluded that medical comorbidity was an important risk factor for survival.

We performed skull base surgery in eight cases with benign tumors. Our general policy was to observe cases of benign tumor without symptoms; however, we judged that patients with some functional loss, such as facial nerve paralysis, needed a reduction of the tumor to allow the recovery of nervous function. We also judged that patients with a premalignant tumor (such as an inverted papilloma) invading the skull base needed craniofacial surgery for total resection. In total, five of the eight cases were treated using the middle fossa approach with a temporal skin incision. These cases had no complications. Only one case of inverted papilloma with anterior craniofacial resection had bacterial meningitis. We therefore concluded that our approach for skull base surgery of benign tumors was safe, although additional attention must be given to complications such as meningitis.

CONCLUSIONS

Craniofacial resection has been developed into a safe and effective procedure for the treatment of tumors involving the skull base. Our analysis showed that dural resection and prior therapy were risk factors for the incidence of perioperative complications. Additional care must therefore be taken with patients who have undergone prior therapy. Furthermore, local complications (45.5%) and meningitis (18.2%) were recognized in dural resection cases. A preoperative and/or postoperative strategy against local infection and meningitis is therefore necessary.

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