Extended orbital exenteration for sinonasal malignancy with orbital apex extension: surgical technique and clinical analysis

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OBJECT The majority of sinonasal malignancies present with advanced disease, and cure rates are generally poor. Surgical extirpation remains the mainstay of treatment. In cases of sinonasal malignancy with orbital apex extension, gross-total tumor resection requires orbital exenteration and bony skull base resection around the orbital apex to provide sufficient margins. In this retrospective study, the authors describe their surgical strategy in and technique for orbital exenteration with orbital apex resection in patients at Tokyo Medical and Dental University who had sinonasal malignancy with orbital apex extension. They also analyzed the clinical features of and the results in these patients.

METHODS Between February 2001 and August 2012 at the authors' institution, sinonasal malignancy with orbital apex extension was treated using craniofacial tumor resection with orbital exenteration including skull base bone around the orbital apex. The authors describe this technique and analyze the surgical indications, extent of resection, primary tumor location, outcome, pathological findings, and neoadjuvant and adjuvant therapies of the patients who underwent the technique.

RESULTS The patients consisted of 12 men and 3 women with a mean age of 47.7 years (range 14–79 years). The longest postoperative follow-up was 9.5 years, and the shortest was 0.67 year (mean 3.0 years). Tumor originated at the ethmoid sinus in 6 patients (40%), maxillary sinus in 5 (33%), nasal cavity in 2 (13%), and orbital cavity and maxillary bone in 1 patient each (7%). Histological analysis of tumor specimens revealed squamous cell carcinoma in 9 patients (60%), rhabdomyosarcoma in 2 (13%), and small cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, and Ewing sarcoma in 1 patient each (7%). Two patients experienced recurrences at 1 and 5 months after treatment; these patients died at 5 and 10 months after surgery, respectively. Estimated 5-year recurrence-free survival (RFS) was 86.7%, and estimated 5-year overall survival (OS) was 86.2%; there was no perioperative mortality. None of the patients had new neurological deficits as a result of the surgery, but 5 patients suffered infectious complications from the graft transplanted into the cavity after resection. There were no other perioperative complications.

CONCLUSIONS These authors are the first to describe a technique for extended orbital exenteration with orbital apex skull base resection. The technique provided sufficient margins for gross-total resection of the sinonasal malignancy with orbital apex extension. The estimated 5-year OS and RFS rates were high, and the perioperative complication rate was acceptably low, demonstrating the safety and efficacy of this technique.

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KEY WORDS craniofacial resection; orbital exenteration; sinonasal malignancies; surgical technique
The majority of sinonasal malignancies present with advanced disease, and cure rates are generally poor because early diagnosis is difficult. Surgical extirpation is the mainstay of treatment. Orbital involvement in sinonasal malignancies, especially of the orbital apex, is associated with a significant reduction in survival. In cases of sinonasal malignancy with orbital apex extension, tumor resection with orbital exenteration and bone resection of the skull base around the orbital apex is required to provide sufficient resection margins.

In this study, we describe our surgical strategy and technique for orbital exenteration with orbital apex resection. We also analyze the clinical features of and the results in patients who underwent this technique.

Methods

All patients in this case series provided informed consent for inclusion of their clinical data in this paper. Between February 2001 and August 2012 at our institution, 65 patients with sinonasal malignancy underwent craniofacial tumor resection performed by a multispecialty skull base team consisting of neurosurgeons, head and neck surgeons, and plastic surgeons. Of these 65 patients, 15 had sinonasal malignancy with orbital apex extension. These patients underwent craniofacial tumor resection with orbital exenteration and bony resection of the orbital apex. We reviewed the surgical indications, extent of resection, primary tumor location, outcome, pathological findings, and neoadjuvant and adjuvant therapies for these 15 patients.

Computed tomography and MRI were performed preoperatively in all patients to determine tumor size, tumor location, and relationship of each tumor to adjacent tissues.

Surgical Strategy

Indications for attempted gross-total resection of these lesions were as follows: no metastasis to other organs, invasion of the intraorbital tissue around the orbital apex, and absence of invasion into the cavernous sinus or dura mater. A thorough evaluation of preoperative imaging was required to determine if orbital apex resection was required. This cancer invasion stage corresponds to the T4bN0M0 stage (International Union Against Cancer Staging System, 7th edition) without dura mater invasion.

Step 2: Craniotomy and Exposing the Frontal Fossa

A semi-coronal skin incision, bifrontal craniotomy, and temporal craniotomy on the affected side were made, and the supraorbital bar was removed. Modifications of the skin incision and supraorbital bar removal were done based on the variation in tumor location and size. The anterior cranial fossa was exposed to the end of the jugum sphenoidale, exposing the optic sheath bilaterally (Fig. 2A). Opening the dura and subsequent sacrifice of the bilateral olfactory nerves were performed to achieve adequate exposure of the frontal cranial fossa to the posterior edge of the jugum sphenoidale. The dural defect was repaired with temporal fascia as described previously.

Step 3: Exposing the Middle Fossa

Dolenc’s approach was first described in 1985; this technique is used for exposure of the optic nerve, internal carotid artery, and ophthalmic artery. The dura of the middle fossa was peeled from the skull base to expose the middle meningeal artery. This artery was coagulated and cut at the foramen spinosum. The superior orbital fissure and optic canal were unroofed with a high-speed drill and micro-rongeur. Epidural dissection of the lateral wall of the cavernous sinus was started by dissection at the meningo-orbital band to the third branch of the trigeminal nerve. The bleeding was controlled by gently packing with oxidized cellulose (Surgicel, Ethicon) soaked in fibrin glue. The dural dissection was extended to the anterior clinoid process. The anterior clinoid process was then removed to expose the optic sheath widely (Figs. 2B and C and 3).

The anterior wall of the foramen rotundum was drilled, and the second branch of the trigeminal nerve was exposed to prepare for ligation and transection of the nerve together with the dura mater. The falciiform ligament was cut, and the optic sheath was longitudinally opened to expose the internal carotid artery and ophthalmic artery (Fig. 4A). The optic nerve was then cut, followed by ligation and cutting of the ophthalmic artery (Fig. 4B and C). The oculomotor nerve, trochlear nerve, first branch of the trigeminal nerve, and abducens nerve were transected together with the dura mater at the transition between the dura mater and the peri-orbita near the superior orbital fissure while taking care not to damage the internal carotid artery (Fig. 5A). After this transection of cranial nerves, the dura mater of the middle fossa floor is peeled further posteriorly to expose the superior and lateral wall of the

FIG. 1. A: Sagittal view of 3D CT bone image with tumor (green). Red line signifies the resection line. B: Coronal view of the T2-weighted MR image. C: Endoscopic view in the left nasal cavity. T = tumor. Figure is available in color online only.
sphenoid sinus (Fig. 5B and C). The opened dura mater around the optic sheath was tightly repaired with the temporal fascia before opening the sphenoid sinus. Illustration of this widely exposed middle fossa is depicted in Fig. 6

Step 4: Resecting the Tumor With a Safety Margin

The line of resection at the frontal and middle fossa skull bases included more than 5 mm of margin and was cut using a high-speed drill (Fig. 7A and B). In cases of sphenoid sinus tumor invasion, the posterior border included the foramen ovale so that the resection would be posterior enough to include the sphenoid sinus (Fig. 8A1–A3). In such cases, the root of the pterygoid process between the foramina rotundum and ovale was drilled off to create a corridor to the posterior part of the sphenoid sinus. It was sometimes difficult to determine adequate margins from the frontal and middle fossae view. In these cases, endoscopic lighting from the nasal cavity transmitting through the ethmoid and sphenoid sinus wall served as a guide (Fig. 7B and D). If tumor did not invade the sphenoid sinus, the lateral wall of the sphenoid sinus was drilled off at the foramen rotundum to set the posterior boundary for excision in the anterior part of the sphenoid sinus (Fig. 8B1–B3). In our series, we defined ample margins at the skull base as a sufficient amount of tissue left surrounding tumor to prevent exposure of the tumor during resection.

A palpebral conjunctiva incision was made (Fig. 9A), and the facial skin and subcutaneous tissue were peeled from the maxillary bone in a downward direction. The maxillary bone was cut using a bone saw without exposing the tumor (Fig. 9B and C). The tumor along with orbital content was then resected en bloc with a margin (Fig. 9D).

Step 5: Reconstructing the Defect After Tumor Resection and Making the Ocular Prosthesis Bed

Anterolateral thigh free flap or rectus abdominis myocutaneous free flap was harvested and transplanted to the cavity after resection (Fig. 10B). If feasible, the ocular prosthesis bed was made at the same time (Fig. 10C).

Statistical Methods

Estimated overall survival (OS) rate and recurrence-free survival (RFS) rate were calculated using the Kaplan-Meier method. “Recurrence free” was defined as no evi-
Results

A summary of characteristics for 15 patients is listed in Table 1. The patients consisted of 12 men and 3 women, with a mean age 47.7 years (range 14–79 years). The longest postoperative follow-up was 9.5 years, the shortest was 0.67 year, and the mean was 3.0 years. Extended orbital exenteration surgery was the first procedure for tumor resection in 11 patients. In the 4 remaining patients, the surgery indexed for this report was the second surgery for 1 patient and the third, the fourth, and the fifth surgery for 1 patient each. The pathology of the 2 lesions that required fourth and fifth reoperations was rhabdomyosarcoma. Ethmoid sinus was the most common primary tumor location. Tumor originated from the ethmoid sinus in 6 (40%) of 15 patients, maxillary sinus in 5 (33%), nasal cavity in 2 (13%), and orbital cavity and maxillary bone in 1 patient each (7%). Histological analysis of tumor specimens revealed squamous cell carcinoma in 9 patients (60%), rhabdomyosarcoma in 2 (13%), and small cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, and Ewing sarcoma pathologies in 1 patient each (7%). Thirteen patients received neoadjuvant chemotherapy; 2 patients did not, and their pathologies consisted of mucoepidermoid carcinoma and adenoid cystic carcinoma. Patients with squamous cell carcinoma and rhabdomyosarcoma (11 patients total) underwent preoperative radiation therapy, and the remaining patients with different pathologies (4) did not receive preoperative radiation.

Only 2 patients (Cases 2 and 8) experienced early recurrence at 5 and 1 months; these patients died at 10 and 5 months after surgery, respectively. Case 2 was a 79-year-old man with small cell carcinoma, and Case 8 was a 60-year-old man with squamous cell carcinoma. The patient in Case 2 had tumor invasion of the dura mater and brain that was observed intraoperatively but was not seen on preoperative CT or MRI studies. In this series of advanced-stage patients, estimated 5-year RFS was 86.7% and estimated 5-year OS was 86.2% (Fig. 11). In addition, there was no perioperative mortality. All of the patients without recurrence at 8 months remained disease free. Univariate analysis of factors, including age (p = 0.11), histology (p = 0.20), extent of resection (with or without the foramen ovale; p = 0.20), and intracranial invasion (p = 0.37) as the outcome predictors, revealed no significance.

Five patients suffered infectious complication around the graft transplanted to the cavity after resection. This infection originated from the ocular prosthesis bed in all 5 of these patients. This infection resolved with irrigation of
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the abscess in 3 patients, and 1 patient had a small incision made at the infection site prior to irrigation. One patient needed to undergo removal of the infected skull bone flap and irrigation of the abscess 1 month after surgery. No patient suffered neurological or any other complication attributable to the surgical procedure.

Discussion

Cancers of the nasal and paranasal sinuses are rare and reported to be only 3%–5% of all head-and-neck cancers. The asymptomatic growth of these tumors into the air-filled nasal and ethmoidal sinus spaces makes their early diagnosis difficult. Hence, many patients are admitted to the hospital with an advanced stage of the disease. Craniofacial surgery for this type of sinonasal malignancy is difficult to perform adequately and requires a team consisting of neurosurgeons, head and neck surgeons, and plastic surgeons.

Five-year OS for patients with sinonasal malignancy who have undergone anterior craniofacial resection has been reported to range between 40% and 58%. Five-year RFS has been reported as 24.4%–52.8%. The perioperative death rate has been reported as 3.6%–4.7%. These data indicate that anterior craniofacial surgery is still a challenging operation.

Suarez et al. reported that survival for patients with sinonasal tumors treated using craniofacial resection was 40% at 5 years and that the clinical outcome for these patients with Stage T2 and T4 disease was almost the same. These authors also showed that 5-year survival was significantly affected by tumor histological findings, with 5-year survival rates of 71% in patients with esthesioneuroblastomas, 65% in those with squamous cell carcinoma, 31% in those with adenocarcinoma, 17% in those with undifferentiated carcinoma, and 0% in those with melanoma. Patel et al. showed that the histology of the primary tumor, the extent of intracranial extension, and the status of the surgical margins were significant independent predictors of RFS.

The poor prognosis associated with malignant tumors of the paranasal sinuses is mainly a consequence of local recurrences in the skull base. Some reports have shown that orbital involvement significantly affects survival, particularly if the orbital apex is involved. These studies have suggested that orbital apex involvement positively correlates with higher recurrence rates and shorter survival. Therefore, we believe that en bloc resection with margins, especially at the skull base around the orbital apex, is necessary to avoid local recurrences and contributed to our high estimated OS and RFS rates. Suarez also reported that involvement of the lateral wall of the sphenoid

FIG. 8. Case 12. Axial T1-weighted Gd-enhanced MR images (A1 and A2) showing tumor invasion of the sphenoid sinus. The resection line was made to include the foramen ovale (A3). Case 11. Axial T1-weighted Gd-enhanced MR images (B1 and B2) showing no tumor invasion of the sphenoid sinus. The resection line was made just anterior to the foramen ovale (B3). Figure is available in color online only.

FIG. 9. A: Palpebral conjunctiva incision was made. B: Facial skin and subcutaneous tissue were peeled off, and the lateral resection line of the maxillary bone was cut using a bone saw. C: Medial side of the resection line was cut using a bone saw and flat chisel. D: Tumor with orbital content was resected en bloc without tumor exposure. Figure is available in color online only.

FIG. 10. A: Defect after tumor resection below the frontal fossa. B: Anterolateral thigh free flap (asterisk) was transplanted to the defect after resection. C: The ocular prosthesis bed was made (arrow). Figure is available in color online only.
## Table 1. Summary of clinical characteristics in 15 patients with sinonasal malignancy

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Primary Tumor Site</th>
<th>Histology</th>
<th>Prior Treatment</th>
<th>Adjuvant Therapy</th>
<th>Complication</th>
<th>Outcome</th>
<th>Follow-Up (mos)</th>
<th>Recurrence/Bed/Complication</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Mucoepidermoid carcinoma</td>
<td>CT+RT (50 Gy)</td>
<td>—</td>
<td>Inf</td>
<td>−/−</td>
<td>−/alive</td>
<td>Inf</td>
</tr>
<tr>
<td>2</td>
<td>79</td>
<td>F</td>
<td>Ethmoid sinus</td>
<td>Small cell carcinoma</td>
<td>5/−+</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>3</td>
<td>77</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Squamous cell carcinoma</td>
<td>SR+CT+RT (35 Gy)</td>
<td>—</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (50 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Adenoid cystic carcinoma</td>
<td>SR+RT (65 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>−/−</td>
<td>−/alive</td>
<td>−/−</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>M</td>
<td>Orbital cavity</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (40 Gy)</td>
<td>—</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>Nasal cavity</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (50 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Adenoid cystic carcinoma</td>
<td>SR+RT (65 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>M</td>
<td>Nasal cavity</td>
<td>Rhabdomyosarcoma</td>
<td>CT+RT (50 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>M</td>
<td>Maxillary sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (50 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>11</td>
<td>31</td>
<td>F</td>
<td>Maxillary sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (50 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>12</td>
<td>55</td>
<td>M</td>
<td>Maxillary sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (50 Gy)</td>
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<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
<tr>
<td>13</td>
<td>62</td>
<td>M</td>
<td>Maxillary sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (40 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>−/−</td>
<td>−/alive</td>
<td>−/−</td>
</tr>
<tr>
<td>14</td>
<td>54</td>
<td>M</td>
<td>Ethmoid sinus</td>
<td>Squamous cell carcinoma</td>
<td>CT+RT (70 Gy)</td>
<td>−</td>
<td>Inf</td>
<td>+/−</td>
<td>−/alive</td>
<td>+/−</td>
</tr>
</tbody>
</table>

CT = chemotherapy; RT = radiation therapy; SR = surgery. — = no; + = yes; − = not applicable.

In our series, the estimated 5-year OS for patients with sinonasal malignancy who had undergone extended orbital exenteration was 86.2%, and estimated 5-year RFS was 86.7%. These survival rates are better than those in previous reports. Furthermore, our 5-year OS rate was better than the 70.3% 5-year OS in the 50 sinonasal malignancy patients (mean age 49.1 years) with no invasion of the orbital apex who also underwent craniofacial resection in the same time period at our institution. The surgical strategy for patients without orbital apex invasion was as follows: When the tumor did not invade orbital bone, the periorbita and orbital contents were preserved, and the medial side of orbital bone was resected with the tumor. When the tumor invaded orbital bone, the orbital contents, excluding the orbital apex, were resected with the tumor. Histological analysis of specimens from these 50 patients without orbital apex resection revealed olfactory neuroblastoma in 15 patients (30%), squamous cell carcinoma in 13 (26%), adenoid cystic carcinoma in 6 (12%), rhabdomyosarcoma in 4 (8%), adenocarcinoma in 2 (4%), osteosarcoma in 2 (4%), and other pathologies in 8 (16%). Patients with olfactory neuroblastoma have better outcomes than patients with other sinonasal malignancies. When we excluded the 15 patients with olfactory neuroblastoma from these 50 patients, 5-year OS decreased to 58.7%. Nonetheless, this rate is still better than previously reported rates but worse than the rate for our 15 cases with orbital apex tumor extension who had undergone extended orbital exenteration. Although these results were initially surprising, we believe that our orbital apex resection allowed for more complete resection of tumor from the sphenoid sinus. Tumor resection from the sphenoid sinus is one of the most technically difficult parts of the excision in most cases but is also one of the most crucial steps in preventing recurrence. Total tumor resection with ample safety margins became feasible using our surgical technique of extended orbital apex resection, providing wide exposure of the posterior part of the sphenoid sinus. There was no perioperative mortality in our patient series, and the postoperative infectious complication rate was 33.3%. All of these infections involved the lacrimal gland around the ocular prosthesis bed. However, these infections were easily controlled in most cases. Irrigation alone cleared the infection in 4 patients, and only 1 patient required an additional operation such as removal of the infected bone flap. There were no neurological and systemic complications. This perioperative complication rate is within an acceptable limit for this type of surgery. There were no factors that independently predicted outcome. However, the number of patients was too small (only 2 of 15 patients died) to draw any unequivocal conclusions.

A limitation of this study is the short mean follow-up period of 3.0 years while calculating the estimated 5-year OS and RFS rates. However, 5 patients are alive and have been recurrence free for more than 50 months after tumor resection. The OS and RFS were not decreased after a few years postresection, as shown in Fig. 11. The use of histori-
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Statistical controls to compare outcome is also a limitation of this study. We intend to accumulate more cases and monitor them for a longer period.

Conclusions

We are the first to describe the surgical strategy and procedures for extended orbital exenteration with skull base bone resection around the orbital apex having a sufficient resection margin for sinonasal malignancy with orbital apex extension. The estimated 5-year OS and RFS were high, and the perioperative complication rate was acceptably low because it was possible to make sufficient resection margins using this procedure. We plan further characterization of the effectiveness of this technique with longer patient follow-ups and the accumulation of more case experience.

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References


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Conception and design: Sugawara, Aoyagi, Tamaki, Ohno, Maehara, Kishimoto. Acquisition of data: Sugawara, Ogishima, Kawano, Tamaki, Yano, Tsunoda. Analysis and interpretation of data: Sugawara. Drafting the article: Sugawara. Critically revising the article: Sugawara, Aoyagi, Ohno, Maehara, Kishimoto. Reviewed submitted version of manuscript: Aoyagi, Ohno, Kishimoto. Statistical analysis: Sugawara. Administrative/technical/material support: Aoyagi, Tsunoda, Kishimoto. Study supervision: Sugawara, Aoyagi, Ohno, Maehara, Kishimoto.

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