

Combined craniofacial resection of anterior skull base tumors: long-term results and experience of single institution

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Received: 1 March 2010 / Revised: 6 May 2010 / Accepted: 5 July 2010 / Published online: 29 September 2010
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Abstract In this article, the authors are presenting their experience and the results with combined craniofacial resection of anterior skull base tumors based on a review of 27 constitutive cases. Our data are evaluated in comparison to other major centers in other parts of the world, and possible factors that might influence surgical outcome and survival are discussed. Twenty-seven patients diagnosed with anterior skull base tumors between 1999 and 2009 were treated by combined craniofacial resection. Of these patients, there were 19 males (70, 3%) and eight females (29, 7%). The age ranged between 11 and 75 years (mean=45.9±17.6 years). The follow-up period ranged between 14 and 123 months (average=74 months). The most common presenting symptoms were nasal obstruction and vision disturbance (11 patients for each –40.7%). Total resection was achieved in 24 patients (89%), while subtotal resection was done in three patients (11%). The most common complication was CSF fistule with rhinorrhea, which occurred in five patients (18.5%). Eight patients had recurrences at the time of this long-term follow-up. There were two mortalities in the early postoperative period and seven deaths in the long-term follow-up (overall mortality, 33.3%). The overall 5-year overall survival for all patients in our series was 70.4%. The 5-year overall survival was 62% for patients with malignant tumors and 100% for

patients with benign tumors. Combined craniofacial resection of tumors of the anterior skull base is an effective approach for the management of these pathologies. The effectiveness is clearly demonstrated by the clinical results and outcomes of these patients' groups. The favorable prognosis is enhanced by significantly by total resection with negative tumor margins.

Keywords Anterior skull base tumor · Combined craniofacial approach · Skull base · Surgical treatment

Introduction

The anterior skull base is a common location of many intradural and extradural cranial and/or facial pathologies. The transbasal approach was first applied by Dandy [17] to resect a large frontal meningioma involved with the ethmoid sinus. Since the introduction of this approach, numerous modifications have been made, aiming to less brain retraction, wide exposure of the tumors and better functional and cosmetic outcomes [29]. The development of skull base surgical approaches has improved the treatment of malignant tumors and other lesions of the anterior skull base and allowed successful resection of many tumors once considered inoperable. As a result, a remarkable increase in the survival rates of the patients with malignant tumors of the anterior skull base is achieved after proper modern surgical treatment. Also, appropriate reconstruction and isolation of the anterior cranial fossa from the contaminated areas is a critical surgical step for the prevention of ascending infection, thus, decreasing the rates of the postoperative morbidity and mortality [1, 28, 35, 56, 57, 60].

In this article, the authors are presenting their experience and results with combined craniofacial resection (CFR) of

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anterior skull base tumors based on a review of 27 consecutive cases. Although there are many articles discussing the anterior skull base tumors and their treatment options in our country, these studies mentioned subgroups of few numbers of patients who were treated with combined craniofacial resection. On the other hand, this is the first case series study in Turkey specifically evaluating the results of combined craniofacial resection for the treatment of anterior skull base tumors, with the largest number of patients operated with this approach. Our data are evaluated in comparison to other major centers in other parts of the world, and possible factors that might influence surgical outcome and survival are discussed.

Patients and methods

Twenty-seven patients diagnosed with anterior skull base tumor were operated with combined craniofacial resection between 1999 and 2009. Of these patients, there were 19 males (70.3%) and eight females (48.1%). The age ranged between 11 and 75 years (mean=45.9±17.6 years). The follow-up period ranged between 14 and 123 months (average=74 months). Five patients were previously operated by transcranial approach alone, three patients with transfacial approach alone and five patients with combined craniofacial approach. On the other hand, 14 patient were newly diagnosed with anterior skull base tumors. All patients were radiologically evaluated in the pre- and postoperative periods by brain computed tomographic (CT) scans and magnetic resonance imaging (MRI). Also, in some cases in which the tumor was invading major vascular structures, digital subtraction angiography (DSA) was performed. The pre- and postoperative neurological status, the extent of resection and early outcomes and the long-term results were evaluated with regard to the Karnofsky score. None of the newly diagnosed patients underwent radiotherapy before surgery. The patients' data are summarized in Table 1.

Surgical technique

Under general anesthesia, the patient is intubated and an orogastric feeding tube is placed. The patient's head is placed on a horseshoe holder, which permits free manipulation and changing of the head position intraoperatively as the surgical team demands. We do not prefer fixation of the head, as this will restrict the head manipulation, which is mostly required, especially for the facial surgeon. The head is held in neutral position and with minimal extension to help in self-retraction of the frontal lobe by gravity with minimal surgical manipulation. This can be assisted by administration of mannitol in the early stages of the

operation before completing the craniotomy when necessary. Skin incision is made behind the hairline and drawn down to the zygoma, which is a good landmark and useful to be exposed intraoperatively. The skin flap is then dissected in the perigaleal plane until the superior borders of the orbital bar. This dissection is not preferred to extend toward the supraorbital foramen, as the deep branches of the supraorbital and supratrochlear arteries originate nearly 10 to 15 mm above the supraorbital rim [73]. In this way, these arteries are protected, and galeal vascularization is preserved. The galea frontalis is then dissected from the skull in subperiosteal fashion and retracted separately. Galeal dissection is continued toward the supraorbital foramen to expose the orbital bar, the glabella, and the supraorbital artery, vein and nerve. The neurovascular structures within the supraorbital foramen are carefully dissected and mobilized as a whole with the galea frontalis. The tips of the temporal muscles are retracted posteriorly enough to expose only the site of pterional key burr hole. The bifrontal craniotomy is aimed to extend as low as possible to expose the anterior skull base with the least possible projections in its anterior limit, which can hinder the exposure of the anterior skull base and requires more frontal lobe retraction with resultant brain tissue injury. Regardless of the pathologic lesion, because of the opening of the frontal sinus in this approach, cranialization of the frontal sinus by removing its posterior wall and mucosa is performed routinely. The nasofrontal ducts are plugged with a piece of muscle taken from the temporal muscle and wrapped with Surgicel®. This step is critical to obliterate the connection between the intracranial and nasopharyngeal cavities [50]. Depending on the localization of the pathology, tumor exposure is done under the operating microscope extra- and/or intradurally. To achieve maximum exposure of the anterior skull base, olfactory nerves are cut. This is done under the operating microscope with controlled coagulation and resection of the olfactory fibers. The anterior skull base approach generally results in complete and permanent anosmia because the olfactory fila are resected. For further exposure, the crista galli is resected, and extradural dissection is continued posteriorly until exposure of the tuberculum sella. Reconstruction is started with the dural repair in watertight fashion. For larger defects, duraplasty with temporal muscle in-between the dural sutures or fascia lata graft is performed. The dura is then sealed with Tisseel® fibrin glue (Baxter Healthcare Corp, Deerfield, IL). According to the size of the bone defect, small defects are closed with inner-table graft from the frontal bone or non-methyl methacrylate Cortoss® (Orthovita) with good results [56]. Larger defects are closed with either the inner-table bone graft from the frontal bone or, as we prefer, by using free flaps [60]. To achieve the best cosmetic results, bone flap must be fixed

Table 1 Summary of the patients' data in our series

Case no.	Age(years)/sex	Symptoms and signs	Tumor location	Previous surgery	KS
1	52/F	Nasal obstruction, vision loss of right eye	Right frontal sinus, ethmoid sinus, tuberculum sella, and sphenoid sinus, destructed sella	C-CFR	90
2	17/M	Proptosis of left eye, vision loss of left eye, headache	Fully filled nasopharyngeal cavity and extending towards to left sphenoid bone, left cavernous sinus, and left optic canal	TC	90
3	53/M	Right forehead lump, nasal obstruction	Right nasal cavity and extending towards to Ethmoid sinus, frontal sinus, and frontal lobe	TC	90
4	41/F	Diplopia, headache, right facial lump	Fully filled nasopharyngeal cavity, right orbita, and maxillary sinus	TC	90
5	18/M	Left facial lump, vision loss of left eye	Fully filled nasopharyngeal cavity and sphenoid sinus, engulfing both cavernous sinuses	TF	90
6	63/F	Epistaxis, left facial hypoesthesia	Filled right nasal cavity and invades anterior skull base	TC	90
7	52/F	Nasal obstruction, facial pain	Anterior cranial fossa and ethmoid and sphenoid sinuses	–	90
8	30/M	Nasal obstruction, epistaxis, diplopia	Filled nasal cavity and invading frontal sinus	TC	90
9	57/M	Nasal obstruction, proptosis, facial pain	Filled nasal cavity and invading right medial orbita, frontal, and ethmoid sinuses	TF	90
10	65/M	Epistaxis, nasal obstruction	Anterior skull base, filling the nasal cavity	–	90
11	68/F	Nasal obstruction, headache, vision loss of right eye	Extends from frontal sinus to anterior skull base and nasal cavity	–	90
12	51/M	Proptosis and vision loss of right eye	Filled nasal cavity and extends to anterior skull base and right orbita	C-CFR	90
13	25/F	Right eye lump	Frontal sinus, right orbita, with dural and intracranial extension	–	90
14	11/F	Vision loss of left eye, anosmia	Frontal sinus, nasal cavity with intracranial extension	–	90
15	44/M	Diplopia, nasal obstruction	Anterior and posterior ethmoid sinuses, sphenoid sinus, and nasal cavity	TC	90
16	26/M	Nasal obstruction, anosmia	Anterior skull base, nasal cavity with frontal lobe invasion	–	90
17	51/M	Anosmia, nasal obstruction, vision loss of right eye, headache	Anterior skull base, nasal cavity, and frontal sinus	C-CFR	80
18	41/F	Right eye lump, vision loss of right eye	Right nasal cavity, sphenoid sinus, ethmoid sinus, frontal sinus, right orbita, and frontal lobe invasion	C-CFR	90
19	40/M	Proptosis and vision loss of left eye, nasal obstruction	Nasal cavity, right orbita, and ethmoid sinus	–	90
20	48/M	Vision loss of left eye, left facial lump	Left maxilla, left orbita, ethmoid sinus, and frontal sinus	–	90
21	44/M	Headache, diplopia	Anterior and middle cranial fossa, compressed temporal lobe, and mesencephalon	–	90
22	55/M	Nasal obstruction, diplopia	Left retroorbital region, anterior skull base, and nasal cavity	–	90
23	69/M	Left forehead lump, headache	Frontal sinus, left orbital roof with compressed frontal lobe	–	90
24	52/M	Diplopia, nasal obstruction, left facial pain	Nasal cavity, ethmoid sinus, frontal sinus, and left orbital lateral wall	–	90
25	69/M	Right facial lump, vision loss of right eye	Right orbita, ethmoid, sphenoid and frontal sinuses, nasal cavity, neck, dura, and soft tissue	–	90
26	75/M	Left facial lump	Left nasal cavity compressed left temporal pole and destructed mandibula	C-CFR	80
27	22/M	Right facial lump	Right orbital medial wall, anterior skull base, and right maxillary sinus	TF	90

TC transcranial approach, TF transfacial approach, C-CFR combined craniofacial resection, KS Karnofsky score

tightly in the craniotomy site; thus, free movement of the flap and resultant malunion, asymmetry, and stair-like shape in the borders of the flap are prevented. This can be achieved by using tight sutures, CranioFix, or miniplates. Maximum efforts must be done to ensure an ideal skull base reconstruction with total separation of the anterior skull base from the nasal and the paranasal cavities. After skin closure, if skin flap pulsation synchronized with respiration is noticed, immediate reoperation must be performed without awakening the patient. If left untreated, this situation can lead to a life-threatening pressure pneumocephalus.

For transfacial approach, we prefer midfacial degloving (MD), transnasal and lateral rhinotomy approaches. Lateral rhinotomy is performed in advanced disease stages, especially when orbital resection is attempted; otherwise, midfacial degloving or transnasal approaches are performed. We prefer the use of modified MD, which in contrast to standard MD, the classic rhinoplasty incisions are not performed [14]. This modification considerably decreases the operation time because the closure of the incisions is important and must be performed with care to avoid complications such as fistula and vestibular stenosis, which is time consuming. Meanwhile, this approach also constitutes adequate exposition, depending on the tumor involvement [14].

Sublabial incision with electrocautery extending between the maxillary first molars is performed. Wide subperiosteal dissection along the anterior wall of the maxilla and piriform aperture to the level of the infraorbital foramen is performed bilaterally. Meanwhile, mucoperiosteal flaps are elevated along the floor of the nose bilaterally. The anterior nasal spine and 1-cm anterior portion of the maxillary crest are separated off the maxilla with a chisel. Heavy turbinate scissors are used to transect the septal cartilage and overlying mucosa along the nasal septal base through the previous nasal mucosal incisions. Bilateral or unilateral anterior maxillary walls are removed, depending on the tumoral invasion. For the best exposition, medial maxillectomy is performed adequately, preserving the inferior orbital wall. Frontal process of the maxilla is removed, and nasal septal cartilage is deviated toward the opposite side of the tumor. Thus, sufficient exposure of the nasal cavities, paranasal sinuses, and nasopharynx is obtained. Posterior wall of the maxillary antrum and ascendant process of the palatine bone can also be removed for the wide exposition of the nasopharynx. However, meticulous dissection is important in this region not to injure the greater palatine artery. Pterygoid muscles, posterior wall of the sphenoid sinus, and clivus can also be identified with this approach. Palatectomy or inferior or total maxillectomy can be performed. Once the tumor is removed, the anterior maxillary crest is replaced to its normal anatomical position. In addition, the septum can be deviated toward the tumor side and suspended with 2–0 chromic suture to

reduce the size of the cavity. We usually do not perform osteosynthesis of the frontal process of the maxilla at the end of the procedure. Nasal cavities are packed with vaseline gauze; more packing is needed on the nontumoral side and is left for 2 more days on this side to reduce the size of the cavity and diminish nasal crusting.

To prevent subcutaneous and epidural collections, we routinely place two silicone drains under the skin flap, facing the epidural space. These drains are left for 24 h, with caution not to apply negative pressure; otherwise, reconstructive materials may become displaced. Also, to avoid cerebrospinal fluid (CSF) fistule development postoperatively, means to prevent increasing of the intracranial pressure, such as elevating the head, antitussives, and laxatives, are applied.

Results

The postoperative neurologic status, the extent of the surgical resection, course, and complications were evaluated and summarized in Table 2.

Symptoms and signs

The most common presenting symptoms were nasal obstruction and vision disturbances (11 patients for each –40.7%), followed by external palpable mass in six patients (22.2%), proptosis and diplopia in five patients (18.5%), headache in four patients (14.8%), epistaxis in three patients (11.1%), anosmia and facial pain in two patients (7.4%), and facial hyposthesia in one patient (3.7%). The preoperative Karnofsky score was 90 in 25 patients (92.6%) and 80 in two patients (7.4%).

Radiological findings

All patients were radiologically evaluated by brain CT scans and MRI. Also, in some cases in with tumor invading major vascular structures, especially internal carotid artery and cavernous sinus, digital subtraction angiography was performed. Extension to the middle fossa was found in eight patients (29.6%), with cavernous sinus infiltration found in two patients (7.4%). Intracranial extension was found in 13 patients (48.1%) and orbital involvement was found in 12 patients (44.4%).

Surgery

All patients were operated by combined craniofacial approach. Total resection was defined as total removal of the tumor with negative macroscopic and/or microscopic margins with immediate postoperative MRI scan not showing any postoperative enhancement. Total resection was achieved in

Table 2 Summary of the surgical resection, histopathologic results, the early postoperative course, and the complications in our series

Case no.	Tumor resection	Enucleation	Pathology	Complications	KS
1	ST		Squamous cell carcinoma	Hydrocephaly and CSF fistule, treated with VP shunt	90
2	T	+	Juvenile angiofibroma	Right hemiparesis (3/5)	90
3	T		Meningeal originated malignant desmoplastic small round cell tumor	Pneumocephaly, CSF fistule, abscess (reoperated)	Excitus
4	T		Adenoid cystic carcinoma	–	90
5	T	+	Juvenile angiofibroma	CN 3 paralysis	90
6	T		Sinonasal adenocarcinoma	CSF fistule (treated with lumbar drain)	90
7	T		Atypical meningioma	–	90
8	T		Squamous cell carcinoma	–	90
9	T		Squamous cell carcinoma	–	90
10	T		Hemangioendothelioma	–	90
11	T		Fibroblastic osteosarcoma	CSF fistule (treated with lumber drain)	90
12	T	+	Squamous cell carcinoma	–	90
13	T		Chondrosarcoma	–	90
14	T		Olfactory neuroblastoma (esthesioneuroblastoma)	–	90
15	T		Atypical meningioma	–	90
16	T		Rhabdomyosarcoma	–	90
17	T		Anaplastic meningioma	Myocardial infarction	Excitus
18	T	+	Sinonasal adenocarcinoma	–	90
19	T		Squamous cell carcinoma	–	90
20	T		Epidermoid carcinoma	–	90
21	ST		Adenoid cystic carcinoma	–	90
22	T		Sinonasal adenocarcinoma	–	90
23	T		Transitional meningioma	–	90
24	T		Transitional meningioma	–	90
25	ST		Epidermoid carcinoma	–	90
26	T		Inverted papilloma	CSF fistule (treated with lumbar drain)	80
27	T	+	Mesenchymal type chondrosarcoma	–	90

T total resection, *ST* subtotal resection, *VP* ventriculo-peritoneal, *KS* Karnofsky score

24 patients (89%), while subtotal resection was done in three patients (11%). Enucleation was performed in five patients (18.5%). The most important factor influenced the amount of the resection was the posterior extension of the tumors toward the middle fossa, and subsequent involvement of the major neurovascular structures, such as the cavernous sinus, the orbital apex, the superior orbital fissure, the base of the pterygoids and the cavernous and the supraclinoid segments of the internal carotid artery (ICA).

Pathology

Squamous cell carcinoma and meningioma were the most common histologic variants, which were found in five

patients each (18.5%), followed by sinonasal adenocarcinoma in three patients (11.1%), benign juvenile angiofibroma, cystic adenoid carcinoma, epidermoid carcinoma, and chondrosarcoma in two patients each (7.4%). Other lesions were osteosarcoma, rhabdomyosarcoma, inverted papilloma, esthesioneuroblastoma, and a rare tumor of meninx originated desmoplastic malignant small round cell tumor. Most of the lesions were malignant tumors (21 patients, –77.8%), with the most common malignant tumor being squamous cell carcinoma. On the other hand, all cases of meningeal tumors (meningioma and desmoplastic malignant round cell carcinoma), chondrosarcoma and rhabdomyosarcoma showed intraparachymal extension.

Postoperative course

In the early postoperative period, the vast majority of the patients did not show change in their Karnofsky score (25 patients, -92.6%). There are two mortalities in the early postoperative period in our series. One patient developed postoperative CSF fistule, followed by cerebritis and abscess, which caused death although reoperated. The other patient had good performance without surgical complications in the early postoperative period. However, he suffered from myocardial infarction in the postoperative day 7 and resulted in death. Excluding postoperative anosmia related to the surgical technique, additional morbidity was seen in four patients (14.8%), in which one patient had left oculomotor nerve paralysis, one patient had right hemiparesis, one patient developed hydrocephalus and CSF fistule which required treatment with ventriculo-peritoneal (VP) shunt, and patient was reoperated for CSF fistule. Loss of the eye was not considered an additional morbidity as enucleation was performed in patients with tumors invading the orbital contents and causing total vision loss. Postoperative CSF fistule developed in five patients (18.5%). In one patient, it was related to hydrocephalus and treated with VP shunt. One patient was reoperated, and three patients were treated successfully by lumbar CSF divergence. All newly diagnosed patients without previous radiation therapy and with malignant pathology had received radiation therapy.

Remission and survival

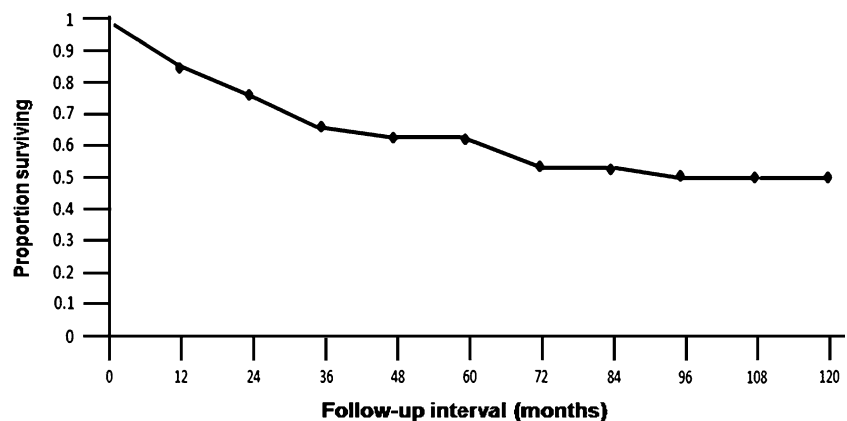
The follow-up period ranged between 14 and 123 months (mean=74 months). At the time of this review, 18 patients (66.7%) were alive without any residual lesion and nine patients (33.3%) died. The death group included four patients (14.8%) with recurrences of the malignant tumor after total resection, three patients (11.1%) with progression of the residual malignant tumors after subtotal resection

(microscopic and/or macroscopic positive tumor margins) and the two patients who died in the early postoperative period. The median time of recurrence was 17 months (range between 6 and 46 months). The overall 5-year overall survival for all patients in our series was 70.4%. The 5-year overall survival was 62% for patients with malignant tumors and 100% for patients with benign pathology (Fig. 1).

Illustrative case

A 48 year-old man, presented with 1-year history of nasal obstruction, vision loss, and proptosis of the left eye. The patient had no significant medical history. Physical examination revealed restriction of the left eye's movements, with decreased visual acuity. Brain and paranasal CT scan and MRI showed a mass lesion invading the left ethmoid sinus, the sphenoid sinus, the left cavernous sinus, the left maxillary sinus, and the left retroorbital area, with heterogeneous dens contrast enhancement and multiple cystic areas (Fig. 2a, b, c). We preferred to approach to the tumor by combined craniofacial approach due to involvement of the cribriform plate, left orbital apex, left superior orbital fissure, left temporal fossa, and left cavernous sinus with the suspicion of dural invasion on preoperative imaging. The endocranial surface of the anterior and middle skull base was exposed by bifrontal craniotomy. The tumor was found soft, well vascularized and lobulated with cystic components and fair surgical cleavage plans. The tumor was dissected and resected in the extradural space. The tumor portion located in the roof of the left ethmoid sinus, the superior and medial orbital wall, the tuberculum sella, the antero-superior part of the sphenoid sinus and around the left cavernous sinus was resected. The exocranial part of the anterior and middle skull base was exposed by modified facial degloving described above, without performing classical rhinoplasty incisions, and the tumor parts located in the left maxillary sinus, inferior and medial left orbital wall and ethmoid sinus were resected. By this combined approach, total resection of the

Fig. 1 Survival outcomes after combined craniofacial surgery for patients with malignant skull base tumors in our series



tumor was achieved and anterior skull base reconstruction was performed with vascularized galeal flap (Fig. 2d, e).

In the postoperative period, no additional neurologic complications were observed, and the patient was discharged in the postoperative day 10. Histopathologic examination revealed epidermoid Ca. The patient was then referred to the radiation oncology clinic for further evaluation and treatment. Follow-up examination after 2 years showed improvement in the movements, and the visual acuity of the left eye, while radiologic follow-up showed no residual or recurrent tumor (Fig. 3).

Discussion

Anterior skull base tumors are a heterogeneous group of pathologies, with more high risk to surgery-related complications [27, 38, 69]. Moreover, the incidence of the same

complications associated with any skull base procedure in surgery for malignant skull base lesions is generally higher [27, 38, 48, 52, 71]. It is a result of the increased invasiveness of malignant lesions, poorer condition of the patient, and the need for multiple surgeries and adjuvant therapies such as radiotherapy [38]. Thus, appropriate strategies aiming to minimize the occurrence of these complications must be considered when planning surgery.

Before the application of CFR, malignant lesions involving the anterior skull base were usually treated by combined extended maxillectomy and external irradiation, and the 5-year survivals were 23–38% [25, 26, 40, 41, 43, 44, 47, 70]. Dandy [17] was first to apply the transbasal approach to resect a large frontal meningioma involved with the ethmoid sinus. Since the introduction of this approach, which consisted of a low bifrontal craniotomy with extradural exposure, numerous modifications have been made, aiming at less brain retraction, wide exposure of

Fig. 2 **a** Axial T2-weighted, **b** coronal post-contrast, and **c** sagittal post-contrast brain MRI of the patient demonstrating a mass lesion invading the left ethmoid sinus, the sphenoid sinus, the left cavernous sinus, the left maxillary sinus, and the left retroorbital area, with heterogeneous dens contrast enhancement with multiple cystic areas. **d** Intraoperative picture showing the anterior skull base after transcranial resection and reconstruction with galeal flap. **e** A picture showing the tumor after resection

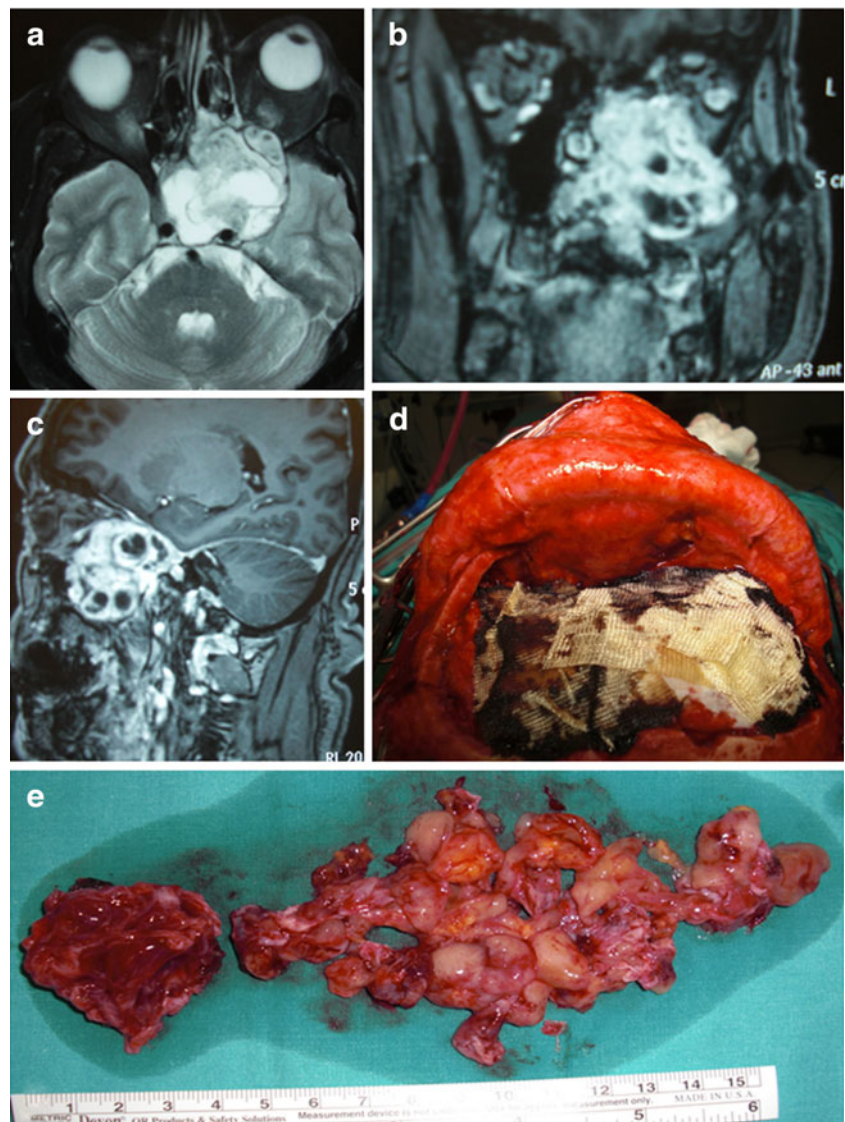
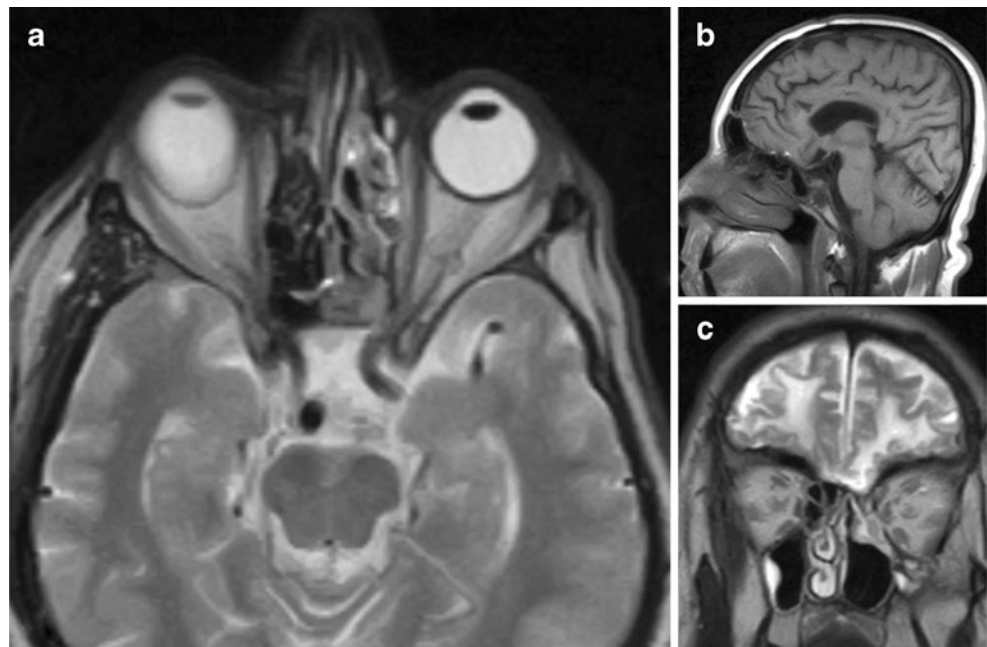


Fig. 3 Follow-up brain MRI after 2 years of surgery, demonstrating no recurrence or residual tumor. **a** Axial T2, **b** sagittal T1, and **c** coronal T2-weighted images



the pathologic lesions, and better functional and cosmetic outcomes. Janecka [29] described that lesions located anterior to the neuroaxis should be treated surgically by means of an anterior approach, which requires the transfacial route due to the anteroinferior anatomic relationship of the facial structures to the cranial base. Kryzansk et al. [38] performed craniofacial resections using a bifrontal flap, a separate orbitonasal bar, and routine cranialization of the frontal sinus with reconstruction of the anterior skull. With their proposed surgical technique, they documented decreasing of the complications rate. Ozlen et al. [50] described the use of low-profile one-piece bifrontal craniotomy for anterior skull base approach, in which the orbital bandeau and the frontal sinus are elevated along with the frontal bone in en bloc fashion. They emphasized that with this technique wide exposure of the anterior skull base can be achieved while the need of facial osteotomies can be lessened, which is potentially important when trying to minimize potential osteomyelitis. Hence, the cosmetically important orbital bar is at less risk of loss due to infection [21].

Smith et al. [64] were the first to use this approach in anterior craniofacial resection of a tumor of the frontal sinus; however, Ketcham and Van Buren [34] and Van Buren et al. [68] were the first to address cure rates and 5-year survival rates in patients with paranasal sinus cancers. They found that combining an anterior skull base approach with a transfacial approach in a craniofacial surgery offered safe and effective removal of sinonasal malignancies [34, 68]. They also documented more favorable survival rates for the first time in these patients when they were treated with this approach. Moreover, adding orbital and/or

zygomatic osteotomies can provide a lower routes to access the suprasellar and cavernous sinus lesions [6, 9, 18, 47, 49, 58, 59, 65, 67].

Our series includes 27 patients with anterior skull base tumors (21 with a malignant tumor). Combined craniofacial resection was indicated in these patients due to ethmoidal sinus and/or cribriform plate involvement by tumor or due to suspicion of dural invasion on preoperative imaging. Transcranial approach alone can be performed for purely ethmoidal tumors. On the other hand, transfacial approach alone can be performed for tumors of the paranasal sinuses extending to the nasal cavity, maxillary sinus, and/or the pterygopalatine and infratemporal fossae, without dural invasion. Extension to the middle fossa was found in 29.6%, intracranial extension in 48.1%, and orbital involvement in 44.4% of the patients. All patients of the series were operated with combined CFR. This approach offered wide exposure of the lesions, which allowed total resection in most cases. The major limiting factor for resection in our series was the extension of the tumor to the middle cranial fossa with invading the vital neurovascular structures, such as the cavernous sinus, the orbital apex, the superior orbital fissure, the base of the pterygoids and the cavernous and the supraclinoid segments of the ICA. On the basis of our experience and clinical observation in this series, we emphasize that the operative resection margin is an important independent prognostic factor that adversely affects survival in patients with malignant tumor in the skull base, as demonstrated in other studies [8, 24, 36, 51, 72]. In our series, there were nine deaths. Of these cases, three patients (11.1%) had recurrences after subtotal resection of malignant tumors. On the other hand, exclud-

ing the early two mortalities, of the 16 patients with total resection of malignant tumor only four patients (25%) had recurrence and died in the long-term follow-up. The remaining 12 patients with malignant tumors and six patients with benign tumors are alive with good performance at the time of this review. Suarez et al. [66] proposed that involvement of the surgical margin was not a negative prognostic factor. This finding was based on different histological patterns in different patient groups, as more than half of the patients in the study of Suarez et al. had adenocarcinoma.

With the use of CFR, the reported 5-year survival from major centers in the world for malignant anterior skull base tumors ranged from 40% to 77.6% [13, 19, 43, 45, 46, 60, 61, 62, 66, 72]. In a recent international collaborative study for CFR for malignant skull base tumor, the reported overall 5-year survival was 54% [51]. In our series, the overall 5-year survival for malignant tumors was 62%, which was considered favorable according to previous reports.

In spite of the favorable prognosis of the benign lesions involving the anterior skull base, their anatomic relations to the vital neurovascular structures would potentially cause significant surgical morbidities. These include blindness and loss of consciousness and may even progress to death if the lesion is left untreated [72]. Although the number of patients with benign skull base tumor in our series was small, CRF showed to be an effective approach with excellent prognostic results, as the overall 5-year survival rate of these patients was 100%.

According to our experience, some important surgical pitfalls are essential for reconstruction in order to reduce the risk of complications. The anterior skull base approach generally results in complete and permanent anosmia because the olfactory fila are resected. For this reason, Spetzler et al. [65] described the circumferential osteotomy to the cribriform plate for the preservation of olfaction. Performing this procedure in selected patients, they were able to preserve olfaction in more than 90% of the time [65].

Preservation of tissue viability during surgery is important to achieve successful reconstruction of the defect. The dissection in the perigaleal plane is not preferred to extend toward the supraorbital foramen, as the deep branches of the supraorbital and supratrochlear arteries originate nearly 10 to 15 mm above the supraorbital rim [73]. In this way, these arteries are protected, and galeal vascularization is preserved. The utilization of vascularized temporalis muscle and pericranial flap transfer to provide vascularized coverage of the surgical site. This also increases the chances for a seal of the CSF-containing space and the elimination of surgical dead space [50, 55]. Also, efforts must be done to avoid aggressive cauterization of the sublabial mucosa, as it forms an important barrier [14]. In

cases with large defects requiring grafting, we prefer autologous grafts because of their advantages upon synthetic dural patches, such as low risk of infection, more profound healing, and incorporation [1]. According to the defect size, small defects are closed with inner-table graft from the frontal bone or non-methyl methacrylate Cortoss® (Orthovita) with good results [55–57]. Rodrigues et al. [53] reported that large defects, measuring at least 3.0 to 4.0 cm, must be reconstructed rigidly to prevent frontal lobe herniation into the paranasal sinuses, while also preventing pulsatile exophthalmos. For this purpose, they used split calvarial bone graft. The fate of bone grafts inserted without any overlapping vascularized tissues has not been well understood. Hao [25] mentioned that the incidence of necrosis of the bone graft was higher in the free-bone-graft group (26.2%) than in the vascularized-bone-graft group (7.1%); however, the difference was not statistically significant. In patients with a free bone graft, postoperative radiotherapy significantly increased the incidence of necrosis of the bone graft, whereas soft-tissue reconstruction significantly decreased the incidence of bone graft necrosis. According to our experience, we found that firm fixation of the bone graft to the anterior fossa makes the graft more resistant to resorption. The free flaps technique has revolutionized skull base reconstruction by providing replacement of tissue that can protect the dural closure and, in result, may protect patients against the appearance of serious surgical complications such as a CSF fistule, meningitis, intracranial abscess, or a wound infection [7, 11, 12, 60].

CSF leakage is the most common complication after CFR. Major series of craniofacial resections where complications were reported in-depth have CSF leak rates from 3% to 20% [22, 33, 34, 39, 42, 63, 69]. In addition, postoperative meningitis occurs in 1% to 10% of cases [15, 19, 20, 23, 34, 54, 70]. Infections of the bone flap, epidural, or subdural space all may occur after craniofacial resection and cause significant morbidity and mortality. A review of craniofacial resection for malignancy found that most operative mortalities among several large series occurred from meningitis or intracranial abscess [10], which also had occurred in one of our cases. It is believed that most complications in anterior skull base surgery are related to bacterial contamination at the time of surgery or inadequate dural and skull base reconstruction [16, 37]. Systemic complications such as cardiac events, as seen in one of our cases, or pulmonary embolism were the next most common cause of operative mortality.

Excluding the postoperative anosmia which is related to the surgical technique, the overall complication rate in our series was 26%, and the common complication was CSF leakage, which occurred in five patients (18.5%). In one patient, it was related to hydrocephalus and treated with VP

shunt. One patient was reoperated, and three patients were treated successfully by lumbar CSF divergence. Operative treatment of CSF fistule is performed when pneumocephaly is present either before or during applying lumbar CSF divergence or failure of CSF drainage after 72 h of application. In the early postoperative period, the vast majority of the patients did not show change in their Karnofsky score (25 patients, –92.6%). Permanent neurologic deficits were seen in three patients (14.8%), in which one patient had left oculomotor nerve paralysis, one patient had right hemiparesis, and one patient developed hydrocephalus and CSF fistule which required treatment with VP shunt. Loss of the eye was not considered an additional morbidity as enucleation was performed in patients with tumors invading the orbital contents and causing total vision loss.

Recently, many studies reported the use of the endoscopic endonasal approach with its significantly wider field of vision that allowed further expansion of the technique to access the full extent of the midline cranial base from the cribriform plate to the anterior foramen magnum [2–5, 30–32, 40]. The main advantages include the more direct midline exposure from below, no need for any brain retraction or neurovascular manipulation, early devascularization of the lesion, and the ability to readily access deep-seated lesions [2–5]. However, endoscopic resection for malignant anterior skull base tumors is controversial since it defies the oncological definitions of resections with negative margins. Also, the rate of CSF leak and resultant morbidity tends to be higher in endoscopic resections since it has a steep learning curve and standardization is yet to occur for it to be included in the standard of care for anterior skull base malignant tumors [5, 30, 32]. The long-term results are still under evaluation.

Conclusion

Combined craniofacial resection of the anterior skull base tumors is an effective approach for the management of these pathologies. The effectiveness is clearly demonstrated by the clinical results and outcomes of these patients' groups. The favorable prognosis is enhanced by significantly by total resection with negative tumor margins. Extending of the tumors to the middle cranial fossa with invading the vital neurovascular structures has potential increase in the surgical morbidity and mortality and may limit the tumor resection, thus has a negative effect on the prognosis. Also, the authors' long experience in the surgical treatment of these tumors led them to define the low-profile one-piece bifrontal craniotomy and the modified midfacial degloving, which were performed in the recent patients of this group and showed favorable surgical results.

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Comments

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Abuzayed et al. report their experience with tumors of combined craniofacial resection for the treatment of anterior skull base tumors from Turkey. It is the first to be published in the English literature from Turkey.

Combined craniofacial resection is performed with an aim to achieve an oncological cure for tumors straddling the anterior, lateral, or posterior fossa skull base. Excision of the tumor along with negative oncological margins is the paramount to justify the radical nature of surgery. A sound anatomical knowledge of the anterior, lateral, and the posterior skull base is necessary. The surgery is best performed in a tertiary oncology center by a multidisciplinary team comprising of a neurosurgeon and otolaryngologist having exposure to and training in skull base surgery. In anterior skull base tumors, combined craniofacial resection is indicated in patients with suspected

cribriform plate involvement or dural invasion. In fact, a good negative margin could be achieved in tumors which involve the cribriform plate but do not erode it.

The authors correctly emphasize that the operative resection margin is an important independent prognostic factor affecting survival in patients with malignant tumor in the skull base. The overall 5-year survival was 54% for malignant tumors and 100% for benign tumors which is comparable with the international literature. However, the pathological and aggressive behavior of the tumor also has an impact on the overall prognosis.

Proper selection of the patient for anterior craniofacial resection is important for an optimal outcome. A midfacial degloving approach and a low bifrontal craniotomy can also provide wide exposure of the anterior skull base and help lessen facial osteotomies. Endoscopic resection for malignant anterior skull base tumors is controversial since it defies the oncological definitions of resections with negative margins. Also the rate of CSF leak and resultant morbidity tends to be higher in endoscopic resections since it has a steep learning curve and standardization is yet to occur for it to be included in the standard of care for anterior skull base malignant tumors.

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The authors retrospectively analyze a 10-year institutional experience with 27 consecutive patients harboring a benign or malignant tumor of the anterior cranial base. Fourteen patients were newly diagnosed with anterior skull base tumors, and 13 were operated on previously: five through the transcranial approach alone, three with the transfacial approach alone, and five with the combined craniofacial approach. The tumor extended toward the orbit in 12 patients, the middle cranial fossa in eight, and the cavernous sinus in two.

A combined craniofacial resection—a bilateral frontobasal approach combined with a lateral rhinotomy or modified midfacial degloving or the transnasal approach—was the approach used in this series. The authors do not report how many patients underwent each type of transfacial approach.

Total resection was achieved in 24 patients, with subtotal in three patients. The authors state that the most important negative factor influencing the degree of resection was an extension toward the middle fossa, cavernous sinus, orbital apex, or superior orbital fissure and the involvement of the internal carotid artery. Nevertheless, in one of the three patients having subtotal resection, none of these structures was involved.

The series presented is heterogeneous. Histopathological examination revealed two juvenile angiofibromas, two transitional meningiomas, two atypical meningiomas, one anaplastic meningioma, five squamous cell carcinomas, two epidermoid carcinomas, two adenocystic carcinomas, three sinonasal adenocarcinomas, one hemangioendothelioma, one fibroblastic osteosarcoma, one chondrosarcoma, one mesenchymal type chondrosarcoma, one rhabdomyosarcoma, one esthesioneuroblastoma, one malignant desmoplastic small round cell tumor originating in the meninges, and one inverted papilloma.

Large dural defects were repaired with a duraplasty of the temporal muscle or a fascia lata graft. The report does not mention how many patients needed this procedure.

Only two patients had preoperative anosmia, but all patients had postoperative anosmia due to the bilateral frontobasal approach. Of the five patients having a postoperative CSF fistula, three required lumbar drainage while two needed a second surgical look. One patient died after the development of a CSF leak, which caused an abscess and cerebritis.

The 5-year overall survival for patients with benign tumors was 100%. Those with malignant tumors had a 5-year survival of 62%. The median time to recurrence was 17 months. While four patients died of recurrences, three died after progression of the residual tumor.

The authors present a relatively large surgical series of anterior cranial base tumors and we congratulate them for dealing with this complex topic with great success in terms of the percentage of patients

having total removal. The best treatment and surgical approach to anterior cranial base tumors are still a matter of debate. We would like to discuss the different philosophies and surgical strategies we use in these cases.

First of all, analyzing benign and malignant tumors in the same series can be confusing. In fact, benign and malignant tumors of the anterior cranial base differ in many fundamental aspects, such as the patient's age and clinical status at presentation, the tumor's natural history, and the overall philosophy of the use of surgical and adjuvant treatment.

In our opinion, meningiomas of the anterior cranial base rarely require a combined craniofacial approach to be resected totally. For meningiomas arising from the olfactory groove, tuberculum sellae, or the medial or lateral sphenoidal ridge, we prefer a pterional-transsylvian exploration and avoid a bilateral subfrontal approach. A subfrontal approach requires retraction of both frontal lobes and causes bilateral frontal lobe damage and postoperative anosmia because both olfactory nerves are usually damaged during this approach. On the other hand, the pterional approach provides a better orientation for the relationships between the meningioma and adjacent vital structures around the sella, without retraction of the frontal lobes. The pterional approach with dissection of the contralateral olfactory nerve from the capsule of the tumor allows the preservation of olfactory function, even in patients with olfactory groove meningiomas. If a surgeon prefers greater working space, the cranio-orbital zygomatic approach can be used.

Juvenile nasopharyngeal angiofibromas (JNAs) are rare, benign, vascular tumors. The blood supply to these lesions is most commonly from the maxillary artery, but may also come from the external carotid artery, the internal carotid artery, the common carotid artery, or the ascending pharyngeal artery. The case of JNA described by the authors involved the nasopharyngeal cavity with extension towards the left sphenoid bone, cavernous sinus, and optic canal. This patient was previously operated on with a combined craniofacial resection and the authors have chosen the same approach for the second surgery. In this case, however, we would prefer to selectively embolize feeding vessels preoperatively. The authors achieved only a subtotal resection with a combined craniofacial resection. Even though JNAs are benign lesions, the recurrence rate is high with residual pathology.

Malignant tumors, such as squamous cell carcinomas or sinonasal adenocarcinomas, require totally different management

than benign tumors. In malignant cases, oncological resection is accomplished when *en bloc* resection includes at least 5 mm of normal tissue beyond the tumor, as determined through histological examination. Moreover, adjuvant therapies such as radiotherapy or, less commonly, chemotherapy must be administered. Treating patients with malignant tumors more complex than benign tumors. Unfortunately, some patients with malignant lesions of the anterior cranial base have already undergone radiotherapy or only partial surgical removal before the tumor reaches the skull base. Previous radiotherapy is correlated with an overall decrease in the 5-year survival and adjuvant radiotherapy carries a high risk of morbidity and local recurrence. Moreover, a delay of surgical treatment may allow the tumor to progress or invade the dura.

In patients with malignant tumors of the anterior cranial base, the combined craniofacial approach can be useful to effect an oncological resection. The modified midfacial degloving used by the authors provides a more cosmetically acceptable surgical route with respect to the lateral rhinotomy. However, in patients with extensive infiltration of the orbital structures, an *orbital exenteration* with prosthesis reconstruction may be necessary. We likely would have used a left cranio-orbital zygomatic approach to resect the epidermoid carcinoma presented by the authors as the illustrative case. The use of this approach could have gained the same total oncological resection but avoided retraction of the frontal lobes, sparing the contralateral olfactory nerve and preserving the mucosa of the nasal cavities. Unfortunately, this is the only case for which the authors present images. It would have been useful to have other cases to discuss.

The use of intraoperative lumbar drainage in selected cases, which is not mentioned in this paper, allows a good release of cerebrospinal fluid to minimize the need for brain retraction. We then make every effort to prevent cerebrospinal fluid rhinorrhea, which could be life-threatening. We prefer to close the dural defects with pericranium and fill major sinuses with autologous fat. In patients undergoing radiation therapy preoperatively or if a potential for CSF leakage occurs during surgery, we leave the lumbar drain in place for 5–7 days postoperatively.

We congratulate the authors for their efforts with these formidable lesions. Unfortunately, the controversies concerning their treatment will not be resolved in the near future.