Sinonasal Malignancy and Orbital Exenteration Sparing Cancer Surgery

Camilo Reyes[1] Mihir Patel[2] C. Arturo Solares[2]

[1] Division of Rhinology and Endoscopic Skull Base Surgery, Department of Otolaryngology - Head and Neck Surgery, Augusta University, Augusta, Georgia, United States
[2] Department of Otolaryngology - Head and Neck Surgery, Winship Cancer Institute at Emory University, Emory University, Atlanta, Geogia, United States

Address for correspondence C. Arturo Solares, MD, Professor, Department of Otolaryngology - Head and Neck Surgery, Emory University, Medical Office Tower (MOT), 9th Floor, 550 Peachtree Street NE Atlanta, GA 30308, United States (e-mail: clementino.arturo.solares@emory.edu).

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Abstract

This article reviews the most common locations and natural history of sinonasal carcinomas. It also reviews surgical indications and current evidence regarding adjuvant and neoadjuvant therapies. In the past, orbital clearance was generally done for ethmoid and maxillary cancers, even without a marked neoplastic infiltration; however, such indications have changed in the recent years due to advances in our understanding of the disease, as well as new chemotherapeutic and radiotherapy protocols. Surgical resection of tumors close to the orbit exhibits the challenging task of balancing treatment goals and patient's desires.

Keywords

- periorbita
- periorbital fat
- extraocular muscles
- maxillary sinus carcinoma
- squamous cell
- carcinoma
- paranasal sinuses
- orbital exenteration

Introduction

Sinonasal tumors account for 3 to 5% of head and neck malignant neoplasms and 0.2 to 0.8% of all tumors.[1] There are different histological types with distinctive clinical behavior. The most common primary tumors are squamous cell carcinoma (SCC), intestinal-type sinonasal adenocarcinoma, sinonasal tract adenoid cystic carcinoma (StACC), sinonasal undifferentiated carcinoma (SNUC), and neuroendocrine carcinoma (NEC). Orbital involvement is common in advanced disease. Indications for orbital exenteration continue to be broadly discussed. Complete surgical resection with negative oncologic margins is the goal of treatment. Several factors need to be considered with orbital compromise: (1) organ preservation, (2) tumor resection, and (3) functional status.

Pearls and Tips

- Indications of orbital exenteration include gross invasion of the orbit, optic nerve, extraocular muscles, and skin overlying the muscles.
- Tumor histology is a fundamental factor in disease treatment.
- Extended endonasal approach can be used to resect sinonasal cavity carcinomas; however, orbital exenteration always mandates an open approach.

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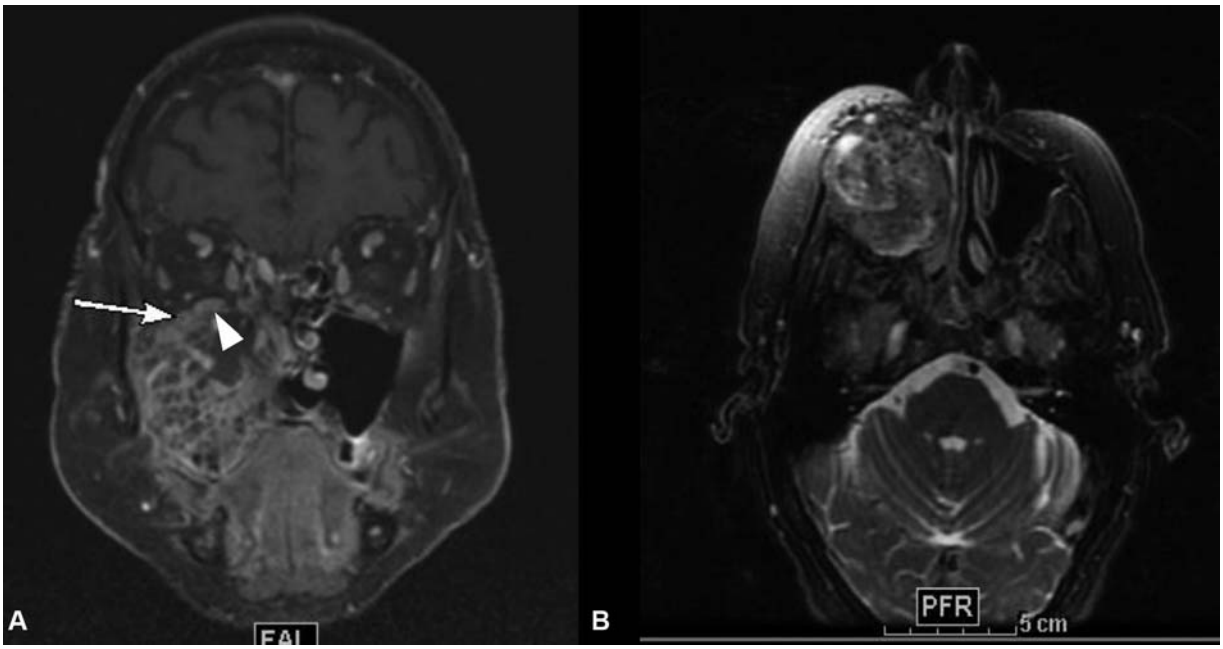

Fig. 1 (**A**, **B**) Coronal T1 and axial T2 contrast-enhanced MRI demonstrating a mass centered in the right maxillary sinus (arrow). There is likely erosion of the orbital floor; however, there is no clear invasion of the inferior rectus (arrowhead). MRI, magnetic resonance imaging.

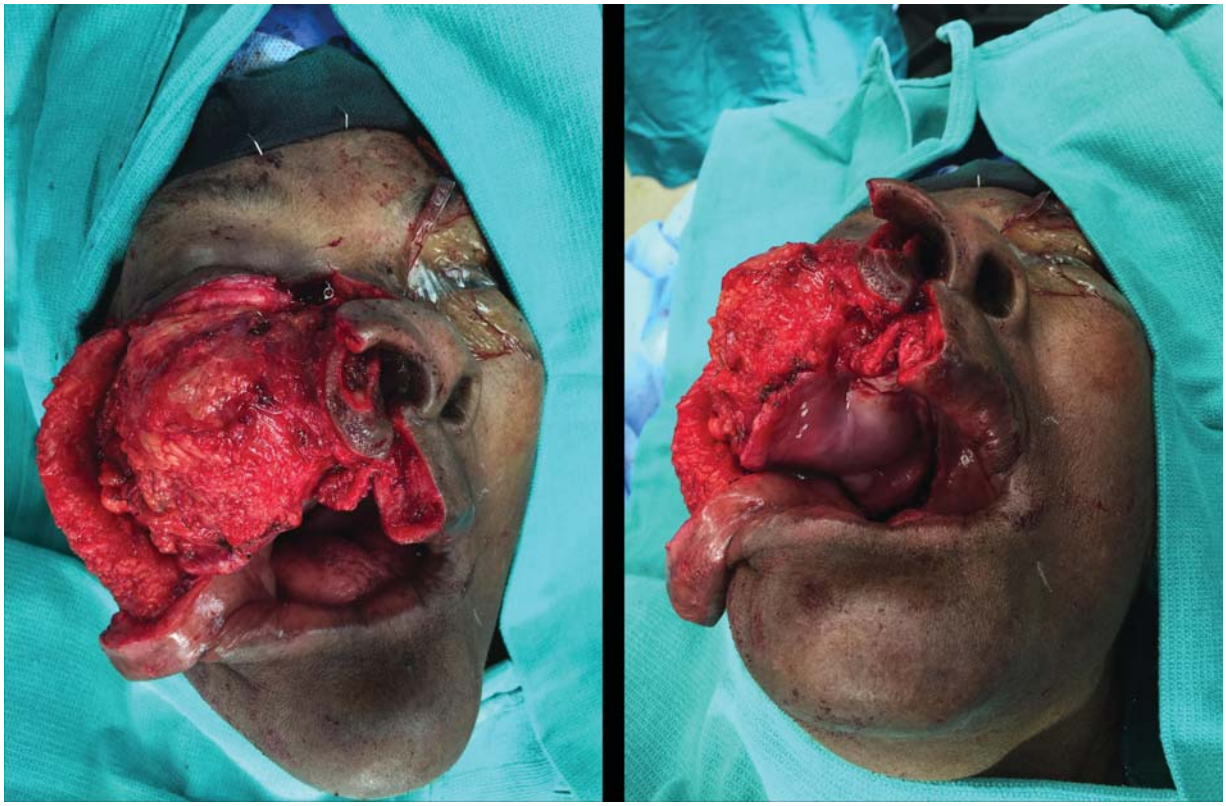

Fig. 2 Open maxillectomy by a Weber–Ferguson approach. The lesion compromised the maxilla, palate, and orbital floor.

Case Examples

Case 1

An 82-year-old woman presented with a sinonasal tumor originating in the maxillary sinus. Preoperative contrast-enhanced magnetic resonance imaging (MRI) showed no definitive orbital invasion (►**Fig. 1**). Nasal endoscopy revealed tumor invading the turbinates but not the septum. Biopsy performed at this time demonstrated sarcomatoid carcinoma. The patient underwent open surgical resection with extended maxillectomy sparing the orbit while removing the orbital floor (►**Fig. 2**). Margins were negative after en

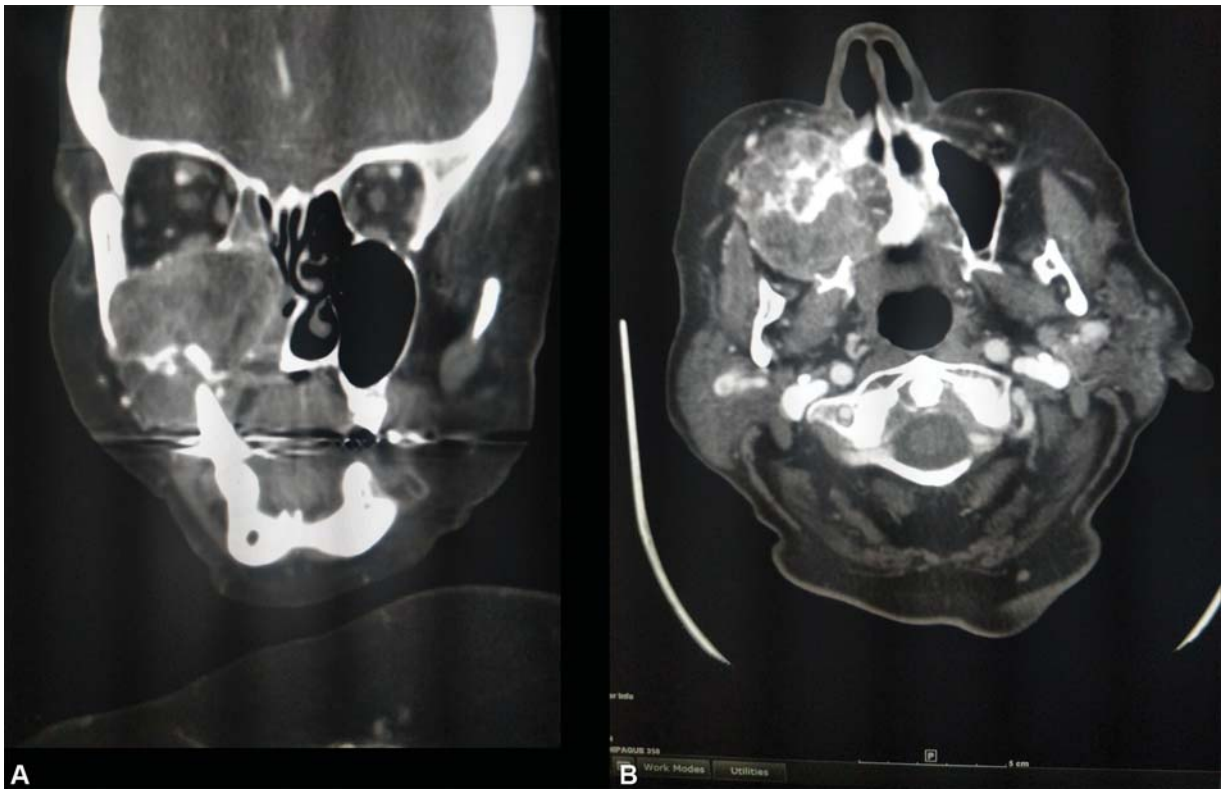

Fig. 3 (**A, B**) Coronal and axial contrast-enhanced CT scans demonstrating a mass centered in the right maxillary sinus. There is erosion of the orbital floor and apparent involvement of the inferior rectus. CT, computed tomography.

bloc resection. The orbital floor, midface, and palate were reconstructed at the time of resection with a scapula free flap. Final pathology was a T4bN0 sarcomatoid carcinoma and treatment plan included adjuvant radiation. She continues to follow-up and is disease free for 4.5 years after the treatment.

Case 2

A 73-year-old woman with a sinonasal tumor concerning from orbital invasion based on computed tomography (CT) depicting a large aggressive mass centered in the right maxillary sinus measuring $\sim 4.7 \times 5.0 \times 4.9$ cm. The mass demonstrated heterogeneous enhancement with areas of central necrosis. Anteriorly, the mass eroded the anterior maxillary wall and extended into the right premaxillary soft tissues. Medially, the mass destroyed the medial maxillary sinus wall and extended into the nasal cavity. Posteriorly, the mass destroyed the posterior maxillary wall, the pterygoid base, extended into the retroantral fat, and bulged into the pterygopalatine fossa. Superiorly, there was multifocal erosion of the right orbital floor with apparent minimal extension into the right extraconal fat and inseparable from the right inferior rectus. Inferiorly, there was destruction of the right maxilla and hard palate (►**Fig. 3**). The tumor was resected en bloc with orbital exenteration given the concern for inferior recurs invasion (►**Fig. 4**). Final pathology revealed invasive SCC measuring $5.0 \times 5.3 \times 4.3$ cm associated with maxillary sinus inverted papilloma demonstrating invasion of resected soft tissue, medullary bone of maxilla, palate, and abuts orbital floor. Final margins were negative. Reconstruction was performed at the time of surgery with a scapula free flap. Postoperative course was complicated with pneumonia and she was unfit for adjuvant therapy. She remained disease free for 18 months at which time she recurred and was treated with chemoradiotherapy (CRT). She remains disease free to date.

Typical Locations (and Approaches)

Overall, the maxillary sinus and nasal cavity are the most common locations for sinonasal carcinomas; however, when orbital compromise is part of the scenario, the ethmoid sinus followed by the maxillary sinus and surrounding structures are the most common origin site.[2] Tumors at the sphenoid sinus and frontal sinuses are rare. The incidence of orbital invasion depends mainly on the site of origin and the histology of the malignancy. Surgical approach depends on location of the tumor and surgeon's preference and experience. Proper patient selection is imperative in decision-making process for whether to utilize endoscopic, open, or combined approaches. Currently, new extended endonasal approaches are being constantly used for the treatment of sinonasal malignancy and continue to evolve. Endoscopic access to the orbital contents is performed through fracture and gentle removal of the entire lamina papyracea. Once the periorbita is cut and excised, the extraconal fat tissue is completely exposed. Removal of the extraconal fat exposes the extraocular muscles. The transnasal endoscopic corridor allows access not only to the intraorbital compartment but also to the medial part of the superior orbital fissure, the

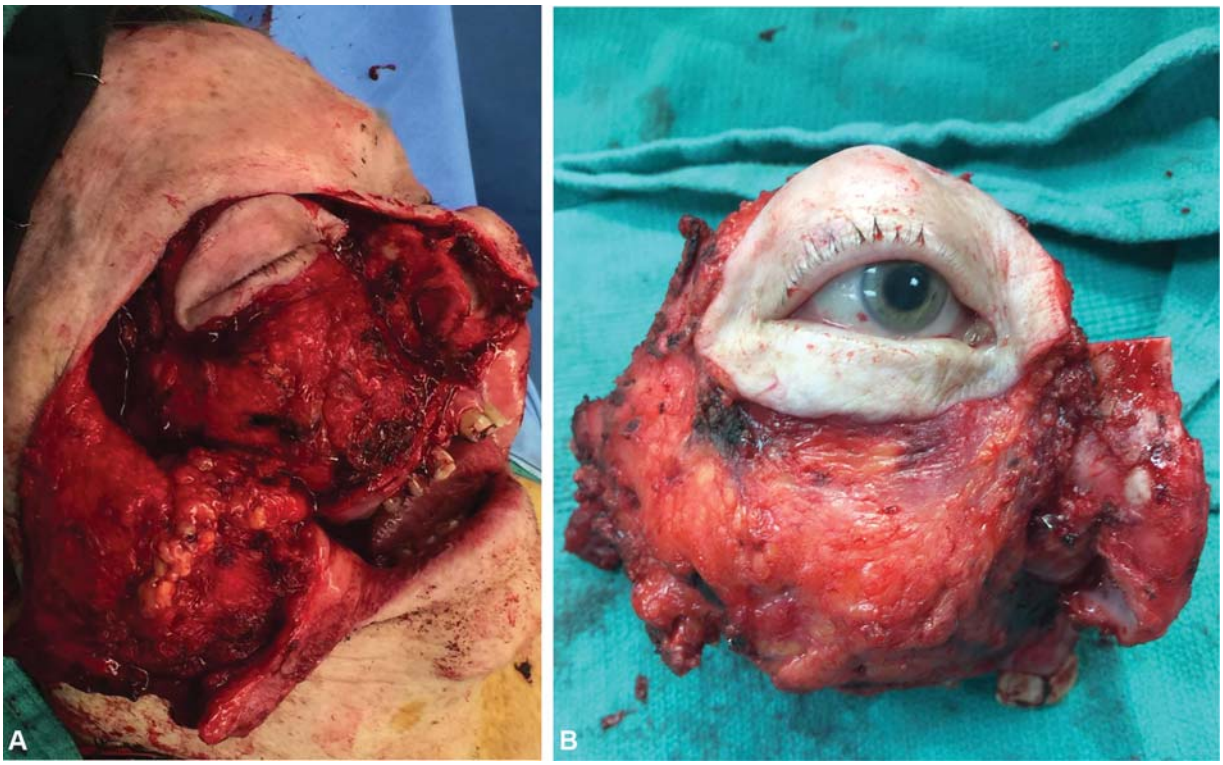

Fig. 4 (**A**, **B**) Case 2 intraoperative pictures. Open maxillectomy by a Weber–Ferguson approach with orbital exenteration.

orbital apex, and the optic nerve. An exclusive endonasal endoscopic approach to sinonasal tumors is contraindicated in some cases, especially when there is invasion of the orbit requiring exenteration, circumferential dissection of nerves and/or vessels, or mobilization of a cranial nerve.[3] However, more experienced centers can achieve complex neurovascular dissection. Two or more approaches may be necessary for orbital exenteration. All patients scheduled for a purely endoscopic endonasal approach must be informed about the possibility of switching to a combined (open and endoscopic) resection, even intraoperatively, if deemed necessary. Tumors that originate or extend to the maxillary antrum require a maxillectomy and an open approach via a lateral rhinotomy incision or a midface degloving. When the tumor extends to the orbital apex, lateral cavernous sinus, or has extensive invasion of the infratemporal fossa, an orbitocranial approach may be required.

Natural History

Sinonasal tumors have an insidious onset and a tendency to present at advanced stages due to their hidden location within the sinonasal cavity. The proximity of the nasal cavity and paranasal sinuses to important neurovascular structures makes these lesions have a high propensity for extension and invasion. Sinonasal tumors present with ocular symptoms at diagnosis in 50% of cases.[2] Erosion of the orbital bone wall is present in 60 to 80% of ethmoidal and 30 to 50% of maxillary sinus cancers.[3,4]

Work-up entails physical and neurological exams, nasal endoscopy, CT scan, MRI, and for some specific cases, angiography. Clinical and imaging findings are crucial for ruling out orbital invasion. In the presence of a sinonasal mass, abnormal physical findings such as decreased extraocular eye movement, conjunctival injection, chemosis, anisocoria, proptosis, vision loss, epiphora, and dystopia are clinical findings suggestive of orbital invasion. Physical exam findings must be correlated with imaging.

The orbit is a quadrilateral pyramid-shaped space that contains the eye and all its related muscular and neurovascular structures. It communicates with the infratemporal fossa through the inferior orbital fissure and to the middle cranial fossa posteriorly through both the optic canal and superior orbital fissure. The rectus muscles define the intra- and extraconal spaces which contain fat and the periorbita with the lamina papyracea as a medial landmark. The lamina papyracea is the wall that separates the orbit from the nasal cavity.

CT scan is the preferred assessment modality of the integrity of the bony orbital rim. Findings can range from contact of a sinonasal mass to the orbital wall, from remodeling/osteitis to erosion. If there is erosion of the bony orbital wall, the chances of orbital invasion increase. Signs of periorbital invasion include focal loss of the continuous hypointensity of the periorbita. Displacement of the periorbita is one of the most accurate radiologic signs of orbital invasion seen on CT showing a negative predictive value of 86% and a positive predictive value of 75%.[4] MRI is a fundamental tool to evaluate the periorbital lining. Regardless of bony erosion, the normal periorbital lining is hypointense on both T1 and T2 sequences. The periorbita can be considered intact when the thin and regular hypointensity is still visible on T2 images between tumor and orbital fat. In

addition, MRI can clearly differentiate tumor from inspissated secretions which cannot be ruled out on CT.[3,5] After the periorbita is violated, the chances of orbital invasion significantly increase. Additional signs of possible orbital invasion include fat invasion (infiltration within the extraconal fat in close relation to the sinonasal mass) and changes in the extraocular muscles (displacement, enlargement, or enhancement). The risk of orbital invasion is higher in the posterior ethmoid cavity in relation to the anterior ethmoid cavity because of the relation of the medial rectus to the lamina papyracea. In the anterior ethmoid cavity, there is a fat plane between the periorbita and medial rectus muscle; this fat plane is missing in the posterior ethmoid cavity, however, is difficult to discern if the tumor origin is within the anterior or posterior ethmoid cavity. Once a nasal cavity mass has been confirmed on physical and radiological imaging, endoscopic tissue sampling should be done to confirm histological diagnosis. We favor biopsy in the operating room instead of the office, as sometimes, due to mucosal inflammation over an overlying mass; in office, biopsy with inadequate sampling can show false-negative results. In addition, there is also significant patient discomfort, risk of severe bleeding, or cerebrospinal fluid leak when an encephalocele has not been ruled out.

Orbital compromise can occur due to direct macroscopic erosion of the bone or by microscopic invasion through vascular and nervous channels. Specifically, for tumors with orbital compromise, an ophthalmology and/or oculoplastic consult is imperative. The functional status of the eye will help in decision making. The eighth edition of AJCC/UICC TNM (American Joint Committee on Cancer/Union of International Cancer Control; Tumor, Node and Metastasis) staging system classifies orbital invasion as T3 when there is invasion of the floor or medial walls of the orbit, T4a when there is invasion of the anterior orbital contents, and T4b when there is invasion of the orbital apex.[6] These staging levels require orbital exenteration. Invasion into the orbit, oral cavity, skin, infratemporal fossa, and dura increases the rate of neck metastasis and has a negative impact over oncologic and functional outcomes in patients with paranasal sinus cancers. Involvement of the orbital soft tissue is also considered an independent factor significantly influencing survival.[7]

Indications for Treatment

There are three stages of orbital invasion: grade I, erosion or destruction of the medial orbital wall; grade II, extraconal invasion of the periorbital fat; and grade III, invasion of the medial rectus muscle, optic nerve, ocular bulb, or the skin overlying the eyelid. In general, grade III is considered an indication for orbital exenteration.[8,9]

Tumor histology plays a significant independent role in patient outcome, irrespective of orbital invasion. Given the long list of sinonasal malignancies, it is inaccurate to define a clear indication for orbital exenteration, as some tumors can be more locally aggressive and show a higher recurrence rate compared with others. In addition, it is crucial to understand which from the long list of sinonasal tumors have a predisposition for perineural spread (e.g., SCC and StACC) and to which nerves they are close (e.g., infraorbital nerve, greater palatine, lesser palatine, pterygopalatine ganglion, and vidian nerve), as this will also play an important role in treatment. For SCC, some authors have found that preservation of the orbit was not associated with a significantly higher rate of local recurrence[10,11] and even some have concluded that preservation of the orbit does not affect survival significantly.[12] Adenocarcinomas can be either colonic, papillary, solid, or mucinous. Colonic and papillary have better prognosis, and generally, treatment is complete surgical resection and chemotherapy, so the use of induction chemotherapy (ICT) can aid in organ preservation. StACCs have a high incidence of postoperative positive margins (63–85% of cases) and recurrence rate up to 94%,[13] so having orbital invasion in an advanced StACC makes the decision of exenterating the orbit fairly straightforward. Mucosal melanoma (MM) is one of the most aggressive tumors and, despite radical resection and adjuvant radiation therapy (RT), patients with MM still face a very unfavorable prognosis (5-year overall survival [OS] ~30%) with high rates of locoregional recurrence and distant metastasis. The role of immunotherapy on orbital preservation for MM has not been analyzed. Neuroendocrine tumors can be divided into esthesioneuroblastoma (ENB) and non-ENB tumors (NEC, SNUC, and small cell carcinoma). ENB with local treatment often leads to locoregional and distant controls. SNUC is highly aggressive with generally poor prognosis as it usually has skull base (50% of patients) and orbit invasion (47% of patients) upon presentation.[14] Specifically, for MM and SNUC, orbital exenteration is not going to significantly affect outcome.

Goals of Treatment

In general, there is no argument on the indication for orbital exenteration in cases of gross infiltration of the extraconal muscles, globe, and orbital apex. Orbital preservation in cases of limited orbital fat involvement is still a matter of debate. Specifically for SCC, there is a slight nonstatistically significant inclination toward preserving the orbit, as there is no difference in survival between orbital exenteration and preservation.[2,10–12] As previously stated, tumor histology plays a fundamental role in decision making. A detailed analysis with the patient regarding goals of treatment is essential. Orbital exenteration must be discussed with the patient regarding recurrence rate, survival, emerging functional defects, esthetic deformity, and emotional hardship. On the contrary, balance between complete surgical resection with negative margins and the functional outcome of the preserved eye must be well known. RT has deleterious effects on the eye and its supporting apparatus. The "preserved eye" is potentially subject to optic neuropathy, cataract formation, xerophthalmia, and ectropion. All of these may develop a painful, dry eye and have the potential to result in either reduced or complete loss of vision resulting in a dysfunctional eye in up to 79% of patients.[15] Having all this said, the risk of leaving a nonfunctional eye increasing the risk of incomplete resection must be evaluated.

Neoadjuvant Chemotherapy

Due to the intervention of chemotherapy, including ICT and concurrent CRT (CCRT), the 5-year OS of patients with SCC of the nasal sinus has reached 59 to 76% in recent years.[16–19] In addition, there have been several studies assessing the role of ICT in organ preservation. One of the first published articles included the use of cisplatin and fluorouracil followed by RT (48 Gy) and surgery. Histopathologic analysis of resected specimens showed no vital tumor in eight patients, minimal microscopic disease in three, and infiltrating tumor in one. Local control was achieved in 11 of 12 patients.[20] One of the largest series reported 46 patients with advanced SCC of the paranasal sinuses (67% with orbital invasion). ICT regimens consisted of a combination of a taxane and platinum in 80% of patients. Subsequent treatment after induction consisted of either surgery followed by radiation or chemoradiation or definitive radiation or chemoradiation. Conservative surgery with orbital preservation was achieved in 87% of the patients, 6/46 failed to preserve the compromised eye and the 2-year OS was 67%.[21] Most recently, a study of 21 patients with SCC of the paranasal sinus and nasal cavity treated with a regimen of docetaxel, fluorouracil, and cisplatin reported an overall response rate of 62% and a tumor down-staging of 71%. Among 17 patients with T4 disease, 82% achieved orbital preservation. Following ICT, patients received definitive treatment such as CCRT, RT alone, and surgery. CCRT regimens consisted of conventional standard fractionated RT of more than 60 Gy for primary tumor and regional lymph nodes, with concurrent chemotherapy with weekly administration of cisplatin 35 - mg/m^2. Thirteen patients (61.9%) achieved a partial response after ICT and 15 patients (71.4%) achieved T down-staging. On this study, there could be a potential susceptibility bias as patients who achieved either stable disease or progressive disease after ICT were older, had higher T-stages, and received more salvage operations than patients who achieved a partial response as this cohort could have gotten more aggressive treatment.[22] Another study analyzed 28 patients with locally advanced SCC of the nasal cavity and paranasal sinuses treated with ICT (cisplatin, docetaxel with or without fluorouracil) followed by RT concurrent with chemotherapy or antiepidermal growth factor receptor therapy. After such a multimodal therapy, the rates of orbital preservation were 78%.[23] EA3163, a phase II randomized trial of neoadjuvant chemotherapy followed by surgery and postoperative radiation versus surgery and postoperative radiation for organ preservation of T3 and T4a nasal and paranasal sinus SCC, is currently enrolling patients.

Reconstruction

The purpose of reconstruction is to restore the lost orbital tissue and provide an acceptable esthetic appearance while allowing for adequate cancer surveillance. Reconstruction can be done either primarily or on a second surgical stage. We favor primary reconstruction because reconstruction on a radiated field is more challenging and healing is impaired in these cases. Reconstruction techniques are beyond the scope of this article but include many regional flaps as the temporalis muscle flap, paramedian forehead flap, temporoparietal muscle flap, and split-thickness skin grafts. Free flaps have largely replaced locoregional reconstruction. Our preference is the use of osteocutaneous free flaps from the fibula or scapula. Patients who are not candidate for reconstruction can be rehabilitated with maxillofacial prosthetics.

Conclusion

Sinonasal carcinomas with orbital compromise generally present at advanced stage have a negative impact on OS and compose a challenging situation for both the patient and surgeon. Like in most disease processes,[24] every case must be addressed individually; surgical goals, survival, and treatment expectations must be discussed with every patient. The balance between oncologic control and quality of life cannot be generalized. For SCC, preservation or exenteration of the orbit shows no difference in survival; however, it does affect recurrence rate. ICT has become an important component of medical management and organ preservation. Although external and endoscopic approaches can be considered as competitive for this scenario,[25] we consider them to complement each other. The role of ICT continues to evolve and so far, its results are promising in regard to survival and organ preservation.

Conflict of Interest
None declared.

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