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Surgical resection of a cutaneous squamous cell carcinoma invading the infraorbital maxillary nerve

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ABSTRACT

Surgical resection of cutaneous squamous cell carcinomas with perineural tumor invasion (SCC) represents an oncological challenge. Although perineural tumor invasion occurs in about 3% of all SCC of the skin, it is recognized as a poor prognostic factor and intracranial spread can occur through cranial nerve pathways. We describe in a stepwise fashion our combined approach for a complete resection of the infraorbital maxillary nerve from its skin terminations all the way up to its intracranial portion. The surgery consisted in an orbitozygomatic translocation and a pterional craniectomy, exposure of the intra and extracranial maxillary nerve, an *en bloc* resection of the affected infraorbital branch of the maxillary nerve from the skin up to its pre-cavernous segment, orbital floor bone removal. Patient then underwent reconstruction of the floor and the lateral wall of the orbit with excellent cosmetic results. Due to its rarity, to our knowledge this is the first technical note in the English literature presenting a complete illustrated description of surgical technique for complete oncological resection these type of skin cancers.

1. Introduction

Non-melanoma skin cancer (NMSC) is the most prevalent cancer type in Brazil., corresponding to at least 30% of all malignant tumors. A total of 176,930 new cases were estimated for 2020 [1]. Among NMSC the most frequent types are in order of frequency basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) [1].

For a curative intent, surgery is often offered for treatment of advanced invading NMSC. SCC is the most aggressive type of NMSC and perineural tumor invasion predicts a poor prognostic outcome, especially on the face, due to the possibility of a pathway to an intracranial invasion. Surgical treatment for intracranial perineural spread is a decision-making challenge of what should be the best surgical approach. Soft tissue extra-cranial involvement requires principles of oncological surgery, such as a tumor-free margin. These are rare and challenging lesions; and few centers have experience managing it. Therefore, we present a stepwise description of the complete surgical resection of a cutaneous squamous cell carcinoma (SCC) with an infraorbital/maxillary nerve bulky perineural invasion. For this patient, the histology of the tumor and the tumor free margins were confirmed by a board-certified pathologist. Ethical guidelines were followed and institutional board review and patient consent for the study were obtained for this publication.

2. Clinical report

2.1. Pre-operative clinical presentation

A 66-year-old female patient presented herself to our out-patient clinic with a subcutaneous infra-palpebral lesion of approximately 2 cm at the level of infra-orbital foramen. According to the patient the lesion was progressively growing over the years. The patient denied

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facial pain and referred only infra-palpebral hypoesthesia. After an open surgical biopsy, the lesion was diagnosed as a skin spindle-cell squamous cell carcinoma. The pre-operative MRI imaging showed the lesion with bulky perineural spread of the infraorbital maxillary nerve (Fig. 1).

2.2. Surgical steps

The following surgical steps were used. Initially neurosurgery performed, as previously mentioned, a modified smaller bi-coronal incision extending through the right infra-zygomatic preauricular area was performed (Fig. 2); the cutaneous flap was elevated from the posterior to anterior and from the superior to the inferior direction up to the lateral orbital rim (Fig. 3). The temporal muscle was cut and freed from the temporal line up to the zygomatic arch. Head and Neck Surgery exposed inferiorly the parotid gland, that was achieved with preservation of the facial nerve and its branches. The next step consisted of three osteotomies: one at 1 cm from the posterior edge of the zygomatic arch, one at the lateral orbital rim both performed by neurosurgery and another at the malar region performed by the head and neck surgery. Both neurosurgery and head neck surgery worked to preserve the masseter muscle insertion at the zygomatic arch and to translocate this bone/muscle flap inferiorly. Neurosurgery performed a small 4 cm orbitopterional craniectomy was performed for the extradural access. Then neurosurgery performed the resection of the lateral wall of the orbit. At this point, the entire extradural maxillary nerve pathway is exposed. The head and neck surgery begun the resection of the infraorbital subcutaneous lesion and it proceeded to resect the tumor, part of the orbital floor was included to ensure clear oncologic margins. The surgical specimen was retracted towards the infratemporal fossa. The maxillary nerve was dissected in the pterygopalatine fossa up to the foramen rotundum, and the sphenopalatine artery was carefully preserved. Now, neurosurgery continued the dissection up to the cavernous sinus. The nerve was cut (Fig. 4), and its proximal end was tied to confirm tumor-free margins. The surgical specimen (bone fragments, skin, soft tissue, and nerve trunk) was *en bloc trans*-facially removed by the head and neck surgeon, from the skin all the way distally to the proximal intracranial emergence of the maxillary nerve.

Both neurosurgery and head and neck surgery worked jointly for the reconstruction of the orbital floor and lateral wall, as well the cranial defect. This was carried out with a shaped titanium mesh (Fig. 5) and miniplates were used for the zygomatic arch fixation. The preserved temporal muscle was sutured at the temporal line. The temporal muscle completely covered the titanium mesh used for the reconstruction of the

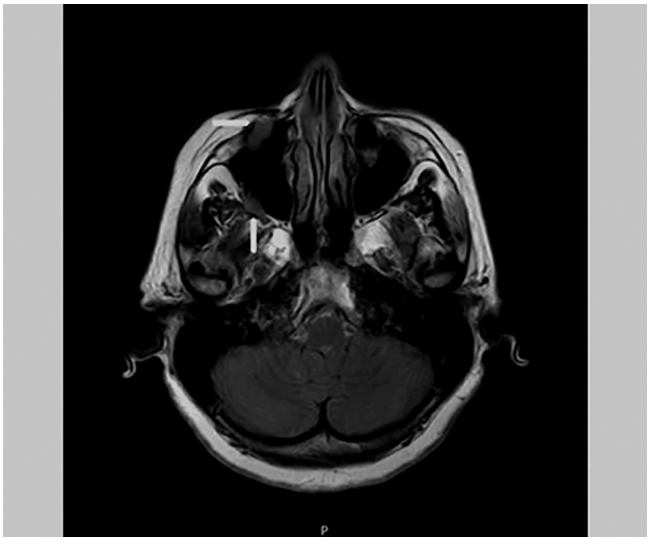

Fig. 1. MRI demonstrating infraorbital/maxillary nerve enlargement.

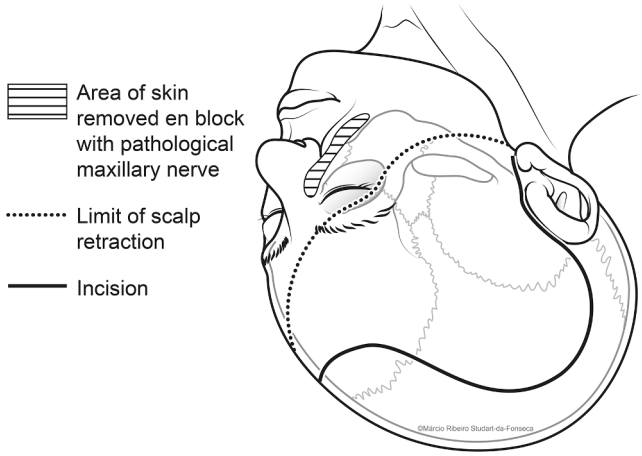

Fig. 2. Surgical incision planning. The temporal curvilinear incision is extended parallel to the hairline to hide the surgical scar. The dotted line represents the limit of detachment of the scalp flap to exposure the orbital border.

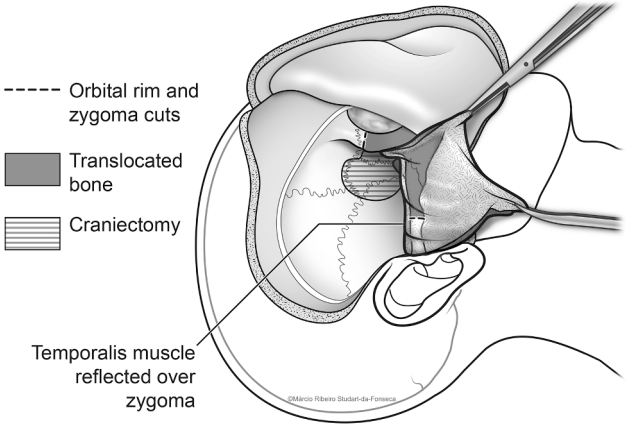

Fig. 3. Illustration of dissection at the rotundum foramen.

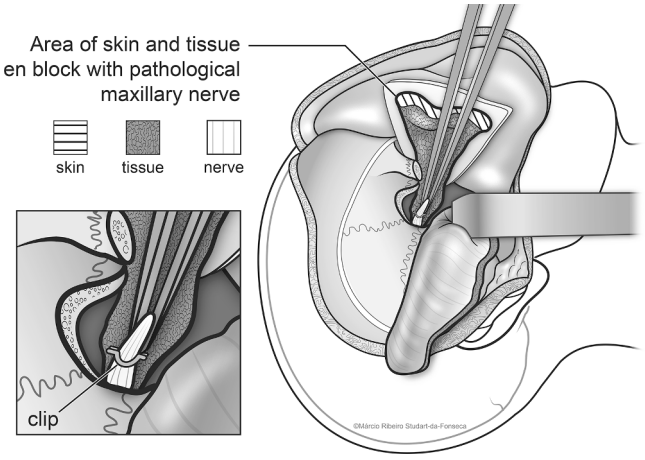

Fig. 4. Maxillary nerve (V2) at the rotundum foramen (detail).

craniectomy and orbital lateral wall. Wound closure followed in traditional stepwise. Suction drains were placed, and the skin area was sutured in a two-layer fashion.

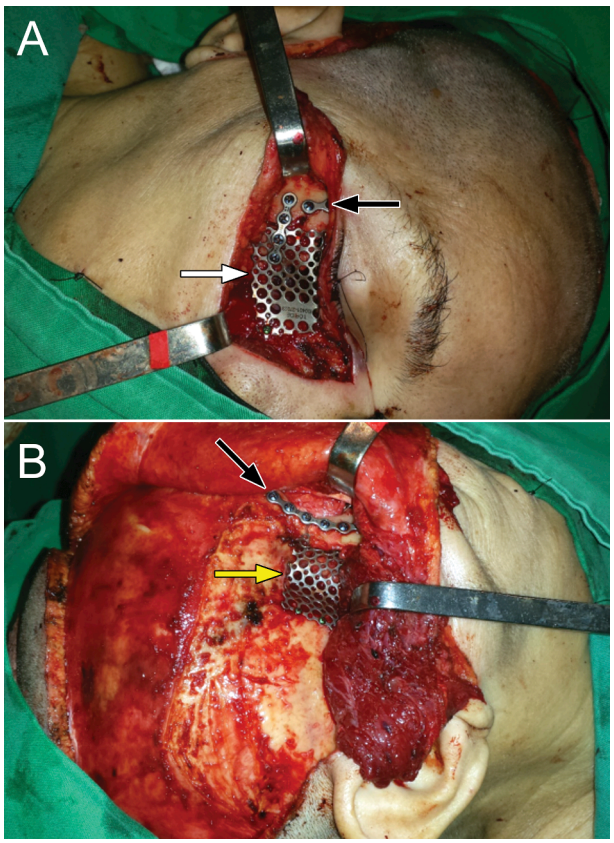

Fig. 5. (A) Titanium mesh reconstruction of the orbital floor and anterior wall of the maxillary sinus (white arrow) orbital rim (black arrow). **(B)** Titanium mesh reconstruction of the craniectomy defect and orbital lateral wall (yellow arrow) and of orbital rim(black arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2.3. Post-operative clinical outcome

There were no postoperative complications. The patient was discharged from our hospital after seven days. The histopathological report showed bulky nerve involvement, but no tumor at the proximal nerve margin and tumor-free margins. The patient was referred to adjuvant therapy and she underwent fractioned conformational radiotherapy of 60 Gy. There is no evidence of tumor recurrence after 5 years of follow-up. There were no new immediate neurological post-operative deficits, visual acuity and eye movements were complete preserved with no diplopia, and the pre-operative facial hypoesthesia on the infraorbital maxillary nerve innervation area remained unchanged. The patient presented very good functional and aesthetic results were with no facial nerve deficits of the frontal and orbicular branches. Currently it is a 5-year follow-up, and the patient remains disease free, but the combination of the surgical reconstruction of the orbit floor and the radiotherapy resulted in soft tissue atrophy and the patient had developed a late enophthalmos (Fig. 6), but the neurological examination showed no clinically relevant diplopia.

3. Discussion

Although many publications address the procedure of fronto-orbitozygomatic approaches for a myriad of vascular lesions and skull base neoplasms, there is not a single publication in the English language describing in detail a case that would require a combined orbitozygomatic translocation, pterional craniectomy and transfacial approaches for a surgical resection of the skin squamous cell carcinoma with

Fig. 6. Patient at a 5 year follow-up and presence of the right side enophthalmos.

perineural involvement of the *maxillary* nerve.

Approximately 70% of all skin SCC occurs in the head and neck area. Perineural tumor invasion is present in about 3% of all skin SCC [2]. Spindle-cell SCC, also known as the sarcomatous variant is a rare and aggressive SCC variant, present in approximately 3% of skin SCC of the head and neck area [3]. Most reports when describing perineural invasion give little clarity whether if it is a microscopic infiltration or involvement of the main named nerve. However, there seems to be a consensus that skin SCC perineural microscopic infiltration is a recognized poor prognostic factor [4]. Additionally, possible main cranial nerve spread is another oncological challenge. It seems to be more infrequent, but it can be underestimated. In a series of 967 squamous cell skin carcinomas of the head and neck treated at the University of Texas M.D. Anderson Hospital and Tumor Institute at Houston, seventy-two (14%) had perineural invasion documented in one or more major nerve trunks(5). The presence of perineural invasion in skin SCC is estimated at between 2.6% and 14% [2,5]. The maxillary nerve (V2) is one of the most affected structures, as well as the facial (VII CP) and mandibular nerves (V3) [4,5]. The risk factors leading to cranial nerve involvement are microscopic perineural infiltration in midface skin tumors, male gender, fast-growing lesions, recurrent and poorly differentiated tumors [6].

According to Panizza, in cases of intracranial extension, surgical access is limited, often compromising surgical resection and cancer outcome [7]. Also, surgical resection associated with radiotherapy for skin cancer with perineural infiltration has better results when compared to radiotherapy alone [5]. Up until the mid-1960 s, tumors were considered not amenable to cure if diagnosed after intracranial dissemination [8]. However, Goepfert et al in 1984 published a series of cases in which an intracranial approach was performed on segments of the trigeminal nerve and ganglion [5] with good surgical outcomes; and Panizza et al in 2012 stated that the resection of the Gasser's ganglion

near the cavernous sinus did not increase morbidity and should be performed, if necessary, to obtain a negative margin [7].

The continuous development of imaging techniques to evaluate disease extension and improved surgical resources have allowed the resection of the cranial nerves in their intracranial segments to be performed safely and good results. To the best of our knowledge no randomized trial has confirmed the advantage of surgery plus radiotherapy when compared to exclusive radiotherapy in cases of clinical-radiological infiltration of nerve trunks. Gupta and colleagues in a review article suggested that radical resection plus adjuvant radiotherapy is likely to offer the best chance for cure for patients with head and neck skin SCC and clinical perineural invasion with symptomatic or with radiographic evidence [9].

Recently, Okholm and colleagues have described three cases of perineural invasion of the infraorbital nerve. No radical surgical treatment was performed, adjuvant radiotherapy was performed in both operated cases and exclusively in the only case with evidence of extension to the cavernous sinus. Only one patient was alive at three months of follow-up [10].

Other surgical techniques for resection of the infraorbital and maxillary nerve have been described, including for some cases of skin cancer. Under a surgical microscope, the *trans*-maxillary route [11] was used in seven cases. All but one case were primary tumors of the maxillary sinuses, and one case of osteoradionecrosis was reported after surgery. In addition to resection of the maxilla, the authors described a more medial approach, including resection of the lateral wall of the sphenoid bone. It was not clear whether the resection was *en bloc* or fragmented. More recently, endoscopic resection of the maxillary nerve has also been described through the nasal fossa (medial approach) [12]. However, it was not clear how much bone resection was done on the orbital floor. The authors opted for a medial maxillectomy, but there was no open surgical approach at the level of the infraorbital foramen. The Orbito-zygomatic translocation, instead of the *trans*-maxillary and endoscopic approaches described, it adds a lateral view to a limited but necessary anterior approach of the infraorbital foramen without extended maxillectomy or even medial maxillectomy. When the resection of the cavernous portion of the maxillary nerve is not necessary there is no concern about the internal carotid artery using the lateral approach through the orbito-zygomatic translocation here described. In addition, no devitalized bone is repositioned, as adhesion to soft tissues maintains bone viability. Furthermore, there is no need to extend the resection to the lateral wall of the nasal fossa and the lateral wall of the sphenoid bone as in the endoscopic and *trans*-maxillary resection described above.

The addition of orbitozygomatic osteotomies improves the working area to a fronto-temporo-sphenoidal approaches [13]. Few papers describe orbitozygomatic translocation for advanced skin cancer [14,15]. Enophthalmos and diplopia are common post-operative problems after orbital floor reconstruction and particularly after radiotherapy. Destruction of the surrounding orbital fat tissue occurs after radiotherapy [16] and is also common after the surgical reconstruction [17], these can cause enophthalmos and residual diplopia [18]. These are issues that should not preclude utilization of complex approaches because of the clear benefit of disease-free survival.

For this case our surgical rationale was the following: confronted with a malignant infra-palpebral skin lesion with perineural invasion of the infra-orbital maxillary nerve all the way up the cavernous sinus, we made the decision that the best option for this patient would be an *en bloc* resection of the affected infraorbital maxillary nerve from the skin up to its pre-cavernous segment. A simple pterional approach would not have allowed access to the infra-orbital maxillary nerve, and because the surgery aimed to approach the temporal, infratemporal and pterygomaxillary fossa in a single stage procedure, this would only be possible through a combined transfacial and transcranial approach. Therefore, even extended approaches as the fronto-orbito-zygomatic would not have sufficed for a complete resection of the malignant lesion originating from the facial skin. Thus, the patient was submitted to an orbitozygomatic translocation, in addition to a limited pterional craniectomy extending to the lateral orbital wall and the transfacial approach. Although we performed limited craniotomy, the orbitozygomatic approach required to access the sub-temporal fossa made us opt for a smaller bi-coronal skin incision to avoid any type of skin tension, skin tears, and preservation of the facial nerve function without any excessive skin retraction. The combined surgical approach through orbitozygomatic translocation and pterional craniectomy at the greater wing of the sphenoid bone allows good exposure of the entire extension of the maxillary nerve from the infraorbital foramen up to the cavernous sinus. Another important technical note is that the maintenance of the masseter muscle insertion at the translocated zygomatic arch associated with limited craniectomy reduces the risk of osteoradionecrosis after adjuvant radiotherapy, since no de-vascularized bone fragments will appear in the radiotherapy field. As described above, the patient did develop a late enophthalmos, but the five-year disease free of the malignancy clearly shows the benefit of the radical surgical resection. The radicality was only attainable through the Also, although endoscopic instrumentation is extremely useful for lesions arising from or invading into the naso-facial sinuses, for this case that was not an option because the cancerous tumor originated itself from the mid face skin and the oncological aim was to obtain complete resection with tumor free margins.

Therefore, this report and its technical note offers a practical description for a combined surgical approach that allows the resection of the affected infraorbital maxillary nerve with excellent oncological, functional, and good aesthetic results. It illustrates the surgical technique used by neurosurgery and head and nek surgery for removal of a challenging cranial-facial malignancy. The limitations of this surgical report with the presented surgical description are the classical disadvantages of all small series and case reports including but not limited to biases, uncontrolled methodology, difficulties for generalization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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