CASE REPORTS

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Orbital exenteration – a salvage procedure?

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Abstract

Orbital exenteration is a procedure performed usually for malignancies. The subsequent reconstructive efforts are directed towards rapid and stable healing but allowing detection of recurrent disease, obliteration of any communication between the orbit and surrounding cavities and above all a good quality of life. The surgical options must be tailored to each patient; we have to achieve first disease control and to compensate a 3D defect as best as we can. In the following, we present a series of three patients with aggressive tumors of the midface, admitted in our clinic in the last four years. For each case, orbital exenteration was performed in order to achieve tumor clearance. The results were good excepting one case (a relapse at three years interval) with a squamous cell carcinoma and perineural invasion.

Keywords: orbital exenteration, temporal muscle flap, squamous cell carcinoma, basal cell carcinoma, perineural invasion.

Introduction

Orbital exenteration is a disfiguring procedure performed usually for malignancies, but also for unresponsive orbital infections and local control of recurrent benign tumors; sometimes, it represents a palliative procedure [1–4]. Orbital exenteration implies removal of the orbital content along with the periosteum. It is generally an oncological procedure performed for malignancies arising from the eyelids (basal cell carcinoma, squamous cell carcinoma, conjunctival malignant melanoma), the lachrymal gland (adenoid cystic carcinoma) or the surrounding sinuses (in which case is usually part of a orbitomaxillectomy) [5–7].

According to Mouriaux F *et al.* (1999) [8], orbital exenterations may be subdivided into three categories: total, sub-total and enlarged (extended). The resection of adjacent bone is labeled as extended orbital exenteration. Total exenteration means removal of all tissues within the orbit including the globe and periorbita. Subtotal procedures are performed when orbital tissues are partially removed with sacrifice of the globe.

Patients and Methods

Our clinical experience regarding orbital exenteration in the last four years is depicted in the Table 1.

Table 1 – ***Our series of seven cases treated by exenteration and reconstruction***

Case No.	Gender	Age [years]	Diagnosis	Anatomical defect	Reconstruction method
1.	F	61	Squamous cell carcinoma of the lower left eyelid.	Orbital exenteration defect.	Fronto-temporal flap.
2.	M	56	Recurrent squamous cell carcinoma of the maxillary sinus extended into the orbit.	Orbital exenteration defect.	Fronto-temporal flap.
3.	M	70	Squamous cell carcinoma of the left inner canthus.	Orbital exenteration defect.	Fronto-temporal flap.
4.	M	52	Basaloid squamous cell carcinoma of the maxillary sinus.	Orbital exenteration defect.	Fronto-temporal flap.
5.	M	61	Recurrent squamous cell carcinoma of the dorsum nasi and inner canthus with maxillar extension.	Orbital exenteration, maxillar hemiresection.	Latissimus dorsi free flap.
6.	M	60	Recurrent infraorbital basal cell carcinoma.	Orbital exenteration maxillar hemiresection.	Latissimus dorsi free flap.
7.	F	64	Lower eyelid basal cell carcinoma.	Orbital exenteration.	Temporal muscle and free graft.

Our series includes patients between 52 and 70 years old, most of them with significant comorbidities, with multiple prior surgical interventions.

The tumor material has been obtained after surgical resection followed by formalin-fixation (10% formaldehyde) and paraffin embedding. The process was carried out using the standard histopathological method. For the histopathological examination, samples were colored with Hematoxylin–Eosin, which represents a routine method.

Regarding the immunohistochemistry analysis,

histological tissue sections paraffin-embedded were deparaffinized, rehydrated and washed in phosphate buffered saline (PBS), with a pH of 7.4. The immunohistochemistry staining is made using Dako EnVision system along with Dual Link System-HRP (Dako, Carpinteria, USA), pursuant to the producer's instructions and it is controlled afterwards with Meyer's Hematoxylin. The immunohistochemistry technique included the following steps:

- deparaffinization in xylol and section rehydration;
- endogenous peroxidase blocking (5–10 minutes);
- primary antibody incubation in optimal dilution;
- polymer HRP incubation during a period of 30 minutes, at room temperature;
- 3,3'-diaminobenzidine (DAB) development, 5–10 minutes;
- counterstaining with Meyer's Hematoxylin, 2–3 minutes;
- dehydration, clearing and cover slip mounting (Eukitt).

The samples presenting a squamous cell carcinoma were tested with cytokeratin antibodies 34βE12 (produced by Dako, clone 34βE12, 1:50 dilution) and Ki67 nuclear growth factor (produced by Dako, clone MIB 1, 1:75 dilution) using immunohistochemistry. 34βE12 is positive membranary as well as cytoplasmatic, undefined in tumor cells; Ki67 is nuclear positive and located in 60% of the poorly differentiated tumor zones.

Results

We present three cases of patients investigated and operated in our department.

Case No. 1

The fist case was a 64-year-old female admitted in our clinic for an ulcerated tumor involving the lower eyelid, the inner canthal area and the left nasal lateral wall. The MRI revealed the tumoral extension inside the left orbit (at the inferior rectus muscle, the lateral rectus muscle, the lachrymal gland). The decision was to perform an exenteration; the complex defect of the orbital cavity was covered with a rotated temporalis muscle flap covered by a split skin graft. The histopathological exam showed a keratotic basal cell carcinoma infiltrating the dermis and hypodermis down to the muscular plane, with extension to the ocular extrinsic muscles and the orbital fat (Figure 1). The postoperative evolution was good; she followed afterwards the adjuvant therapy.

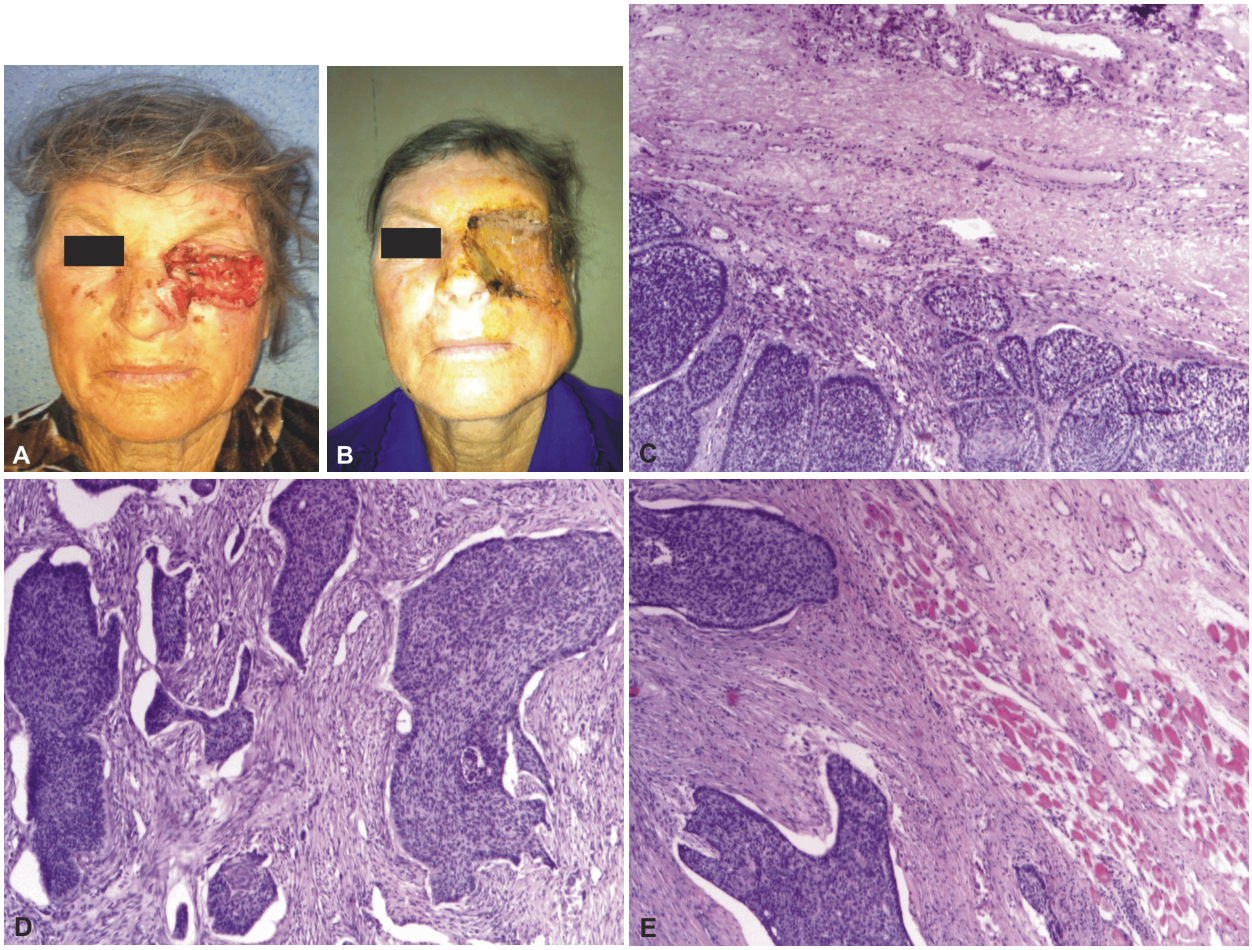

Figure 1 – ***Case No. 1. A 65-year-old female with lower eyelid basal cell carcinoma extended to the inner canthal area and the left nasal lateral wall. (A) Preoperative aspect. (B) Fourteen days postoperative aspect. (C–E) Histopathological aspects: (C) Basal cell carcinoma and nasal mucosa with seromucinous glands, HE staining, ob. ×4; (D) Basal cell carcinoma – infiltrative pattern, HE staining, ob. ×10; (E) Basal cell carcinoma – skeletal muscle invasion, HE staining, ob. ×4.***

Case No. 2

The second case was a 61-year-old male patient with a history of a tumor recurrence at the level of the nasal pyramid with extension at the inner canthus and intraorbital, which necessitated enucleation of the left eye socket, excision of the anterior wall of the maxillary sinus and hard palate.

At hospital admission, he had tumoral invasion in the malar area with extension to the mandible and the pterygoid muscles; he was almost unable to open the mouth.

Excision of the tumor at the level of left malar region was performed; total parotidectomy with conservation of the mandibular branch of the facial nerve; hemiresection with disarticulation of the vertical ramus of left mandibular bone; coverage of the resulting defect through a microsurgical myocutaneous free flap of latisimus dorsi; the oral mucosa was restored by a split thickness skin graft collected from the anterior surface of the right thigh. The pathology exam confirmed a squamous cell carcinoma infiltrating the dermis down to the facial muscles and the bony skeleton with perineural invasion (Figure 2).

After reconstruction, he followed the radio-chemotherapy protocol; he was disease-free for three years; at the annual follow-up in the third year, he developed recurrence in the pterygopalatine fossa with extension to the temporal bone.

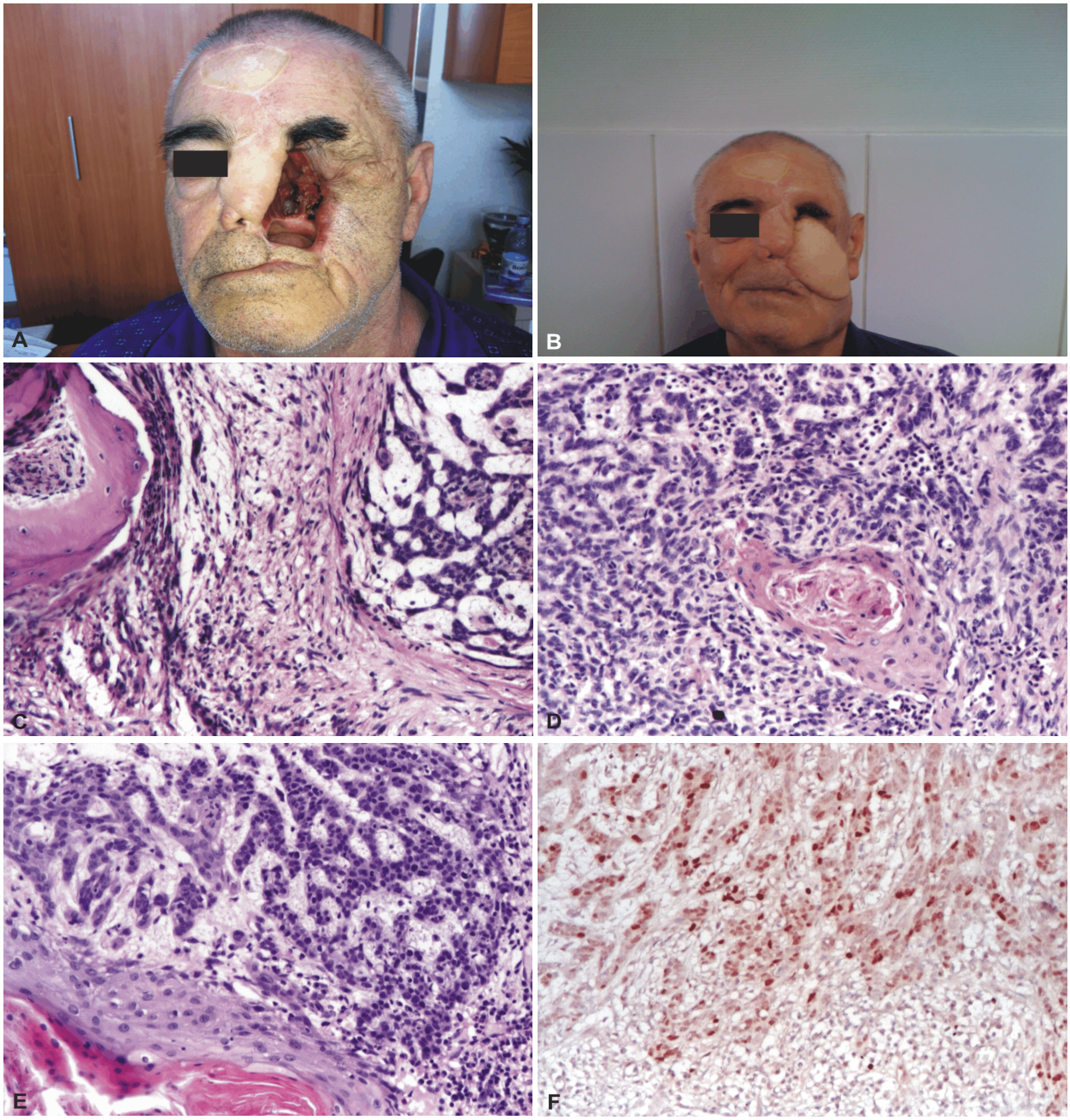

Figure 2 – ***Case No. 2. A 61-year-old male patient with a history of a tumor recurrence at the level of the nasal pyramid with extension at the inner canthus and intraorbital, which necessitated enucleation of the left eye socket, excision of the anterior wall of the maxillary sinus and hard palate. (A) Preoperative aspect. (B) Post-operative aspect at 21 days. (C–F) Histopathological exam: (C) Squamous cell carcinoma – bone invasion, HE staining, ob. ×10; (D) Squamous cell carcinoma, HE staining, ob. ×10; (E) Squamous cell carcinoma – poor differentiation, HE staining, ob. ×10; (F) Squamous cell carcinoma, Ki67 immunostaining, ob. ×10.***

Case No. 3

The third case was that of a 60-year-old patient operated in another clinic one year ago for a basal cell carcinoma of the lower left eyelid that had infiltrated the orbit. When he presented in our clinic, he has had the left eye enucleated and partial resection of the left maxilla; the defect was covered by means of a temporal muscular flap and a split-thickness skin graft. He presented with an ulcerated tumor that extended from the left nasal ala across the cheek up to the left eye socket.

The CT scan showed tumoral invasion of the remaining maxillary bone with extension to the pterygopalatine muscles; no cerebral tumoral masses were detected.

We performed radical excision – orbitomaxillectomy (resection of the remaining maxilla along with exenteration). A free latissimus dorsi flap connected to the facial vessels covered the defect. The excisional specimen was sent to pathology; it was found a poorly differentiated spinocellular carcinoma infiltrating full thickness the facial soft tissues (skin, fatty tissue, muscular fibers) with perineural invasion (Figure 3).

The postoperative evolution was slowly favorable.

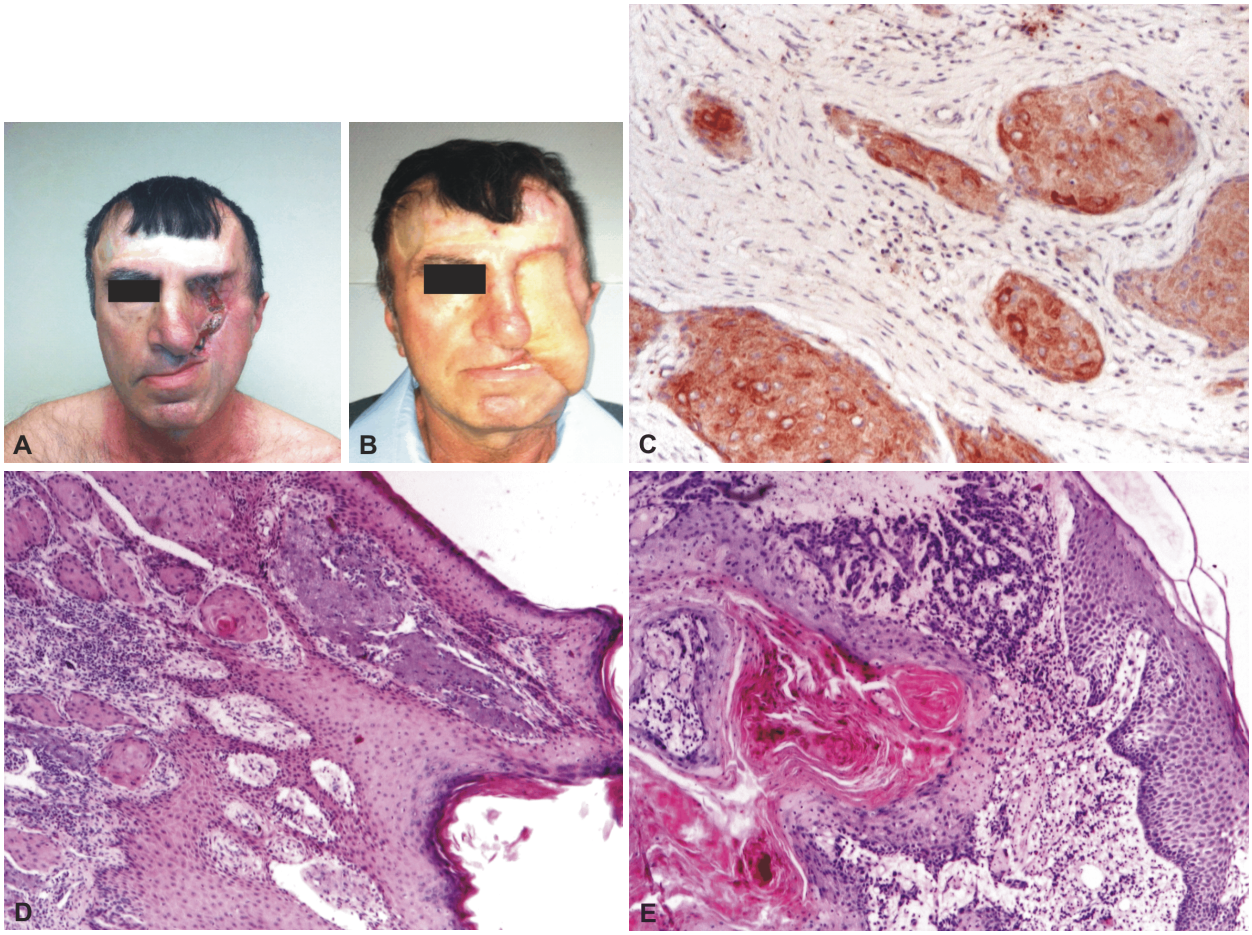

Figure 3 – ***Case No. 3. A 60-year-old patient operated in another clinic for a carcinoma with the left eye enucleated and partial resection of the left maxilla, covered by temporal muscular flap and a split-thickness skin graft. He presented with an ulcerated tumor that extended from the left nasal ala across the cheek up to the left eye socket. The excisional specimen showed a poorly differentiated spinocellular carcinoma infiltrating full thickness the facial soft tissues (skin, fatty tissue, muscular fibers) with perineural invasion. (A) Preoperative aspect of the ulcerated tumor. (B) Thirty days postoperative aspect with a musculo-cutaneous latissimus dorsi flap covering the hemifacial defect. (C–E) Histopathological aspects: (C) Squamous cell carcinoma, 34βE12 immunostaining, ob. ×10; (D) Squamous cell carcinoma, HE staining, ob. ×4; (E) Squamous cell carcinoma, HE staining, ob. ×4.***

Discussion

Basal cell carcinoma is the most common eyelid malignancy for which exenteration is usually performed. From the literature, we have that basal cell carcinomas count for 80–90% of all malignant tumors of the eyelids [9–12], the most common locations being the lower eyelid and the medial canthus; only 0.8% to 3.7% (T3 tumors, according to *AJCC* staging) of these lesions extend to the orbit, requiring exenteration [9, 11, 13].

Basal cell carcinomas are locally invasive tumors. Morbidity is increased in neglected tumors with large size and extension into deep soft tissue and bone. Recurrences are associated with infiltrative morphology at head and neck location, in part due to the difficulty in achieving free surgical margins.

The second most common malignancy of the eyelids is squamous cell carcinoma (5–10%) [14]. Squamous cell carcinomas are locally aggressive tumors with the capacity for metastasis. Aggressivity in SCC correlates with disease extension and poor differentiation. Narrow surgical margins are a risk factor for recurrence (Table 2).

Table 2 – ***Comparison of orbital exenteration series from the literature, showing duration of studies, number of cases and indications [1, 6–8, 10]***

Indication	Naquin, 1927–1953	Rathburn, 1940–1971	Simons, 1951–1964	Bartley, 1967–1986	de Concilis, 1976–1986	Levin, 1969–1988	Moriaux, 1981–1993	Goldberg, 1983–1999	Shields, 2001	Pushker, 1990–2000	Simon, 1999–2003	Nassab, 2005
Total no. of cases	48	48	31	102	39	99	44	25	56	26	34	32
Basal cell carcinoma	11	14	11	21	9	8	11	2	4	2	6	17
Squamous cell carcinoma	4	6	3	33	7	32	15	7	5	10	9	3
Malignant melanoma	12	8	7	16	8	18	7	6	31	5	9	6
Sebaceous carcinoma	0	1	0	6	0	6	0	3	3	6	3	4
Other epithelial tumors	6	8	5	9	10	15	0	7	0	1	1	2
Rhabdo-myosarcoma	2	5	2	2	2	2	2	0	0	0	0	0
Infection	1	0	0	1	0	6	0	0	0	1	0	0
Other	12	6	3	14	3	12	9	0	13	1	6	0

To reconstruct an exenteration defect, we have a large area of options. Many have chosen spontaneous granulation, split or full thickness skin grafts [15, 16]. The healing achieved by means of spontaneous granulation often takes several months; we have to accept a certain infection risk that delays the final result [15].

By skin grafting, the healing process is fast and we can apply early an orbital prosthesis [16]. As regional surgical options, we have the temporalis muscle flap associated with skin graft [17, 18], the cervicofacial flap [19], the temporoparietal fascial flap and the frontal flap [20–22]. Local skin flaps provide better color and contour match. In these cases, the associated bony defects may be reconstructed with split calvarial bone grafts. An important landmark is the medial canthal position; it must be fixed in place for accurate placement of a later prosthesis.

At last but not least, we have the free tissue transfer alternative using the rectus abdominis [23], latissimus dorsi [24], radial forearm [25], lateral arm [26], antero-lateral thigh flap.

In patients of high anesthetic risk, reconstruction by means of skin graft and orbital prosthesis must be considered. Life-like prosthesis can be made; sometimes, after exenteration, the craniofacial reconstruction with bone-anchored epithesis is a safe way towards social reintegration. The prosthesis must have accurate globe placement and good texture and color [27, 28]. By means of osseointegrated implants, we have good positioning for the prosthesis and comfort. It is best to place the implants at the same time with the tumoral resection when surgical exposure is best. This decision may be influenced by a consecutive radiotherapy. The success rate of implants in irradiated bone varies between 33% and 96% [28, 29]. There are various concerns; either the tumor site receives a lower dose of irradiation because it is shielded by the implants, either that the implants converge a higher dose of irradiation to surrounding areas, with possible radionecrosis involving the soft tissues and even the bone with implant failure [30].

The reconstruction of exenteration defects with epithesis offers the advantage of easy visualization of the tumor site and early recurrence detection, especially in cases when the pathology exam confirms perineural invasion.

Reconstruction methods by free tissue transfer are often used when the exenteration is associated with maxillectomy. One of the first used flaps was the rectus abdominis or the latissimus dorsi [23, 24, 31–34]. They provide sufficient bulk to obliterate the postexcisional cavity, thus making a barrier between the oral, nasal and orbital cavities. Intraoral mucosalisation of the muscle surface occurs in 3–4 weeks and no skin grafting is necessary [35]. There are disadvantages: they do not provide bony malar support and a certain mid-face projection and we cannot provide dental rehabilitation by means of osseointegrated implants. Attempts have been made regarding this latter aspect with a fibular osteocutaneous flap [34, 36]; even in the "double barrel" fashion, it does not have the sufficient height for the implant fixtures. Another alternative is the iliac crest-internal oblique free flap. We have enough muscle bulk and necessary bone stock to insert implants. There are shortcomings: a variable vascular anatomy and a short pedicle, which may need interpositional vein grafts – a consecutive higher percentage of flap failure; the skin island of this flap gives a poor aesthetic outcome in midface reconstruction [33, 37].

Various authors have described the use of chimeric flaps in midface reconstruction. Among these, the latissimus dorsi-scapular/parascapular flap gives a better fit for mid-facial projection and enables bony reconstruction of the alveolar ridge, malar eminence and orbital floor [38, 39].

We can thus perform a three-dimensional reconstruction using the flap units, each of them having its own vascular pedicle with separate arcs of rotation.

In our patient's series, most of them were classified after anesthetic evaluation as ASA grade II or more. This implies that we performed exenteration in cases with significant comorbidities; some of the reconstructive alternatives are long procedures, not very well tolerated in old patients; however, increasing microsurgical experience may allow a single stage reconstruction by free flap transfer.

The early results were favorable in all cases. Still, we

have a short follow-up (between four and 36 months). In every case, the orbital involvement was indicated by at least one of these: bone fixation of the mass, limitation of ocular motility and globe displacement. In one case, we have a relapse at three years interval; the pathology exam in this case had emphasized the perineural invasion, which we believe to be the worst prognosis factor. For squamous cell carcinoma, longitudinal studies have shown that although tumor diameter and tumor thickness are both risk factors for metastatic spread only the latter is an independent risk factor for local recurrence.

The question is if it is not better to excise the tumor and wait for the pathology exam (especially in advanced cases like the ones described). If the perineural invasion is confirmed, we should use a simpler coverage method or just an epithesis in order to detect early a possible recurrence. The adjunctive radiotherapy in these cases is mandatory. However, there are no studies up to date to assure that CT/MRI scans are a reliable instrument to assess a possible disease relapse.

Conclusions

The reconstruction after orbital exenteration is still a debatable subject. The perineural invasion, when detected at the pathology exam, occurs mainly on the infraorbital nerve. We believe that for better and safer results the length of the perineural invasion should be assessed; given this parameter, we should decide to restrict to an epithesis and to inspect periodically the postexcisional cavity or to proceed to other methods of reconstruction. We should also consider the cases when the patient is not surgically curable and the excision-reconstruction procedure is done only to improve the quality of life.

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