Original Articles

Management of periocular tumors with Mohs micrographic surgery

Manejo dos tumores perioculares com cirurgia micrográfica de Mohs

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ABSTRACT

Introduction: Due to the risk of invasion of the orbital cavity and involvement of noble structures, the periocular region requires specific knowledge related to the anatomy and biological behavior of tumors in this region.

Objective: To present the particularities and complexity of the approach to periocular tumors, through the analysis of cases treated at a Mohs micrographic surgery specialist center.

Methods: A retrospective, observational, cross-sectional study was carried out based on data collected through a review of medical records, operative records, and photographic archives. Thirty-four cases were analyzed between April 2010 and April 2014.

Results: Thirty-one basal cell carcinomas, two squamous cell carcinomas, and one sebaceous carcinoma were operated. Of these, 22 (64.70%) were primary tumors, and 12 (35.29%) were recurrent or incompletely excised. The nodular was the most common type of basal cell carcinoma (38.70%), followed by the micronodular (25.80%), the infiltrating (22.58%), the sclerodermiform (6.45%), the superficial (3.22%) and the adenoid (3.22%). Most of the lesions affected the lower eyelid (44.11%), followed in number by the internal canthus (41.17%), the upper eyelid (11.76%), and the external canthus (2,94%). There was only one recurrence following Mohs micrographic surgery.

Conclusions: Most tumors had an aggressive histological subtype, especially those located in the internal canthus. Despite the study's limitations, the strict histological control of Mohs micrographic surgery, combined with the multidisciplinary approach to patients, provided excellent oncological, functional, and cosmetic results.

Keywords: Mohs surgery; carcinoma, basal cell; carcinoma, squamous cell; eyelid neoplasms; orbit evisceration.

RESUMO

Introdução: *Pelo risco de invasão da cavidade orbitária e comprometimento de estruturas nobres, a região periocular exige conhecimento específico relacionado à anatomia e ao comportamento biológico dos tumores dessa região.*

Objetivo: *Apresentar as particularidades e complexidade da abordagem dos tumores perioculares por meio da análise dos casos operados em um centro de referência em cirurgia micrográfica de Mohs.*

Métodos: *Estudo retrospectivo, observacional, transversal, com dados colhidos por revisão de prontuários, ficha operatória e arquivo fotográfico. Analisados 34 casos entre abril de 2010 e abril de 2014.*

Resultados: *Foram operados 31 carcinomas basocelulares, dois carcinomas espinocelulares (CEC), e um carcinoma sebáceo (CS). Desses, 22 (64,70%) tumores primários, e 12 (35,29%) recidivados ou incompletamente excisados. O CBC nodular foi o mais frequente (38,70%), seguido do micronodular (25,80%), infiltrante (22,58%), esclerodermiforme (6,45%), superficial (3,22%) e adenoide (3,22%). A maioria dos tumores acometia pálpebra inferior (44,11%), seguida do canto interno (41,17%), da pálpebra superior (11,76%) e do canto externo (2,94%). Após CMM, houve somente uma recidiva.*

Conclusões: *A maioria dos tumores apresentava subtipo histológico agressivo, especialmente os localizados em canto interno. Apesar das limitações do estudo, o rigoroso controle histológico da CMM, aliado a abordagem multidisciplinar dos pacientes, propiciou excelente resultado oncológico, funcional e cosmético.*

Palavras-chave: *cirurgia de Mohs; carcinoma basocelular; carcinoma de células escamosas; neoplasias palpebrais; exenteração orbitária.*

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INTRODUCTION

The periocular region is often affected by malignant skin tumors, with basal cell carcinoma (BCC) being the most frequent, followed by squamous cell carcinoma (SCC), and less commonly by sebaceous carcinoma (SC) and Merkel cell carcinoma. Basal cell carcinoma is responsible for 80-90% of all malignant neoplasms of the eyelids.[1] It mainly affects the lower eyelid (50-60%), followed by the medial canthal region (25-30%), and to a lesser extent by the upper eyelid and lateral canthal region.[1,2] In the literature, the mortality rate is variable, estimated at 1.5 to 11%,[3,4] and in general is precipitated by intracranial invasion. Tumors involving the medial canthal region are correlated to an increased risk of intraorbital and intracranial invasion.[1,2]

Although less common, SCC has a more aggressive biological behavior due to its metastatic potential. It is estimated that there is a 24% risk of metastasis to regional lymph nodes secondary to palpebral SCC, and an 8% risk of perineural invasion.[1,2,5]

Perineural invasion can result in a worse prognosis, due to an increased risk of orbital invasion, and an increased recurrence rate. Intermittent or continuous pain, and prickling are symptoms that are often associated with perineural invasion.[1,5]

Sebaceous carcinoma is often undertreated, due to the fact that it often mimics benign diseases such as blepharoconjunctivitis or chalazion. It can simulate a BCC or a SCC, and has great potential to metastasize and be lethal.[5,6] It originates in the meibomian glands in the tarsal plate, or in the Zeiss glands, which are related to the eyelashes. It is more frequent in the upper eyelid, but may cause multifocal lesions, with an estimated orbital invasion of around 15-19% of cases. Metastases can occur in 17% of cases, and mortality is estimated at 6%.[5,6]

Although rare, Merkel cell carcinoma may arise on the eyelids. It has great lethality, grows rapidly, and primarily affects elderly female patients. Metastases may occur early, having a negative affect on the prognosis for recovery. Other malignant neoplasms in this region are even rarer.[1,5]

The surface anatomy of the periocular region classically comprises four anatomical subunits: upper eyelid, lower eyelid, lateral canthal region, and medial canthal region.[2]

Periocular tumors constitute a challenge to the dermatologic surgeon who, while minimizing the functional impairment of the eyelids,[7] should pay attention to the fact that this region is located over the embryonic cleft area, and is therefore less resistant to tumoral spread.[1,8,9] The risk of orbital invasion is greater with biologically aggressive tumors, such as SC and SCC. Although rare in occurrence, it is estimated that the risk of a periorbital BCC invading the orbits varies from 0.8 to 3.6% of cases.[8-10] Among the risk factors are histologic sclerodermiform, micronodular, and infiltrating subtypes, recurrent tumors, development duration in excess of one year, compromise of the medial or lateral canthus, and neural invasion.[9-11] The signs and symptoms that are most frequently linked to orbital invasion are adherence of the tumor to the orbital bone, limitation of the ocular motility, diplopia, displacement of the eyeball due to mass effect, palpebral ptosis and, more rarely, proptosis.[1,12] The tumor spreads through the periosteum of the orbital cavity, but rarely invades the eyeball.[1,11] Intracranial involvement usually takes place via neural invasion through the superior orbital fissure,[13,14] which is the path of the oculomotor (III cranial nerve) and abducens nerves (VI cranial nerve), and lacrimal and frontal branches of the ophthalmic nerve – which in turn is a branch of the trigeminal nerve (V cranial nerve). A multidisciplinary approach, with the presence of an ophthalmologist, and/or head and neck surgeon is essential in such cases.

Mohs micrographic surgery (MMS) is considered the gold standard treatment for periocular tumors due to the fact that it enables accurate histological control of surgical margins, ensuring a higher cure rate, with lower recurrence rates.[10,15,16] An additional advantage of the Mohs' technique is that it allows for a greater economy of the healthy tissue around the tumor, favoring the preservation of important structures and the surgical closure.[9-11]

Although some periocular tumors are easily handled, most of them are difficult to approach due to their size, location, and aggressive biological behavior. Salashe[17] notes that for these tumors, there should ideally be a multidisciplinary team prepared to deal with any tumor size, complex surgical reconstructions, and the management of any possible complications.

The present study is aimed at presenting the particularities and challenges of approaching periocular tumors, through analysis of cases where operations were performed at a Mohs micrographic surgery reference center.

METHODS

A retrospective, observational, cross-sectional study was carried out through a review of medical records, operative records, and a vast photographic archive.

Thirty-four periocular tumors were studied in 33 patients operated on between April 2010 and April 2014, and who were followed up with until September 2014. The patients analyzed had Fitzpatrick skin phototypes II and III. The tumors had the following distribution: 6 in men and 28 in women, 22 were primary tumors, 10 were recurrent, and 2 were incompletely excised.

All patients who underwent surgery had previous biopsies, with paraffin specimens and reports issued by pathologists. Tumors were divided according to histologic type and classified according to the previous biopsy report or the histological analysis performed during surgery (where it was possible to detect remaining tumors in the evaluated margins). In case of an inconsistency between histological subtypes observed in the biopsy reports and those observed in the slides analyzed during surgery, the latter was chosen for the study. This happened in three cases: the previous reports recorded the nodular BCC subtype in two cases and the sclerodermiform BCC subtype in one case; during surgery all three were found to be of the infiltrating BCC type.

In two BCC cases there was no classification of the histological subtype in the report of the incisional biopsy issued by the pathologist. In such cases, the histological slide was requested

and analyzed by the Mohs surgeon, with both having been classified as nodular BCC subtype.

The tumors were still classified into primary, recurrent and incompletely excised, and those that had had their surgical safety margin compromised. This was done according to the histological report drafted after the previous conventional surgery and in consideration of those that were referred to Mohs micrographic surgery for a widening of margins.

The anatomical features of this region impose difficulties for dermoscopic visualization, by hampering the delimitation of margins through dermoscopy. Therefore, a choice was made to delimit margins with the naked eye. In all cases an initial surgical margin was marked based on the clinically apparent boundaries of the lesion. A 2 mm margin was used for nodular BCCs, while a 3 mm margin was used for other BCC subtypes, SCCs, and SCs.

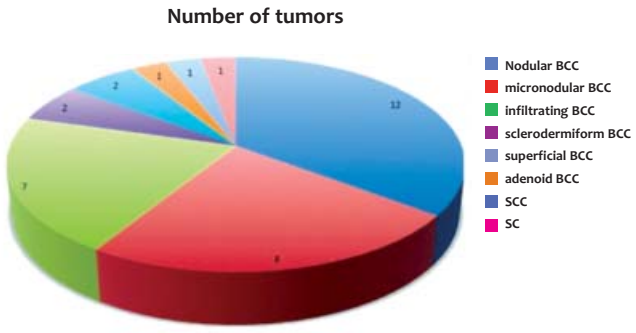
Patients with recurrent or aggressive histological subtype tumors, or with tumors located in the medial or lateral canthal region underwent computerized tomography (CT) with contrast and fine cuts in the topography of the orbit. In all, 10 patients with an increased risk of subclinical invasion of the intraorbital structures were operated on with the participation of an ophthalmologist specializing in ocular plastic. One patient with recurrent SC also had the participation of a head and neck surgeon.

All patients with lesions in the medial canthal region underwent a probing of the upper and/or lower lacrimal canaliculus aimed at minimizing the risk of injury during the tumor resection (Figure 1).

Only two cases were operated on under general anesthesia; the others received tumescent local anesthesia and sedation.

Most tumors operated on were located in the lower eyelid or internal canthus.

Figure 1: Probing of the lower lacrimal canaliculus. This maneuver was always used in tumors located in the inner canthus in order to minimize the risk of sectioning the lacrimal canaliculus



Graph 1: Histological types of operated tumors

RESULTS

BCC was the most frequent tumor, at 31 cases, with the nodular subtype found in 12 patients, followed by the micronodular (8 cases), infiltrating (7 cases), sclerodermiform (2 cases), superficial (1 case) and one with adenoid differentiation. Other

If the most aggressive histological BCC subtypes (micronodular, infiltrating and sclerodermiform) are added to the SCC and SC cases, it is possible to notice a high incidence of aggressive tumors, as compared with subtypes considered less aggressive

Table 1: Histological type of the tumor & location

type of tumor	Upper eyelid	Lower eyelid	Internal canthus	External canthus	Column 6	Recurrent / Including excised	1 phase 1	2 phases	3 phases	4 phases	Total number of tumors
nodular BCC	0	8	4	0	11	1	9	3	0	0	12
micronodular BCC	1	3	4	0	3	5	1	3	3	1	8
infiltrating BCC	1	3	2	1	5	2	4	0	2	1	7
CBC esclerodermiforme	0	0	2	0	1	1	0	1	1	0	2
superficial BCC	1	0	0	0	0	1	0	1	0	0	1
adenoid BCC	0	0	1	0	1	0	0	1	0	0	1
SCC	0	1	1	0	1	1	1	1	0	0	2
SC	1	0	0	0	0	1	1*	0	0	0	1
Total	**4**	**15**	**14**	**1**	**22**	**12**	**16**	**10**	**6**	**2**	**34**

Note the high incidence of recurrent tumors, especially micronodular BCCs.
Note: *Exenteration of SC performed by head and neck surgeon.

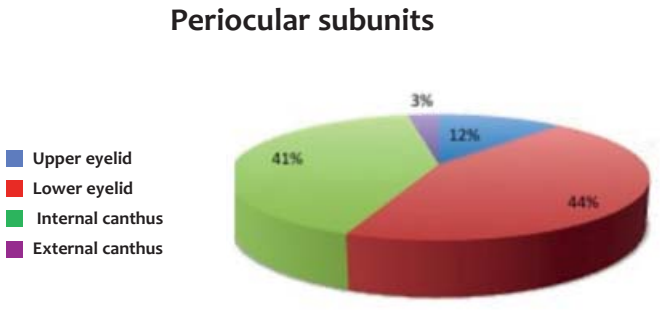


Gráfico 2: Anatomical location of tumors operated on

Most tumors operated on were located in the lower eyelid or internal canthus

tumors operated on were: SCC (2 cases) and one recurrent SC in the upper eyelid (Graph 1).

None of the patients had an image compatible with the invasion of the orbital cavity under CT.

The most affected periocular subunit was the lower eyelid (15 cases), followed by the internal canthus (14 cases), the upper eyelid (4 cases), and external canthus (1 case) (Table 1 and Graph 2).

Regarding the number of stages/phases needed to achieve free margins, only 16 were free of neoplasms, given the initial margin of 2-3 mm. In 10 cases, 2 expansion phases were required; 6 cases needed 3 phases; and 2 cases required 4 phases. (Table 2)

Surgical closure was highly variable according to the size of the surgical defect and location. In lower eyelid tumors, 7 inferior rotation flaps were performed, 1 upper eyelid transposition flap, 1 primary closure, and 6 ear helix chondro-perichondrial grafts.[5] The simple skin graft was used in 9 tumors in the internal canthus, skin flaps were used in 3 cases, and primary closures were used in 2 cases. In the upper eyelid, skin flaps were used in 2 cases, a graft was used in 1 case, and the orbital exenteration was used in 1 case of recurrent SC. In the single case of an external canthus lesion, the tumor occupied 1/3 of the upper eyelid and half of the lower eyelid (Figure 2). An ear helix chondro-perichondrial graft was used for the reconstruction of the inferior tarsus and a periosteal flap for the reconstruction of the superior tarsus, followed by the performance of a lateral advancement skin flap for the closure of the upper eyelid.

The follow-up time ranged from 5 to 48 months, with 1 to 4 years in 26 patients (76.5%) and shorter than 1 year in 8 patients (23.5%). One female patient had recurrence of an extensive micronodular BCC in the nose and internal canthus (Figure 3). Having previously undergone PDT in 2012, she was advised by a dermatologist physician to seek care at the authors' dermatologic service, when the lesion recurred. She then underwent MMS in January 2013, through surgical reconstruction with a simple skin graft. After 8 months a tumor recurrence was identified at the graft's superior border, and she underwent a new MMS in November 2013. The patient had no signs of recurrence up to the date this paper was submitted (10 months of follow-up).

Figure 2: In the single case of a tumor in the orbit's external canthus, the final surgical defect shows a loss of full thickness in 1/3 of the upper eyelid, in 1/2 of the lower eyelid, and of tissue in the temporal region

Table 2: Histological type of the tumor/ number of Mohs stages

	1 phase	2 phases	3 phases	4 phases	Total
nodular BCC	0	8	4	0	11
micronodular BCC	1	3	4	0	3
infiltrating BCC	1	3	2	1	5
sclerodermiform BCC	0	0	2	0	1
superficial BCC	1	0	0	0	0
adenoid BCC	0	0	1	0	1
SCC	0	1	1	0	1
SC	1*	0	0	0	0
Total	**4**	**15**	**14**	**1**	**22**

There was a trend for the aggressive histologic subtypes to need additional expansion phases in order to achieve tumor-free surgical margins.

* SC with invasion of the bulbar conjunctiva was referred to ocular enucleation.

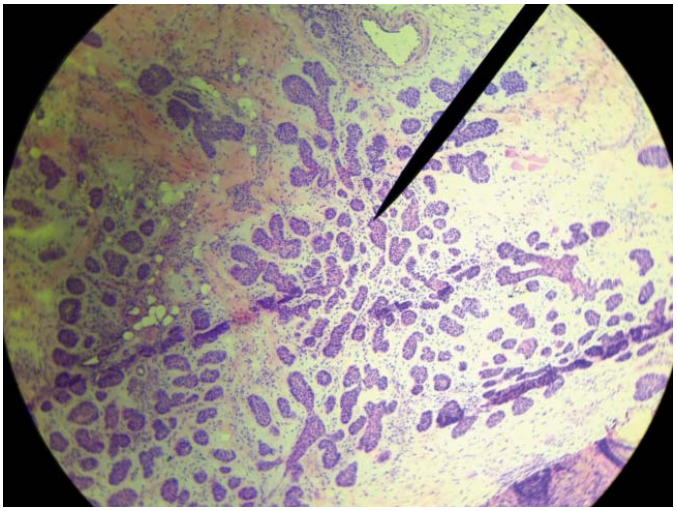


Figure 3: Photomicrography of the recurrent micronodular BCC. It is possible to notice several islets of tumor cells, which are responsible for the high recurrence rate of this histologic subtype.[25]

Regarding complications in the post-operative period, 1 patient had a lower lacrimal canaliculus injury due to tumor infiltration, which progressed to epiphora, and was then referred to the ophthalmologist for evaluation for a possible connective tissue surgery (dacryocystorhinostomy) six months after the CMM. In 5 lower eyelid tumor cases there was a slight scleral show, without relevant functional or aesthetic compromise. One case progressed with chondrite in the donor area of the chondro-perichondrial graft in the ear helix, which was easily resolved with oral corticosteroids.

DISCUSSION

In line with the international literature, BCC was the most common tumor (91.17% of the patients).[12] Considering the fact that the BCC's more aggressive histological subtypes are the sclerodermiform, micronodular and infiltrating[1,3,] the present study will have come across a large number of aggressive tumors (54.83%) – higher than the average found in the literature.[1,8,10] This may be explained by the fact that they were sourced at a reference center for MMS, where most cases have a high complexity level, which also explains the large number of recurrent or incompletely excised tumors, with 12 cases (35.29%) having been operated on during the study's period.

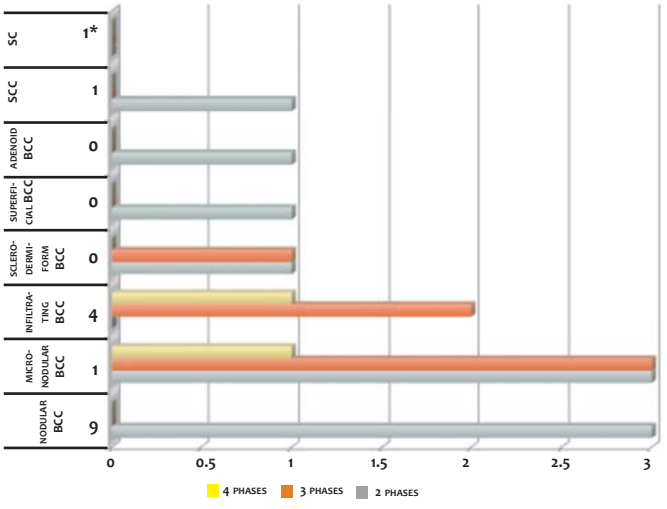
As compared to BCCs, tumors located in the internal canthus have a higher incidence of aggressive subtypes,[1,6,16] with 4 micronodular, 2 infiltrating and 2 sclerodermiform tumors (Table 1). That was also the location of the only case of recurrence after MMS. This confirms data from the literature, which point to internal canthus tumors as having greater invasiveness and a poorer prognosis.[18,19]

As for the location of the lesions, the data from the present study is aligned to the literature,[1,2] with a predominance in the lower eyelid (44.11%), followed by the internal canthus (41.17%), the upper eyelid (11.76%) and the external canthus (2.94%) (Graph 2).

Large surgical margins imply larger surgical defects, requiring complex reconstructions. Most authors recommend using the smallest possible safety margin, sufficient only to completely remove the tumor without generating excessively large defects, thereby minimizing the functional and cosmetic deficits. Hsuan et al.[20] demonstrated that 2 mm margins were insufficient for the complete removal of nodular BCC from the eyelid in about 18% of cases. Chadha et al.[21] recommend 2 mm margins in clearly delimited BCCs, having found incompletely excised surgical margins in approximately 13% of cases and a recurrence rate of 3.3%. Other studies recommend 3-5 mm surgical margins for tumors in the area.[8, 11, 22]

Although the surgical margins recommended for the treatment of BCC with conventional surgery are variable and depend on the histological type and the affected area,[23] in general, most authors consider surgical margins between 2-5mm reasonable for the eyelids.[11, 19-21] With MMS, the authors used an initial margin of 2-3mm, which was not enough to excise the tumor in most studied cases, since 52.94% of tumors needed more than 1 phase of surgical expansion (Graph 3). This finding demonstrates the importance of the histological control of margins through MMS.

Although some authors question the use of MMS for the treatment of SC,[24] the strict histological control achieved by the Mohs technique was important in the management of a case of recurrent SC in the upper eyelid in which a bulbar conjunctival invasion was identified during the procedure. In this case a choice was made for an orbital exenteration during the same surgical event, with the involvement of a head and neck surgeon (Figures 4 and 5). After the exenteration, a new perioperative histological analysis of the margins was performed, in which the tumor was not observed, making it unnecessary to perform a new surgical approach to extend the exenteration. The patient's



Graph 3: Correlation between the histological types of tumors that required more than one phase of margin expansion, and the number of phases to achieve tumor-free surgical margins

Figure 4: Surgical defect after orbital exenteration, including surgical removal of the eyelids for the treatment of recurrent SC. A choice was made for exenteration after histological confirmation of extensive conjunctival compromise

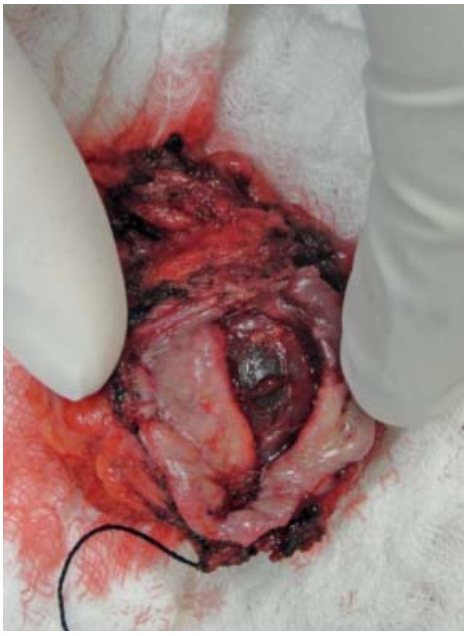


Figure 5: Anatomical specimen containing eye and eyelids, after orbital exenteration for the treatment of a SC. Histological analysis by MMS showed an absence of residual tumor in the surgical margins

follow-up was carried out by the Head and Neck Surgery and Radiotherapy Departments, with no recurrence having been found as of the submission date of the present paper.

The multidisciplinary team effort, which included the contribution of an ophthalmologist and a head and neck surgeon, was critical to the success of the most complex cases, allowing a better approach to deep soft tissues in the orbit and assisting in complex surgical reconstruction and post-operative management.

Notwithstanding the short follow-up time, which ranged from 1 to 4 years in 76.5% of patients – and shorter than 1 year in 23.5% - there was a low recurrence rate, with only one case (2.94%) to date.

Regarding the type of surgical reconstruction, several techniques were used according to the surgical defect's location and size. Five patients developed slight scleral show, with minimal aesthetic impact, and an absence of any recorded cases of ectropion, entropion, or infection.

CONCLUSIONS

The complex anatomy and the peculiar biological behavior of tumors affecting the periorbital region require a specific knowledge on the part of the dermatologic surgeon and the support of a multidisciplinary team.

Most tumors operated on had aggressive histologic subtypes, with roughly 1/3 being recurrent or incompletely excised, evidencing the high degree of difficulty of treating these tumors.

Regarding BCCs, tumors located in the internal canthus showed more aggressive biological behavior, coinciding with the literature data.[1,16,19] This was also the location for the only case of recurrence after MMS – one micronodular BCC, which had a large subclinical size – a fact aligned with the literature that deems this subtype as highly recurrent.[25]

Although surgical margins of 2-3 mm have been performed in all tumors by numerous authors,[18,20,21,22] and considered reasonable for the treatment of primary BCC, most cases in the present study required successive expansion phases in order for neoplasia-free margins to be achieved (Table 2). This datum demonstrates the importance of strict histological control of surgical margins achieved by MMS.

Of the 20 tumors with subtypes considered aggressive, 13 (65%) required more than one expansion phase. Of the 14 less aggressive tumors, only 5 (35.7%) demanded more than 1 expansion phase, demonstrating the relationship between aggressive histological types and subclinical invasion.

Despite the limited size of the sample and the short follow-up time, MMS yielded a high cure rate and a low recurrence rate to date.

The multidisciplinary approach to periocular tumors provided an excellent oncologic management, with maximum functional and aesthetic preservation.

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