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Ocular Medulloepithelioma: Case Report and Literature Review

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Abstract

Medulloepithelioma is a congenital tumor of very low incidence, generally unilateral and rarely bilateral, with very few cases appearing in the global literature. It primarily develops in the ciliary body, and its diagnosis is differential, with retinoblastoma as the primary option for diagnosis. This is the first case of medulloepithelioma identified at the National Institute of Neoplastic Diseases in Lima, Peru, the leading cancer-treatment institution of the nation. A case report of a 4-year-old female with decrease of visual acuity and a spot-like lesion in her right eye, initially diagnosed as glaucoma and cataracts. In October of 2020, the patient was treated surgically with the removal of her right eye once the diagnosis of orbital Medulloepithelioma was confirmed. She had early recurrence three months later. A follow-up MRI confirms recurrence at the surgical bed level, as well as the presence of an ipsilateral parotid node with a metastasis biopsy that tests positive. The patient was subjected to orbit exenteration, right cervical dissection, and homolateral parotidectomy with skin graft. The pathology confirms the diagnosis of orbit medulloepithelioma in the lesion of the surgical site and the parotid region, while the nodal dissection did not report compromised nodes. She received adjuvant chemotherapy and concurrent chemoradiotherapy localized to the tumor bed and parotid region with a dose of 50 Gy in 25 sessions. Once this concurrence ends, she continues with chemotherapy.

Keywords: Ciliary body; Intra-ocular; Medulloepithelioma; Uveal neoplasm; Orbital tumors

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Introduction

Medulloepithelioma is a rare tumor that originates from the primitive medullary epithelium of the Central Nervous System (CNS), is most often located in the ciliary body, and can also occur in the retina and optic nerve [1]. Histologically, intraocular medulloepithelioma is classified into teratoid and non-teratoid, the latter being the most frequent. They are also classified into benign and malignant [2]. The average age of presentation is in childhood between 4 and 5 years, however, cases of adult medulloepithelioma or [3] have been described.

It presents as slow growing and is locally invasive, is typically characterized by presenting a cyst or mass in iris, ciliary body, or anterior chamber with decreased visual acuity, epiphora, pain, leukocoria, exophthalmos, strabismus, iridis rubeosis, cataract, subluxation of the lens and generally tends to be unilateral, predominantly in the right eye [4]. Although bilateral cases have been described [5].

Case Presentation

A 4-year-old female, from Lima, who presented with approximately 2 years of a spot like lesion in her right eye. She was evaluated at the National Institute of Child Health (INSN) where she was diagnosed with glaucoma and cataract of the right eye. Surgical resection was performed, and a valve was placed. Six months after surgery, she presents with growth of conjunctival tissue in the right eye, a biopsy was performed with result of subepithelial connective tissue infiltrated by basaloid pattern carcinoma with basophilic stroma of myxoid appearance and tubular structures with probable differential diagnosis annexal *vs.* pseudoglandular basal cell carcinoma.

The patient was referred to the National Institute of Neoplastic Diseases (INEN), Lima-Peru, where she was evaluated by the Department of Ophthalmology, an increased volume of the right

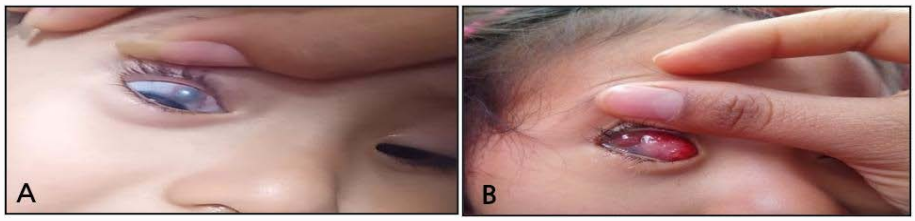

Figure 1: A: Lesion at presentation (May 2020). B: Lesion 4 months later.

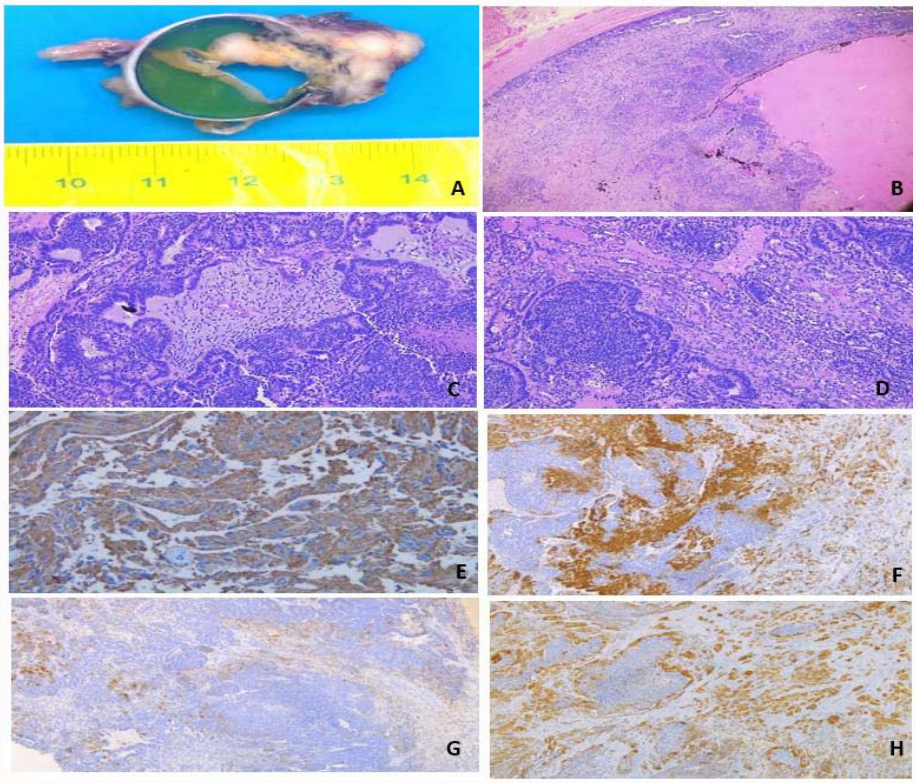

Figure 2: (A) Right eyeball measuring 25.0 mm × 30.0 mm in diameter and optic nerve of 12.0 mm × 3.0 mm, in the anterior part lobular proliferative lesion of 25.0 mm × 20.0 mm was observed, replacing the choroid and compromising the conjunctiva. The eyeball has an upper temporal level Ahmed's valve of 15.0 mm in diameter and 2.0 mm in thickness. At the cut, a grayish-brown tumor was evidenced that replaces the anterior and posterior chamber and extends to the vitreous humor in an area of 30.0 mm × 20.0 mm. B) The tumor was composed of cords, bands and anastomosed ribbons of polarized neuroepithelial cells that resemble the embryonic medullary epithelium (H&E, x400). C and D) The polarized neuroepithelial elements were surrounded by a relatively acellular myxoid stroma. E, F, G and H) Immunoexpression of tumor cells reveals positivity for synaptophysin, S100, HMB45 and LIN28 (IHQ, x400).

eyeball with corneal opacity was found, conjunctival growth located in the nasal sector that protrudes from the palpebral cleft associated with a decrease in visual acuity of the right eye (Figure 1).

On September 19th, 2020, Magnetic Resonance Imaging (MRI) of Orbit showed at the level of the right orbit a solid lesion that compromises the right eyeball in the anterior chamber of 2.6 cm × 2.3 cm, with cystic areas predominating its posterior aspect. At the same time, a review of the initial pathology was carried out; it reported an epithelial malignancy characterized by areas of basaloid appearance, presence of cell cords and myxoid stroma with phenotypic characteristics suggestive of Medulloepithelioma. IHC: SALL4-, CK7-, CK20-, KI67: 40%, P63: -, EMA positive in few cells, S100+, CerbB2-, CD117-, Calponin-, SNP positive in few cells, WT1 cytoplasmic expression in focal population, PGAF positive in some cells, SBP negative. She underwent enucleation of her right eye on October 2020, with pathology report showing malignant medulloepithelioma grade III, absent necrosis, unifocal tumor foci, invasion of absent optic nerve, and free surgical margins (Figure 2).

Post-surgical MRI of the brain in January 2021 a hypointense tissue in the tumor bed that restricts diffusion, measuring 11 mm × 7 mm, non-specific appearance (Figure 3A, 3B).

Follow-up MRI 03 months later showed, a hypointense tissue of 10 mm × 8 mm, suspicious for disease recurrence, associated with an adenopathy in right parotid of 1.6 cm × 1.4 cm. A biopsy of right orbital tumor reported inflammatory tissue and the right intraparotid nodule reported round cells neoplasm in relation to medulloepithelioma.

Two months later, a repeated MRI showed interval size increase of the nodular formation in the surgical bed of 13 mm × 10 mm, and the adenopathy located in the right parotid of 1.8 cm × 0.7 cm is evident, no other adenopathy was found (Figure 3C, 3D).

Due to recurrence of disease on the surgical bed and adenopathy

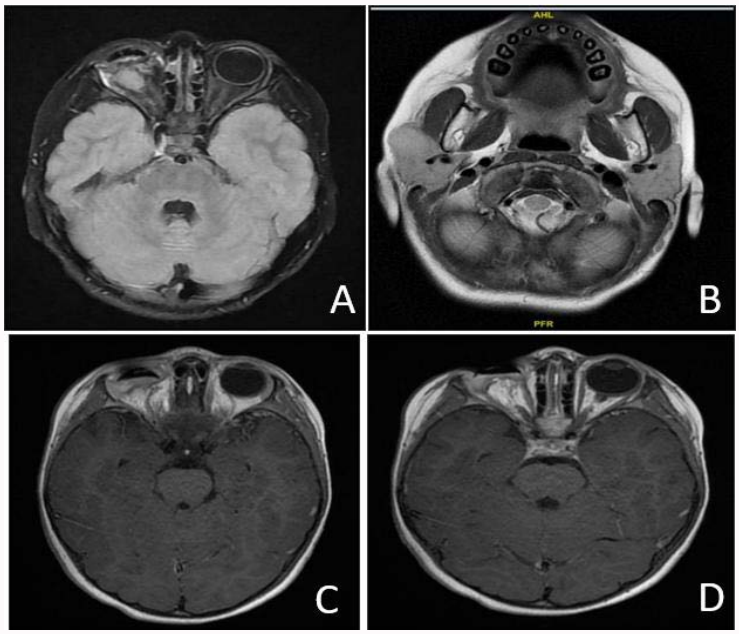

Figure 3: A and B) MRI of the brain January 2021 (T2 with contrast). C and D) MRI of post-surgical brain June 2021 (T1 c/c).

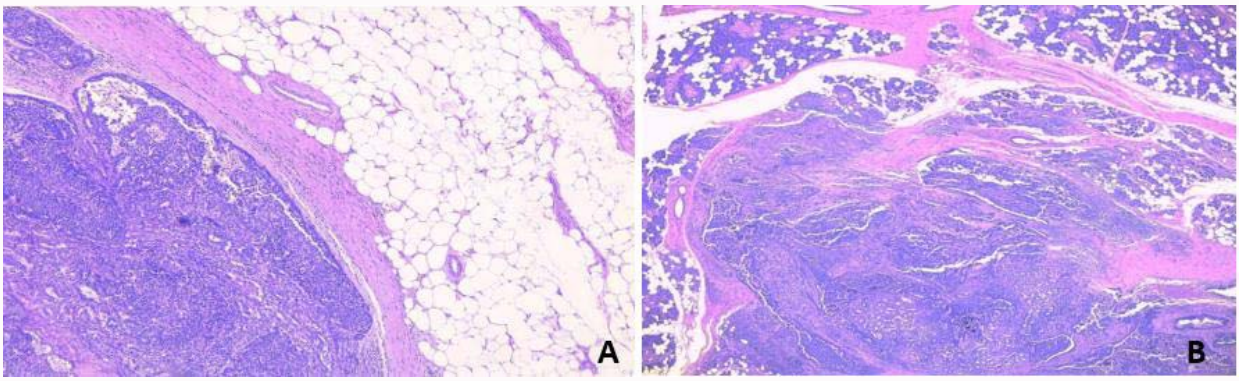

Figure 4: A) The residual neoplasm was surrounded by a hyaline fibrous layer that infiltrated periorbital fat (H&E, x100). B) Additional criteria for malignancy include invasion of ocular tissues and extraocular involvement, the image shows metastasis to parotid (H&E, x100).

at the right parotid, an orbital exenteration, right cervical dissection, right parotidectomy and skin graft were performed with pathology report of non-teratoid malignant medulloepithelioma, committed orbital soft tissue structures, surgical margins less than 1 mm from the posterior edge, parotid gland with metastasis of medulloepithelioma of predominantly defined and partially infiltrative edges. Lymph nodes 0/24 positives (Figure 4A, 4B).

Adjuvant treatment with a course of chemotherapy based on vincristine, etoposide and carboplatin was prescribed, continuing with external beam radiation therapy and concurrent chemotherapy.

Radiotherapy was administered with conventional fractionation schedule at a dose of 5000 cGy in 25 sessions at 200 cGy for each fraction, using VMAT conformal technique to the orbital and parotid surgical bed. She presented skin toxicity grade I limited to the irradiation field; treatment was well tolerated (Figure 5, 6).

Post chemo radiation MRI, 05 months later, showed post enucleation status with scarring tissue at the surgical bed and absence of the right parotid gland without signs of recurrence or persistence of disease (Figure 7).

She completed chemotherapy and is being monitored by the pediatric department (Figure 8).

Discussion

The medulloepithelioma was initially called primitive carcinoma by Badel and Lagrangef in 1892. In 1926 Bayley classified it as a congenital neoplasm, rare that occurs in childhood and rarely in adults [6], Grinker in 1931 called it for the first time medulloepithelioma [7].

Survival in patients operated with enucleation ranges from 1 to 5 years when they have extraocular extension. It may also have the ability to destroy the iris and invade adjacent tissues [8].

Unlike other pathologies, there are no known direct or associated risk factors; however, the literature reports the possibility of presenting *DICER1* gene mutation [9]. The diagnosis is basically histopathological. A CT scan and magnetic resonance imaging of the brain and orbital imaging should be ordered [10].

Differential diagnoses included: Retinoblastoma, Medulloblastoma, PNET, ependymoblastoma, immature teratoma, and metastatic carcinoma [11].

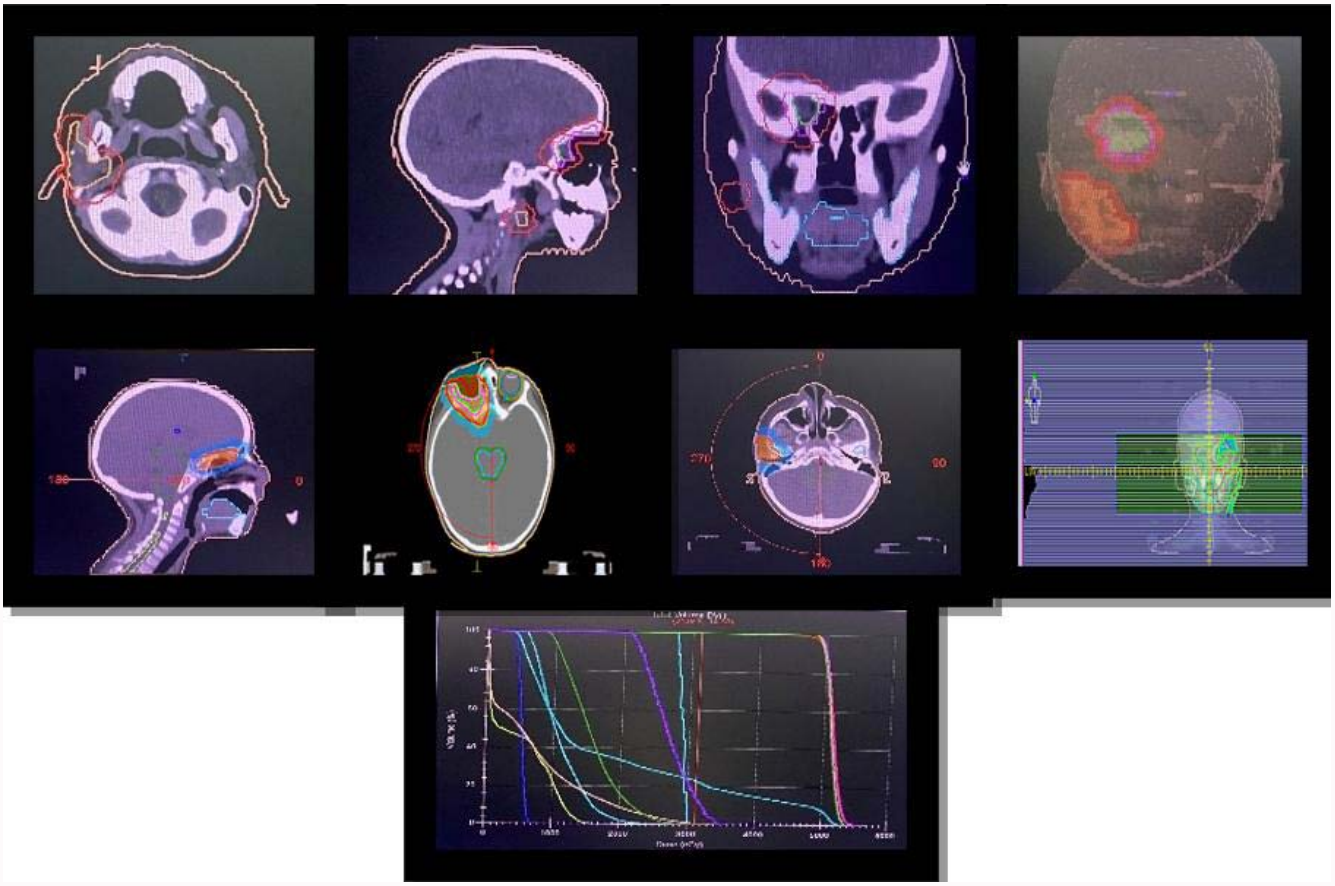

Figure 5: Delimitation and planning in VMAT of treatment.

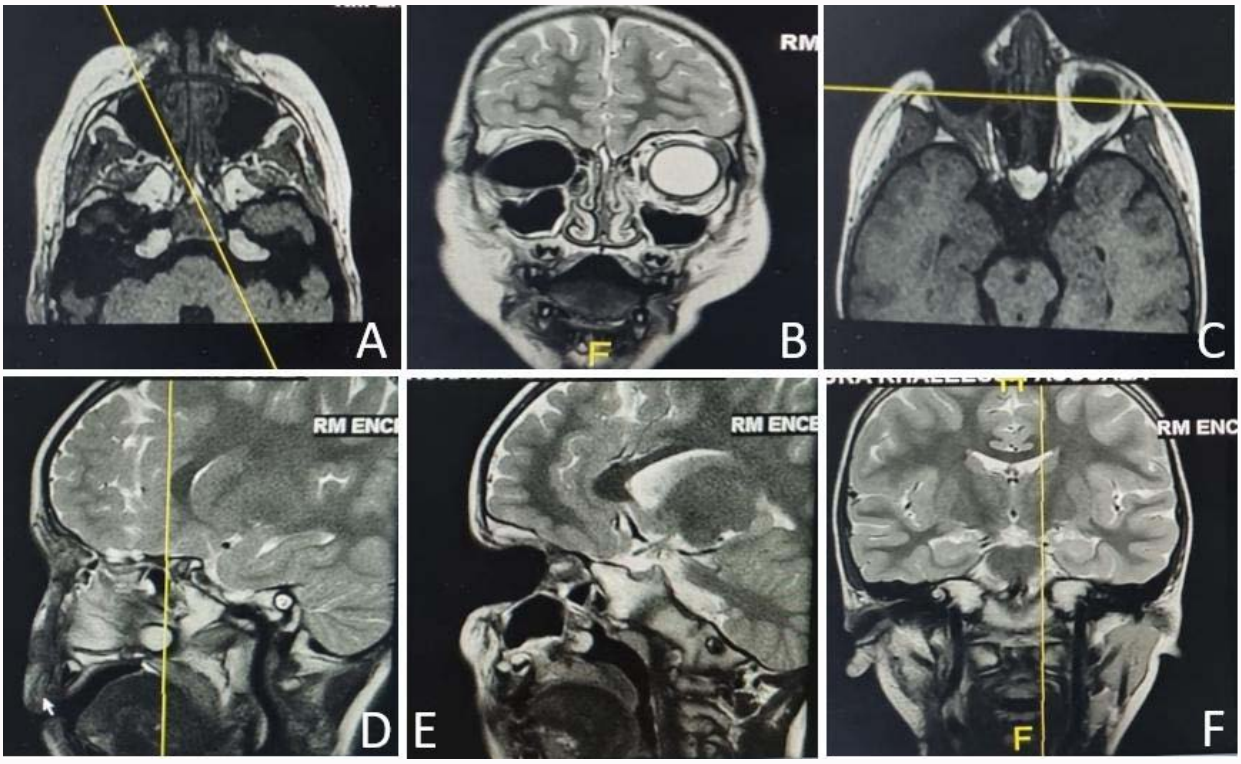

Figure 6: Control brain resonance February 2022.

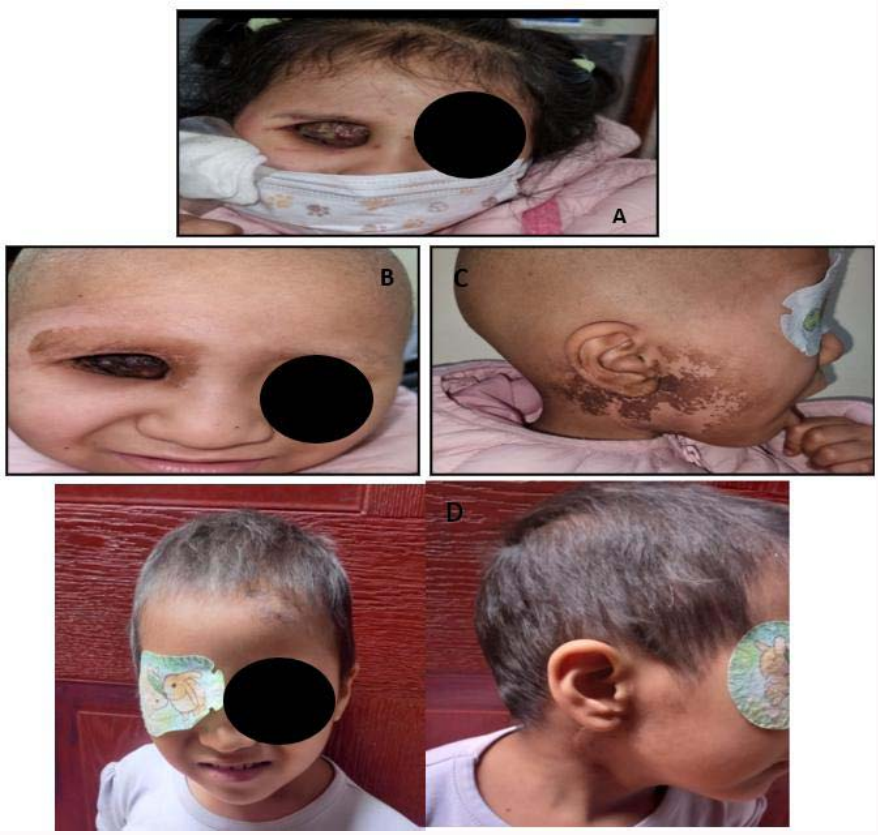

Figure 7: A) Before treatment. B and C) After treatment at 4weeks. D) After completion of radiotherapy at 4 months.

Treatment options include enucleation, exenteration, cryotherapy [12], external beam radiation therapy, brachytherapy, systemic chemotherapy, although it is not established.

The tumor is slow growing; the standard treatment is enucleation when it presents infraorbital tumor growth, vitreous seeding, or extra ocular metastasis. In extra scleral extension it is a poor prognostic factor that can metastasize to regional lymph nodes and distant sites [13]. Subsequently, after surgery on the extra ocular extension of the tumor, systemic chemotherapy and/or irradiation may be given with external radiotherapy or brachytherapy.

Tumors located in the eyeball have an excellent prognosis with a 5-year survival of 90% to 95% after enucleation [14]. Metastatic disease and mortality associated with medulloepithelioma of the ciliary body are very rare; unless extraocular extension or central nervous system involvement is found, the mortality rate increases dramatically resulting in an overall poor prognosis. The main predictor of death is extraocular extension for both teratoid and non-teratoid tumors [15].

In the case presented, the patient presented an early recurrence, which tells us about an aggressive disease with a poor prognosis, so far, she continues complementary chemotherapy. Due to the patient's history of disease, it was decided to supplement with irradiation on the surgical bed of the primary (orbit) and the ipsilateral parotid bed; but not to the regional nodes since it was found that the pathology of the nodal dissection was negative, a conventional fractionation up to 5000 cGy, was used because it was subclinical disease.

Conclusion

Medulloepithelioma is an extremely rare tumor, which occurs in the first decade of life and is much less frequent in adults; the diagnosis is often delayed or confused with other pathologies of orbital or embryonic origin. The management is based on surgical resection, if metastatic disease is present adjuvant or neoadjuvant chemotherapy and/or radiotherapy can be considered in order to reduce the risk of recurrence and increase survival free of locoregional disease.

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