CLINICAL, IMAGING, HISTOPATHOLOGICAL, MUTATIONAL AND THERAPEUTIC CHARACTERIZATION OF REFRACTORY AMELOBLASTOMA IN THE MAXILLA

W.E. Bernaola-Paredes[1]; H.R.M. Veronese[2]; H.F. Köhler[3].

[1]Department of Radiation Oncology, A.C. Camargo Cancer Center, Brazil.
[2]Department of Stomatology, School of Dentistry, UNIFAMINAS, Brazil.
[3]Department of Head and Neck Surgery and Otorhinolaryngology, A.C. Camargo Cancer Center, Brazil.

No conflict of interest

Introduction:
Ameloblastoma is a slow-growth benign epithelial neoplasm, characterized for its aggressive and local invasiveness associated with a high rate of recurrence that will be responsible in almost 10% of odontogenic tumors [1, 2]. It is rare in the maxilla with greater prevalence in the mandible [2]. At imaging assessment, ameloblastoma has been observed from uni- or multilocular radiolucent areas, whose histological classification is based on four subtypes: solid/ multicystic, peripheral, unicystic and desmoplastic [1, 3]. Its treatment is controversial, ranging from conservative surgical treatment such as marsupialization, enucleation and curettage, associated with higher rates of recurrences, to more extensive surgical resections whose rates of recurrence is lower and its mainly complications are related to aesthetic, functional and further reconstructive surgeries[1]. Moreover, mutations detected such as BRAF-V600E were found in refractory ameloblastoma that could participated in the pathogenesis that has been associated to more aggressiveness and recurrence rates [3].

Objective:
This case report aims to describe clinical, imaging, histopathological, mutational and therapeutic characteristics of refractory ameloblastoma in the maxilla.

Case report:
A 74 years-old male patient, who was diagnosed with ameloblastoma in maxilla since 1994 submitted to multiple surgeries (12 in total, including a right maxillectomy), all with compromised surgical margins, that had last recurrence in 2017, complaining for cutaneous fistula placed in the right medial corner of the eye that had started on November 2019.

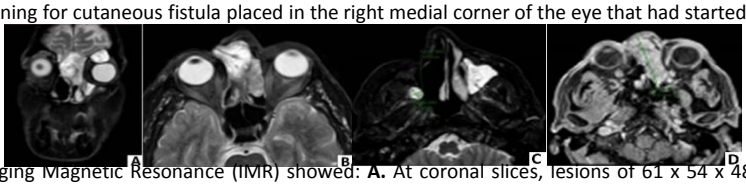

Figure 1: Imaging Magnetic Resonance (IMR) showed: **A.** At coronal slices, lesions of 61 x 54 x 48 mm were observed centered in the left nasal cavity surrounded by areas of cystic and necrotic degeneration. **B.** Invasiveness of the anterior cranial fossa, with thickening and enhancement of dura mater, and **C.** Extending through the anterior ethmoidal area to the right orbital wall (extraconal) and the subcutaneous region onto medial corner and **D.** the roof of the orbit with lowering of the eyeball extended to the left maxillary sinus.

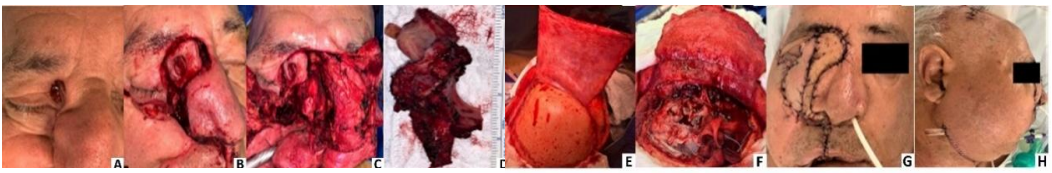

Figure 2: Clinical and therapeutics features. **A.** At extra-oral examination, an ulcerative lesion with 10x10mm is observed in the upper medial corner; **B.** Modified Weber Ferguson approach on the right side to access the remnant maxillary bone; **C.** Meso-suprastructural maxillectomy for exposure of the tumor region; **D.** Surgical specimen after resection; **E.** Scalp flap with large pericranium preservation for Dural and craniofacial reconstruction with pericranial detachment for repair; **F.** Dura mater was opened for early identification of tumor invasiveness at the anterior frontal Dural region through whose entire portion was resected; **G.** Microsurgical reconstruction with musculocutaneous free flap from the anterolateral thigh (frontal view) and **H.** Lateral view at the immediate postoperative.

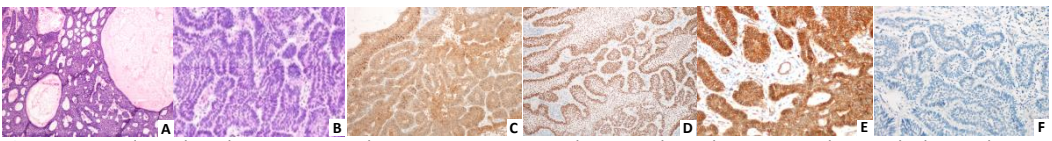

Figure 3: Histological analysis. **A.** 10x and **B.** 20x microscopy and immunohistochemistry analysis with the markers **C.** cytokeratin AE1AE2, **D.** P63, **E.** Beta-catenin and **F.** CDX2, showing a solid/ multicystic pattern of the lesion, negative for mutation at codon 600 of the BRAF gene (BRAF V600E).

Conclusion:
Refractory ameloblastoma diagnosed in maxilla bone is rare and could be a challenge for surgical removal due to its aggressive infiltrated local behavior, associated with higher rates of recurrence and surgery morbidity is increased. Although, the present case was negative for BRAF V600E mutation, further studies are recommended in order to clarify physiopathological role of these mutations.

Bibliography:
(1) Sammartino G, Zarrelli C, Urciuolo V, di Lauro AE, di Lauro F, Santarelli A, Giannone N, Lo Muzio L. Effectiveness of a new decisional algorithm in managing mandibular ameloblastomas: a 10-years experience. Br J Oral Maxillofac Surg. 2007 Jun;45(4):306-10. **(2)** Zhang J, Gu Z, Jiang L, Zhao J, Tian M, Zhou J, Duan Y. Ameloblastoma in children and adolescents. Br J Oral Maxillofac Surg. 2010 Oct;48(7):549-54. **(3)** Duarte-Andrade FF, Silva AMB, Vitório JG, Canuto GAB, Costa SFS, Diniz MG, Fernandes AP, de Toledo JS, André LC, Gomes CC, Gomez RS, Fonseca FP. The importance of BRAF-V600E mutation to ameloblastoma metabolism. J Oral Pathol Med. 2019 Apr;48(4):307-314.