EVENT ABSTRACT

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BRAF gene mutations in odontogenic lesions: a molecular biology analysis

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Aim. Odontogenic tumours are lesions derived from epithelial, ectomesenchymal and/or mesenchymal elements that still are, or have been, part of the tooth-forming apparatus. Their etiopathogenesis is still unknown. Most of them are benign, but local aggressiveness, infiltrative potential and high recurrence rate (15-80%), characterize some entities. V600E mutation accounts for about 90% of BRAF mutations, involved in 78-88% of odontogenic lesions. The study aims to determinate the real frequency of the BRAF V600E mutation in odontogenic lesions, to evaluate its clinical and functional significance. Further, it evaluated the most sensitive gene sequencing technique detecting the mutation itself. Finally, it assessed the role of BRAF as a prognostic marker to clarify the correlations between the mutational status and the clinical-pathological characteristics of the lesions, in order to select patients at greater risk of recurrence.

Materials and Methods. The study included 70 surgical specimens, involved Ameloblastomas, Odontogenic keratocysts, Pindborg's tumours and Odontogenic carcinomas. Data were retrieved from clinical records and from the archive of the Institute of Pathology of Marche Polytechnic University. Serial sections (4 µm), from FFPE, were subjected to gene sequencing by Sanger's sequencing and MALDI-TOF mass spectrometry, Sequenom.

Results. The BRAF V600E mutation involved only Ameloblastomas, recording a frequency of 36.1% by Sanger and 43.6% by Sequenom, while no role was attributable to the BRAF in the pathogenesis of the further lesions examined. The concordance index, Cohen's Kappa, was good (K = 0.786). The mutational status was significantly correlated with tumor localization and histological type, since the mutation had exclusively involved mandibular Ameloblastomas ($p<0.0001$) and the 82.4% of unicistic Ameloblastomas ($p = 0.0153$). A slight predilection for female gender has emerged (52.9%). No correlation neither with the age at diagnosis (46.6 ± 17.2 years V600E vs 49.3 ± 20.4 years WT), neither with the increased dimensions, neither with the histological pattern, nor with the relapses, was found. The relapses also preferred mandibular site (100%), unicistic type (80%) and female gender (60%). No mutated lesions relapsed before 2 years from surgical treatment, however the mutational status was not associated neither with disease-free survival (66.8 ± 32.9 months V600E vs 54.1 ± 44.6 months WT), nor with risk of relapse (80% shortly term and 20% in the long term).

Discussion. These results could indicate the anatomical specificity of the driving mutations, reflected different pathways between mandibular and maxillary ameloblastic lesions. Therefore, they could provide the biological basis for the development of personalized targeted therapies, to reduce the recurrence rate and the aesthetic-functional morbidity of the surgical treatment. Further, targeted therapies could offer a therapeutic alternative for patients not candidate for surgical treatment. Literature data are extremely recent and heterogeneous, so should be conduct further studies to evaluate the prognostic and biological role of BRAF in odontogenic tumorigenesis.

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