CURRENT VIEWS ON METHODS TO DETECT THE BRAF V600E GENE MUTATION IN PATIENTS WITH ODONTOGENIC TUMORS

Annotation: Odontogenic tumors are rare lesions with unknown etiopathogenesis. Most are benign, but some entities are characterized by local aggressiveness, infiltrative potential, and high recurrence rates. Activation of the MAP kinase pathway may represent a primary critical event in odontogenic oncogenesis. In particular, the BRAF V600E mutation is involved in 80-90% of ameloblastic lesions, providing a biological rationale for the development of novel targeted therapies. The study aims to evaluate the BRAF V600E mutation in odontogenic lesions by comparing three different detection methods.

Introduction: BRAF is a serine/threonine protein kinase that plays an important role in the RAS-RAF-MEK-ERK (MAPK) signalling pathway. Activation of this pathway transmits extracellular signals into the cell through a cascade of phosphorylation events, leading to changes in gene expression, growth, cell survival and differentiation in normal and transformed cells. Most BRAF mutations occur in the kinase domain, leading to constitutive activation of BRAF and phosphorylation of MEK, independent of prior activation by tyrosine kinase receptors or RAS. This accounts for constitutive activation of ERK, which leads to stimulation of cell growth and evasion of apoptosis and neoplastic transformation. The most common BRAF mutation, found in more than 90% of tumours with a BRAF mutation, is a valine to glutamic acid substitution at amino acid 600 (V600E) in the kinase domain. This substitution mimics phosphorylation of the activation loop, thereby inducing constitutive BRAF protein kinase activity. BRAF mutations have been described in melanoma (50-60%), colorectal cancer (10%), thyroid carcinomas (30-50%) and non-small cell lung cancer (3%).

Identification of V600E mutation in BRAF gene in different types of metastatic malignant tumours (skin melanoma, colorectal cancer, non-small cell lung cancer) serves as an indication for prescription of ATP-competitive BRAF inhibitors in monotherapy or in combination with MEK inhibitors.

BRAF V600E mutation is the most frequent aberration found in papillary thyroid cancer (40-50% of cases). This mutation is also found in 20-40% of low-differentiated carcinomas and 30-40% of anaplastic carcinomas. The presence of BRAF V600E mutation determines the risk of detection of malignancy in cytological material of Bethesda III-V category in > 95% of cases. BRAF V600E mutation detection is recommended for all patients with highly differentiated thyroid cancer for postoperative risk stratification of recurrence risk in order to determine the management of patients.

Objective: to identify BRAF V600E gene mutations in patients with odontogenic tumours.

Materials and methods of research: The mutation analysis was carried out in 69 patients with odontogenic tumours treated in the Tashkent regional branch of the Republican Specialized Scientific and Practical Medical Centre of Oncology and Radiology. On the basis of anamnestic,
clinical, radiological and histological data we distinguished 2 groups of patients: the first group consisted of 52 patients with ameloblastoma, and the second group consisted of 17 patients with other odontogenic tumours (myxoma, odontoma and cementoma). BRAF V600E mutation was analysed by allele-specific real-time PCR.

**Results.** It was found that 30.43% had V600E mutation in the BRAF gene, and in 69.57% of cases this type of mutation was not detected. The mutation was detected in patients with ameloblastomas and myxomas. The features of histological types of some odontogenic tumours depending on BRAF status were revealed.

It was found that genetic study at the preclinical level of the disease allows to avoid recurrence, also to predict the course of the disease.

**Conclusion.** Thus, the conducted studies have shown that the detection of BRAF V600E mutation increases the risk of odontogenic tumours development by 2.7 times. In this regard, determination of the presence or absence of the V600E mutation in the BRAF gene will allow to predict the course of the disease. Using an integrated clinical, morphological and genetic approach to patient examination, preclinical diagnosis of odontogenic tumours, in particular ameloblastomas and myxomas, as well as individual patient management will be possible.

**References:**