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Congress Abstract

BRAF and TERTp Co-Mutations in Radioiodine-Refractory Differentiated Thyroid Cancer: Association with Aggressive Clinical-Pathological Characteristics

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Introduction: Differentiated thyroid cancer (DTC) is characterized by a favorable prognosis in most cases. However, the development of radioiodine refractoriness significantly worsens the disease course, limits the effectiveness of standard therapy, and is associated with an increased risk of progression. In this regard, the search for molecular genetic markers that allow early identification of patients at high risk of developing an aggressive radioiodine-refractory phenotype is a relevant area of research. Integration of molecular and clinical-pathological characteristics of the tumor may improve the accuracy of risk stratification and contribute to personalization of treatment strategy.

Objective: To evaluate the relationship between molecular genetic alterations, including BRAF and TERT promoter mutations, and clinical-pathological characteristics of radioiodine-refractory differentiated thyroid cancer.

Materials and Methods: A retrospective single-center study was conducted, including 167 patients with DTC treated between 2021 and 2023. The study was performed in the Republic of Kazakhstan among patients treated at the Radionuclide Therapy Department of the Center for Nuclear Medicine and Oncology, Health Department of the Abai Region. Depending on the response to radioiodine therapy, patients were divided into two groups: radioiodine-sensitive DTC (n = 130) and radioiodine-refractory DTC (n = 37). Multivariate analysis was performed to identify independent predictors of radioiodine refractoriness. The discriminatory ability of the prognostic model was assessed using ROC analysis.

Results: The development of radioiodine refractoriness was associated with clinical-pathological signs of aggressive disease course, including elevated levels of thyroglobulin and/or antibodies to thyroglobulin, the presence of lymphogenous metastasis, and the need for more extensive surgical intervention. Individual BRAF and TERTp mutations did not demonstrate independent statistically significant prognostic value. At the same time, the simultaneous presence of BRAF and TERTp mutations was significantly associated with the development of radioiodine refractoriness. The integrated clinical-molecular model demonstrated good discriminatory ability (AUC = 0.796) and outperformed the model based solely on clinical-pathological characteristics, indicating the additional prognostic value of molecular profiling.

Conclusions: The inclusion of molecular genetic profiling in comprehensive clinical-pathological assessment may improve the accuracy of risk stratification, contribute to early identification of patients with potentially aggressive disease course, and serve as a basis for personalization of treatment strategy.

Keywords: Differentiated Thyroid Cancer; Radioiodine Resistance; BRAF; TERTp; Co-Mutation