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BRAF mutations in thyroid tumors from an ethnically diverse group.

Schulten HJ, Salama S, Al-Mansouri Z, Alotibi R, Al-Ghamdi K, Al-Hamour OA, Sayadi H, Al-Aradati H, Al-Johari A, Huwait E, Gari M, Al-Qahtani MH, Al-Maghrabi J.

Center of Excellence in Genomic Medicine Research, King Abdulaziz University, Jeddah, Saudi Arabia. hschulten@kau.edu.sa.

Abstract

ABSTRACT:

BACKGROUND:

The molecular etiology of thyroid carcinoma (TC) and other thyroid diseases which may present malignant precursor lesions is not fully explored yet. The purpose of this study was to estimate frequency, type and clinicopathological value of BRAF exon 15 mutations in different types of cancerous and non-cancerous thyroid lesions originating in an ethnically diverse population.

METHODS:

BRAF exon 15 was sequenced in 381 cases of thyroid lesions including Hashimoto´s thyroiditis, nodular goiters, hyperplastic nodules, follicular adenomas (FA), papillary TC (PTC), follicular variant PTC (FVPTC), microcarcinomas of PTC (micro PTC; tumor size ≤ 1 cm), follicular TC (FTC), and non-well differentiated TC (non-WDTC).

RESULTS:

We identified BRAF mutations in one of 69 FA, 72 of 115 (63%) PTC, seven of 42 (17%) FVPTC, 10 of 56 (18%) micro PTC, one of 17 (6%) FTC, and one of eight (13%) non-WDTC. Most of the cases showed the common V600E mutation. One case each of PTC, FVPTC, and FTC harbored a K601E mutation. A novel BRAF mutation was identified in a FA leading to deletion of threonine at codon 599 (p.T599del). A rare 3-base pair insertion was detected in a stage III PTC resulting in duplication of threonine at codon 599 (p.T599dup). Patients with PTC harboring no BRAF mutation (BRAFwt) were on average younger than those with a BRAF mutation (BRAFmut) in the PTC (36.6 years vs. 43.8 years). Older age (≥ 45 years) in patients with PTC was significantly associated with tumor size ≥ 4 cm (P = 0.018), vessel invasion (P = 0.004), and distant metastasis (P = 0.001). Lymph node (LN) involvement in PTC significantly correlated with tumor size (P = 0.044), and vessel invasion (P = 0.013). Of notice, taken the whole TC group, family history of thyroid disease positively correlated with capsular invasion (P = 0.025).

CONCLUSIONS:

Older age is manifold associated with unfavorable tumor markers in our series. The K601E identified in a PTC, FVPTC, and FTC seems to be more distributed among different histological types of TC than

previously thought. The T599del is a yet undescribed mutation and the rare T599dup has not been reported as a mutation in PTC so far