MUTATIONAL LANDSCAPE OF POORLY DIFFERENTIATED THYROID CARCINOMAS

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Background/Purpose: Molecular studies on poorly differentiated thyroid carcinomas (PDTC) are limited. Our aim was to examine the mutational profile of PDTC and correlate with clinical characteristics and outcome.
Methods: 79 PDTC patients treated primarily at MSKCC (1986-2009) were identified. Mass spectrometry–based genotyping was used to interrogate hot spot point mutations in the most common thyroid oncogenes: BRAF, RET, NRAS, HRAS, KRAS, PIK3CA, AKT1. In addition, common fusions of RET and PAX8/PPARγ were assessed by RT-PCR. Mutational profile was correlated with clinical characteristics by χ^2test and outcome by the Kaplan Meier method.
Results: 67% of patients showed mutations: 23 BRAF (29%), 23 RAS (29%), 2 BRAF/PIK3CA (3%), 1 PIK3CA (1%), 1 AKT1 (1%) and 3 RET/PTC rearrangements (4%). 33% were wild type (wt) without identifiable driver mutation or gene rearrangement. BRAF+ compared to RAS+ and wt tumors had a higher rate of extrathyroid extension (96%, 48%, 54%; p=0.0003) and pN+ (61%, 0%, 46%; p=0.0001). RAS+ tumors were more likely to have distant metastases compared to BRAF+ and wt tumors (61%, 13%, 19%; p=0.0007). 5 year locoregional control was worse for BRAF+ (66%) vs. RAS+ (91% p=0.03) and wt (92% p=0.01). 5 year distant control was worse for RAS+ (35%) vs. BRAF+ (54% p=0.02) and wt (80% p=0.001). 5 year DSS was superior for wt (85%) vs. BRAF+ (70% p=0.02) and RAS+ (56% p=0.04).
Discussion & Conclusion: 33% PDTC have no identifiable driver mutation or gene rearrangement. These tumors show significantly better outcome. Future studies are needed to examine molecular alterations responsible for their favorable prognosis.