A NOVEL VARIANT OF RET/PTC1 REARRANGEMENT IN PEDIATRIC PAPILLARY THYROID CARCINOMA

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Background/Purpose: The development of papillary thyroid carcinoma (PTC) is in about a fifth of cases caused by the rearrangements in the RET proto-oncogene. The intracellular domain of RET is fused to the other gene resulting in expression of a chimeric oncogene RET/PTC. RET/PTC rearrangements are associated with younger age of onset and history of ionizing radiation exposure. 11 fusion partners of RET forming 15 different RET/PTCs has been described. RET/PTC1 is the most prevalent form, where exon 12 of RET is fused to exon 1 of CCDC6(formerly H4) with breakpoints within CCDC6 intron 1 and RET intron 11.

Methods: An eight-year male patient with classical variant of PTC with lung metastasis, without any evidence of exposure to ionizing radiation, underwent total thyroidectomy. Tumour tissue was tested under informed consent. RNA was isolated from fresh frozen tissue by TRIzol and converted into cDNA. RET/PTC1 detection was performed by q-PCR followed by melting curve analysis. The purified PCR product was sequenced.

Results: A novel, larger RET/PTC1 variant characterized by means of a different melting curve than RET/PTC1 positive control was found. cDNA sequence analysis revealed the fusion of CCDC6 exon 1 with intact exon 9 from extracellular domain of RET directly followed by RET exon 12.

Discussion & Conclusion: We found a novel RET/PTC1 variant in a non-irradiated pediatric patient with an aggressive PTC. Surprisingly, the extracellular part of RET, which is normally not present in RET/PTCs, was implicated in this chromosomal rearrangement.

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