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

Halkova, Tereza[1]; Vaclavikova, Eliska[1]; Sykorova, Vlasta[1]; Dvorakova, Sarka[1]; Vcelak, Josef[1]; Vlcek, Petr[2]; Schrumpf, Melanie[5]; van Wezel, Tom[3]; Morreau, Hans[3]; Bendlova, Bela[1]
[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [2]2nd Faculty of Medicine, Charles University and Faculty Hospital Motol, Department of Nuclear Medicine and Endocrinology,, Prague, Czech Republic; [3]Leiden University Medical Center, Department of Pathology, Leiden, South Holland, Netherlands

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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