MEDULLARY THYROID CANCER WITH RET PROTO-ONCOGENE CYS634TRP MUTATION IN A FAMILY WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 2A

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Background/Purpose: Hereditary medullary thyroid cancer (MTC),occurring within multiple endocrine neoplasia type 2A (MEN2A), penetrance of MTC varies in relation to the particular RET proto-oncogene codon affected. MEN2A may be suspected when MTC occurs at an early age or is bilateral or multifocal. We perform a genetic screening for RET proto-oncogen mutation in a family with proband had confirmed with MEN2A and RET mutation.
Methods: We report a family with MEN2A in which the first patient had bilateral pheo associated with CMT. Molecular genetic testing of the RET exon confirmed the mutation at codon 634(Cys634Trp) in RET exon 11. After identification of the proband we screened all her family members with genetic testing for the RET proto-oncogene mutation.The subjects with mutation were further assessed for pheo by measurement of the 24-hour urinary metanephrines and CT-scan. The serum calcium, urinary calcium excretion and PTH secretion were measured.
Results: From the nine family members screened, six have a RET proto-oncogene mutation codon 634 (Cys634Trp); four females: proband, three proband daughters and two children. A boy has normal level of calcitonin identified with RET mutation at 160 days, his mother developed CMT during pregnancy.The second boy-ten years old has high level of calcitonin; his mother has CMT and bilateral pheo.
Discussion & Conclusion: It is widely recommended RET gene mutation testing be performed for all cases of MTC. RET proto-oncogene mutation given the almost 100% risk of developing CMT in MEN2A; it is currently recommended total thyroidectomy before the age of five in children.