Review Article

A Brief Review on The Molecular Basis of Medullary Thyroid Carcinoma

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Abstract

Approximately 5-10% of all thyroid cancers are medullary thyroid carcinomas (MTC). MTC is mainly sporadic in nature, but 20-30% of cases are hereditary. Genetic testing for hereditary MTC is very important for the patient and his family, but the patients must be receiving appropriate genetic counseling. About 98% of patients with hereditary MTC have germline mutations in exons 10, 11, 13, 14, 15, 16 and intron 16 of the REarrangement during transfection (RET) proto-oncogene, but the etiology of the more frequent sporadic form of MTC (sMTC) is not well understood. Recently, it has been reported that apparently sporadic MTC may involve point mutations in BRAF and RAS genes, with an overall prevalence of almost 10%. Also alteration and abnormal expression of miRNA has been described in MTC. In this review, we attempted to mention some mutations and molecular changes in sporadic and hereditary MTC pathogenesis.

Keywords: Medullary Thyroid Carcinoma, RET Proto-Oncogene, miRNA

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Introduction

Medullar thyroid carcinoma arises from the Calcitonin (CT)-producing parafollicular C cells of the thyroid and was first described by Hazard in 1959. Medullary thyroid carcinomas (MTC) accounts for 5 to 10% of all thyroid carcinomas (1, 2). It is important to recognize, because its management is different from follicular thyroid tumors (3). MTC is mainly sporadic and only approximately 20-30% of cases are the hereditary form of the disease. The hereditary forms of MTC were first reported in 1961, in a pair of young siblings whose mother had died previously following surgery for thyroid cancer (3, 4).

The hereditary forms of MTC, referred to as 'multiple endocrine neoplasia type 2' (MEN 2), characterized by MTC in combination with pheochromocytoma and hyperparathyroidism (MEN 2A), or MTC in combination with pheochromocytoma, multiple mucosal neuromas and Marfanoid habitus (MEN 2B). The occurrence of familial MTC (FMTC) in the absence of other neoplasia is also possible (5, 6). All these disorders are transmitted as an autosomal-dominant trait (7-9). Hereditary MTC occurs, in 60% of cases, with either, multiple endocrine neoplasia type 2A and 5% of MEN type 2B, or 35% of familial medullary thyroid carcinoma (9-11).

About 20 years ago it was recognized that the genetic cause was mutations of the REarranged during transfection (RET) proto-oncogene (12, 13). Since that time, the utility of genetic testing for RET mutations has been to confirm the diagnosis of MEN 2. In fact detection of RET mutations in MEN 2 provides a paradigm for genetically guided patient management, genotype-phenotype correlations, patient and family screening and long-term follow-up (9, 14). Also early detection of RET mutation can provide an opportunity for therapeutic intervention prior to advanced disease. In addition to