

Editorial

Characterization of Thyroid Cancer in Pakistan

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EDITORIAL

Introduction

Thyroid is a gland at the front of neck beneath larynx and consists of two lobes which are connected by a piece of tissue, the isthmus. The thyroid makes two important hormones; *thyroid hormone*, which affects heart rate, blood pressure, body temperature, and weight, and *calcitonin*, which keeps the healthy level of calcium in the body.

In Pakistan, papillary thyroid cancer (PTC) is the most common type of thyroid cancer. About 70 of every 100 people with thyroid cancer have this type. It begins in follicular cells and usually grows slowly. It is predominantly driven by certain genetic and epigenetic modifications, including activation of oncogenes and inactivation of tumour suppressor genes. Much still remains unknown about the molecular mechanisms of PTC even though many genetic and epigenetic alterations have been known in thyroid carcinoma, such as aberrant hyper-methylation of CpG islands in promoter regions of tumor suppressor genes. As per previous reports, Tumor-specific rearrangements of the proto-oncogenes *ret* and *trk*, encoding tyrosine kinase membrane receptors, have been detected with a high frequency in human papillary thyroid carcinomas. The oncogenic activation of these genes is accomplished by the fusion of their tyrosine kinase domain with unlinked amino-terminal sequences following intrachromosomal rearrangements involving chromosome 10 and chromosome 1 in the case of *ret* and *trk*, respectively. In particular, a paracentric inversion of the long arm of chromosome 10, *inv(10)(q11.2q21)*, was shown to provide the structural basis for the fusion between *ret* and *DIOS170*. Papillary carcinomas frequently have genetic alterations leading to the activation of the mitogen-activated protein kinase (MAPK) signalling pathway. These include *RET/PTC* rearrangement and point mutations of the *BRAF* and *RAS* genes.

The second most common type is follicular thyroid cancer. A little more than 12 of every 100 people with thyroid cancer have this type. It begins in follicular cells and usually grows slowly. Frequent genetic alterations in follicular carcinomas, the second most common type of thyroid malignancy, include *RAS* mutations and *PAX8-PPARg* rearrangement. *RET* point mutations are crucial for the development of medullary thyroid carcinomas. Many

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Submitted: 07 February 2018

Accepted: 07 February 2018

Published: 09 February 2018

ISSN: 2379-061X

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of these mutations, particularly those leading to the activation of MAPK pathway, are being actively explored as therapeutic targets for thyroid cancer.

Medullary thyroid cancer is not common. About 3 of every 100 people with thyroid cancer have this type. It begins in C cells and can make abnormally high levels of calcitonin. Medullary thyroid cancer tends to grow slowly. It can be easier to control if it's found and treated before it spreads to other parts of the body. Medullary thyroid cancer sometimes runs in families. A change in a gene called *RET* gene can be passed from parent to child. The disease occurs alone, as familial medullary thyroid cancer, or with other cancers, as multiple endocrine neoplasia (MEN) syndrome. The least common type is anaplastic thyroid cancer. About 1 of every 100 people with thyroid cancer has this type. Most people with anaplastic thyroid cancer are older than 55. The cancer begins in follicular cells of the thyroid. The cancer cells tend to grow and spread very quickly. Anaplastic thyroid cancer is very hard to control.

Diagnosis

Physical examination of thyroid is done for lumps (nodules), of the neck and nearby lymph nodes for growths or swelling. Determination for abnormal levels of thyroid-stimulating hormone in the blood is also done. Too much or too little TSH shows abnormal activity of thyroid gland the thyroid. Hence, for medullary thyroid cancer, a high level of calcitonin and other blood tests must be recommended. *Through* ultrasound device, the size and shape of each nodule and whether the nodules are solid or filled with fluid should be analysed. Nodules that are filled with fluid are usually not cancer. Nodules that are solid may be cancer.

By scanning thyroid gland nodules can be differentiated into hot and cold nodules. Hot nodules are usually not cancer but cold nodules may be cancer. A biopsy is the only sure way to diagnose thyroid cancer, which unfortunately is not available everywhere in Pakistan.

Hence, public awareness, biochemical and molecular characterization of thyroid cancer needs to be done in Pakistan.

Cite this article

Jabbar KHAN (2018) Characterization of Thyroid Cancer in Pakistan. *JSM Cell Dev Biol* 6(1): 1024.