

P53 and C-FOS overexpression in patients with thyroid cancer: an immunohistochemical study

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A sequence of genetic events characterized by deletion and expression of several oncogenes may lead progressively to tumorigenesis. The expression of certain oncogenes is believed to be related with thyroid carcinogenesis and tumor progression. We investigated immunohistochemically p53 tumor suppressor gene and c-fos oncogene expression in forty patients with thyroid cancer. Thyroid biopsies from twenty patients with benign thyroid diseases were also examined. The forty patients with thyroid cancer varied histologically; 24 with papillary carcinoma (60%), 12 with follicular carcinoma (30%), 3 with anaplastic carcinoma (7.5%) and one with medullary carcinoma (2.5%). The patients with benign thyroid diseases consisted of 10 with adenomatous goiter (50%), 7 with goiter (35%) and three with Hashimoto thyroiditis (15%). Individual p53 and c-fos expression was more prevalent in thyroid carcinomas compared to benign tumors ($p=0.001$ and $p=0.04$, respectively). A marked increase of p53 and c-fos coexpression was found ($p=0.02$) in patients with thyroid cancer and metastasis to the regional lymph nodes. Furthermore c-fos was overexpressed in only female thyroid cancer patients. In conclusion, p53 and c-fos are significantly overexpressed in thyroid cancer patients, indicating their role in the genetic mechanisms leading to thyroid tumorigenesis. This hypothesis is further supported by the observation that p53/c-fos coexpression was related with more advanced disease status.

Key words: Thyroid cancer, goiter, thyroiditis, adenoma, p53, c-fos.

Thyroid tumors represent an attractive model for the identification of genetic changes involved in tumorigenesis. They show a stepwise progression from hyperplasia to solitary nodule, differentiated and anaplastic carcinoma.

The development and progression of thyroid tumors involve several genetic mechanisms. The mutation of p53 tumor suppression gene located in the short arm of chromosome 17, is frequently reported to be mutated in malignant tumors [15, 23]. This gene encodes, a 53 kDa nuclear phosphoprotein, which plays a role as a check point control for recognising DNA damage, resulting in either a delay in progress through the cell cycle to permit repair process or to initiate apoptosis [16], eliminating this way the abnormal clones of cells that lead to cancer [1]. The half-life of mutated p53 gene is subsequently much longer than wild-type and high levels of mutated p53 protein accumulate in the nucleus. For this reason p53 immunohistochemistry re-

presents a possibility to get inside into the process of neoplastic transformation.

The protooncogene c-fos also plays a central role in cell proliferation and its protein product is an essential component of transcription factor AP-1 [3, 20]. The activity and function of c-fos is also implicated in hormone-dependent transcriptional regulation by fos-steroid receptor fusion proteins [7, 27]. The aim of this study was to investigate the clinical significance of the p53 tumor suppressor gene and c-fos oncogene overexpression in patients with thyroid cancer.

Material and methods

Pathological specimens from 40 patients with thyroid cancer and 20 patients with benign thyroid diseases were