

Retrospective Analysis of the Histopathological Pattern of Thyroid Cancer in the Southern Marmara Region of Turkey and Comparison of the Data with the Data of Previous Decade

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Although thyroid cancers are quite rare in the population, thyroid nodules are common and about 5 % of all thyroid nodules are reported to be malignant. Factors predisposing to thyroid malignancies are different, one of them being ionizing radiation. We evaluated 2225 patients with a thyroid mass between the years 1996-2001 in our thyroid outpatient clinic and fine needle aspiration biopsy (FNAB) was performed to 2012 cases who accepted. Among all cases FNAB revealed malignancy in 59 patients. In this study we aimed to delineate the histopathological pattern of thyroid cancers in the Southern Marmara region in the last decade and compare it with our previous results obtained with a similar analysis conducted between the years 1985-1995. We found a statistically insignificant increment in papillary thyroid cancer frequency while follicular and anaplastic thyroid cancers were decreasing and medullary cancer was unchanged. In conclusion, the increment in papillary/follicular ratio might be due to iodine replacement procedures which were obliged and supported by the government in recent years and more importantly to the possible effect of radiation fallout that occurred in Chernobyl in 1986 which Turkey might be affected as well as the other countries being in the neighbourhood.

Key words: Thyroid cancer, histopathological distribution, iodine replacement, radiation.

Introduction

Thyroid cancer is a rare condition with an incidence of 0.004 % per year according to the Third National Cancer Survey (1). It accounts for approximately 1 % of all malignant tumors. Thyroid nodules are extremely common, particularly among women. In adult population the prevalence rate has been estimated to be 4-7 % with a female to male ratio of 4:1. Although most of the thyroid nodules are benign, it is important to separate them from those that are likely to be malignant. In this context, medical history, physical examination, thyroid

function tests, ultrasonography and radionuclide imaging are of limited use. Fine needle aspiration biopsy (FNAB) is the most reliable method and the major diagnostic tool for the identification, if performed in experienced hands and aspirates evaluated by experienced cytopathologists (2,3).

A medical history of exposure to external radiation for therapeutic purposes, particularly during childhood for benign head and neck conditions, is associated with an increased risk of thyroid cancer (4,5). A thyroid nodule in such an individual was reported to be malignant in 33-37% of the cases (6). The association with internal ¹³¹I exposure is less clear; however, studies conducted after the Chernobyl accident indicate that this exposure increases the incidence of thyroid cancer especially if it occurs in younger ages and this might be related to a greater carcinogenic sensitivity of young thyroid glands, compared to lowered growth

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potential of adult thyroid follicular cells (7). As a result of the accident, an entire population in a large geographic area including Turkey and many other countries in the neighbourhood is under risk. This exposure has raised an important public health problem regarding the medical value of screening for thyroid diseases, particularly nodular ones (4).

The aim of this study is to evaluate the changing histopathological patterns of thyroid cancers in nodular goitre in the Southern Marmara region of Turkey around the city of Bursa after the year 1995 and to determine if there is a change in their frequencies in the last decade compared to the previous one.

Subjects and Methods

During the period 1996 - 2001, 2225 patients were evaluated and followed up in the "Thyroid Out-patient Clinic" of Uludağ University Medical School Department of Endocrinology and Metabolism, with a diagnosis of single or multiple thyroid nodules.

All patients were examined by an endocrinologist on their first admissions. A complete record was filled for each patient including information about the complaints, medical history, physical examination, ultrasonographic and radionuclide imaging findings and blood analysis including TSH, free T3, free T4, thyroglobulin and/or calcitonin.

After these procedures, 2012 patients underwent, 213 refused FNAB. Three experienced endocrinologists performed the FNABs without local anesthesia by using a 21 gauge needle attached to a 20 ml disposable syringe while the patients were positioned supine with the neck slightly hyperextended. Palpable nodules in the thyroid gland were fixed between the 2 fingers of one hand, the needle was inserted into the lesion. If the nodule could not be palpated FNAB was done under ultrasonography. More than one aspirations were made for each nodule. The aspirates were expressed onto microscope slides. All the smears were dried in the air and stained with May- Grünwald Giemsa stain.

All of the smears were interpreted by the same cytopathologist and classified according to World Health Organisation (WHO) classification (8). The cytological diagnoses were classified into four

categories as benign, suspicious, malignant and insufficient material for diagnosis. In cases of insufficient material, patients underwent a second FNAB. Patients with suspicious and malignant cytologies underwent surgery. After the pathological evaluation of these surgical materials; we investigated the age, gender and histopathological distribution of the thyroid cancer cases and compare the results with the previous decade.

The numerical values were given as mean \pm standard deviations. Statistical analysis was done with Chi-square and Fischer exact tests. *p* values < 0.05 were considered to be statistically significant.

Results

Among 2012 patients who underwent FNAB, 59 patients (2.9 %) had suspicious and malignant cytology. Of these 59 patients 37 (62.7%) were females and 22 (37.3%) were males with a F/M ratio of 1.68:1. The mean age of the patients was 48.7 ± 16.3 years. When the records of these patients were reviewed, swelling in the neck, palpitation and dysphagia were the most frequent complaints on admission.

The ultrasonographic examination of these patients revealed multiple nodules in 57.5 % and single nodule in 42.4 %. Among all nodules 31.7 % was solid, 19.5 % was cystic, 9.7 % was calcific in nature. A mixture of solid, cystic and calcific components were detected in 39.1 % of the patients. The radionuclide imaging indicated hyperactive nodules in 8 %, hypoactive nodules in 60 % and normoactive nodules in 32 % of the cases.

All 59 patients underwent thyroidectomy and both histopathological evaluations and tumor, lymph node and metastasis (TNM) classifications were performed (1). Tumor diameter was <1 cm (T1) in 7.8 % , between 1 to 4 cms (T2) in 44.7 % and >4 cms (T3) in 31.5 %. Lymph node involvement was present in 36.8 % of the patients. Distant metastasis (T4), mainly to lungs and bones was present in 15.7 % at the time of diagnosis.

The histopathological evaluation of the thyroidectomy materials according to WHO classification revealed papillary carcinoma in 64.3 %, follicular carcinoma in 16.8 %, medullary carcinoma in 5.1 %, anaplastic carcinoma in 3.4 %, mixed papillary and follicular types in 8.4 % and

lymphoma of the thyroid in 1.7 % of the cases. The histopathological distribution of the cases are indicated in Figure 1 with female and male ratios. In a previous study (2) conducted in our department between the years 1985 and 1995, the percentages of different cancer types were as follows; papillary carcinoma 48.7 %, follicular carcinoma 24.3 %, medullary carcinoma 6.41 %, anaplastic carcinoma 10.2 %, metastatic carcinoma 10.2 %. Comparison of the previous and recent frequencies of different histopathological types of thyroid cancers are shown in Figure 2. There was no statistically significant difference between these two data ($p>0.05$).

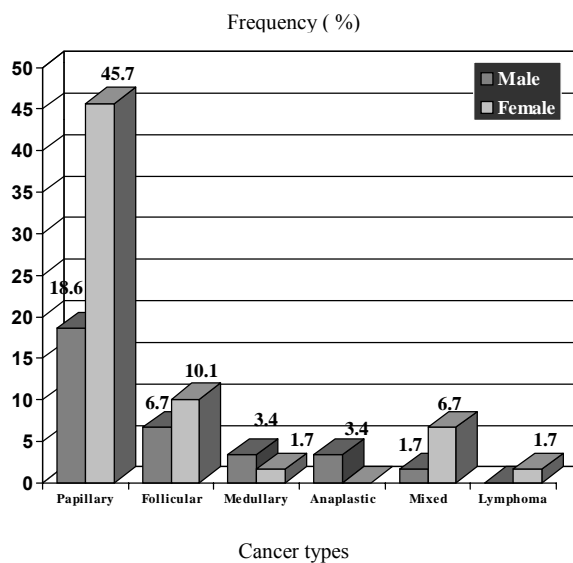


Figure 1. The histopathological distribution of the cases with female and male ratios between the years 1996 - 2001.

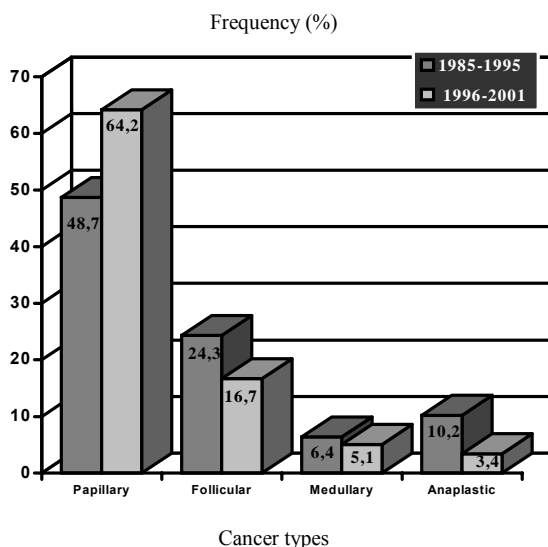


Figure 2. The comparison of the previous and recent frequencies of different histopathological types of thyroid cancers ($p>0.05$).

Discussion

Since Turkey is an iodine deficient country as a whole including Southern Marmara region, thyroid diseases especially thyroid nodules are quite frequent in the population. 90-140 thousand individuals are estimated to have thyroid nodules in our city Bursa, with a population of 1958529. Thyroid nodules range from benign lesions to malignant tumors and it is important to detect and treat the malignant ones to prolong patient's life and increase it's quality.

Initial symptoms such as rapid nodule growth, hoarseness, dysphagia and pain may indicate local tissue invasion by tumor but may not be present in patients with thyroid cancer or may be seen in benign conditions as well (9). This was also the situation for our cases. Although there were symptoms like swelling in the neck, palpitation, dysphagia, hoarseness, dyspnea in our patients with malignant nodules on admission, these were also similar in benign ones.

The first step in the laboratory evaluation for thyroid nodules is the measurement of serum TSH levels. If TSH level is suppressed a scintigraphy should be performed for confirming the diagnosis of a hyperfunctioning nodule in which thyroid cancer is extremely rare (10). In our patient group 8 % of the patients had one or more hyperactive nodules in their scintigraphies. As shown by other studies hypoactive nodules have a higher risk for thyroid cancer as is the case in our study group with a rate of 60 % (1).

Ultrasonography is a noninvasive useful method for evaluating the nature of nodules. Single, solid, hypoechoic, calcific nodules and nodules with irregular or poorly defined margins on ultrasonography are most likely to be malignant (11). The ultrasonographic examination of our patients revealed 31.7 % solid, 9.7 % calcific nodules. A mixture of solid, cystic and calcific components were detected in 39.1 % of the patients. Among all patients 42.4 % had a single nodule. These results indicate that ultrasonography is not a reliable method for the discrimination of benign and malignant lesions.

FNAB is the single most accurate procedure for differentiating benign from malignant thyroid

nodules. It has an important role in the evaluation and management of nodular thyroid diseases (12, 13). In our study FNAB indicated a false-positive rate of 5 %, a false-negative rate of 3 %, a sensitivity of 95 % and a specificity of 93 %. These results are also consistent with data from other centers (14). In a study conducted a decrease in the percentage of surgical treatments from 67 % to 43 % with a 20 % reduction in the cost of care by the introduction of FNAB (15). After performing FNAB routinely in our center, thyroid cancer rate per operation increased. This rate was approximately 4 % and 7.6 % before and after the introduction of FNAB, respectively (2).

Approximately 4-5 % of thyroid nodules are reported to be malignant in different studies (2, 10,16). In our series this was found to be 2.9 %. Among malignant cases 62.7 % were females, 37.3 % were males with a F/M of 1.68:1. F/M in our previous study was 2:1(2). The decrement in the ratio, indicated an increment of thyroid cancer prevalence rate in general in the favor of male subjects with thyroid nodules.

In our study 64.2 % of all malignancies were papillary carcinomas. This percentage is similar to other reports from other countries (17-19). When these data were compared to our data of the previous decade, we observed an increment in the favor of papillary carcinoma although statistically insignificant (2). On the other hand follicular carcinoma showed again a statistically insignificant decrement. The papillary/follicular ratio increased from approximately 2 to 4. One possible explanation may be the increased efforts on iodine replacement procedures in food and salt in recent years in Turkey, including our district (1,4). Another reason may be due to exposure to radiation fallout during and after Chernobyl nuclear reactor accident that occurred in 1986. It has been reported that there is a significant trend for the proportion of different organ cancers including thyroid to increase over time after this disaster (20). Gene mutations involving the RET proto-oncogene and less frequently TRK, have been shown to be causative events specific for papillary cancer. RET activation was found in nearly 70 % of the patients who developed papillary thyroid carcinomas following Chernobyl accident (21). In a study reported from Belarus, F/M ratio was reported to be 1.6:1 which was similar to our result

(18). This point also might indicate the possibility of radiation exposure in our district. The frequency of medullary carcinoma was found to be similar within years. The statistically insignificant decrement in the frequency of anaplastic carcinoma might be due to iodine replacement procedures since a higher frequency of anaplastic carcinoma had been reported in iodine insufficient areas (2).

Our results of the comparison of the data of two decades indicated a change in the histopathological pattern of thyroid cancers although they did not reach statistical significance. Thyroid cancers have an increasing frequency and their relationship with radiation exposure although uncertain, indicates a possibly growing public health problem. To evaluate the underlying factors leading to changes in the frequency of thyroid cancers, effecting their histopathological distribution and the possible role of radiation fallout, long term follow-up periods for patients with nodular thyroid lesions should be carried out.

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