Thyroid Cancer, Clinical and Hystopathological Study on Patients under 25 Years in Tabriz, Iran (2000-2012)

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Abstract: Thyroid cancer comprises a broad spectrum of diseases with variable prognoses. The aim of this study was to assess thyroid cancer in young population using the surveillance, epidemiology and end results database and whether radioactive fallout from the Chernobyl accident in 1986 influenced thyroid cancer incidence among children and adolescents in Tabriz, Iran. Patients aged 5-25 in Tabriz from April 2000 to April 2012 were studied. Using the surveillance and end results database, the study examined the overall incidence of thyroid cancer with variations based on tumor pathology, size and stage, as well as the current surgical therapy of thyroid carcinoma. This study demonstrated a positive correlation between thyroid carcinoma tumor size and stage of disease. Mortality rates were higher among men than women. Recurrence rates are also higher in men. Compared with women, men have greater likelihood of loco regional lymph node involvement and more than twice the rate of distant metastases. Operative treatment for thyroid cancer also has shifted with Radical dissection/Total thyroidectomy replacing partial thyroidectomy as the most common surgical procedure. Our data indicate that the increasing incidence of thyroid cancer cannot be accounted for fully by an increased detection of small neoplasms. This study show the increasing in thyroid cancer incidence related to exposure to radiation from the Chernobyl accident.

Key words: Thyroid cancer, surveillance, epidemiology, chernobyl accident, tumor

INTRODUCTION

Thyroid Carcinoma (TC) is an uncommon disease with an annual incidence ranging from 0.3 to 10 per 100,000 persons, according to official statistics (Akyildiz et al., 2010; Goldust and Rezaee, 2013; Goldust et al., 2013a; Lotti et al., 2013). Morphologically, four main types of thyroid carcinoma are distinguished, with different etiology and prognosis: Papillary Thyroid Carcinoma (PTC) and Follicular Thyroid Carcinoma (FTC) (differentiated) carcinomas (Goldust et al., 2013b, c; Mohebbipour et al., 2012). The Anaplastic Thyroid Carcinoma (ATC) (undifferentiated) type is uncommon at young ages and Medullary Thyroid Carcinoma (MTC), a tumor of the thyroid C cell that secretes calcitonin (Goldust et al., 2013d; Nehs et al., 2010; Sadighi et al., 2011; Vafaee et al., 2012). Numerous studies have described the increasing incidence of thyroid cancer; however, debate continues on whether these findings reflect a true increase of relevant disease or simply an improved diagnostic surveillance or pathologic recognition of incidental neoplasm with little clinical significance (Goldust et al., 2012; Golfrushan et al., 2011; Milan et al., 2011; Pezzolla et al., 2010). Some groups have proposed that the increasing use of cervical ultrasonography and fine needle aspiration contributes to the identification of clinically unimportant cancers (Fardiazar et al., 2012; Goldust et al., 2011; Sadeghpour et al., 2011). If this theory is true, then a greater proportion of earlier stage cancers should be noted. Davies and Welch support this theory by showing that neoplasm <1 cm representing micropapillary thyroid cancer (microPTC) accounted for 49% of the overall increase of thyroid cancer in their study (Davies and Welch, 2006). They did not, however, do any correlation of tumor size to stage of disease. Others have suggested that the increase in thyroid cancer is real and have observed an increase in thyroid cancer of all stages. Enewold et al. (2009) examined demographic changes in thyroid cancer and found a substantial increase in larger cancers (>2 cm). Although, the exact etiology of this trend is not yet known, some investigators have suggested that radiation or other unknown environmental factors are possible contributors to the increase in incidence of thyroid malignancy (Bullock 2010; Ganipour Sales et al., 2012; Nikanfar et al., 2012; Sadeghpour et al., 2012; Spiess, 2010). Exposure to radiation gives rise to differentiated types, notably to the papillary type,
although a causal association for the other types cannot be excluded (Karzar et al., 2012; Martinez et al., 2010; Shakeri et al., 2013; Vahedi et al., 2012). The management of thyroid cancer has changed substantially over the past several decades, largely as a result of the rapid increase in understanding of the genetic pathogenesis of thyroid cancer and the availability of newer diagnostic tools, along with a wealth of epidemiological data (Farhoudi et al., 2012; Nourizadeh et al., 2013; Seyyednejad et al., 2012; Sipos and Mazzaferr, 2010). As a result, there has been a gradual evolution of the diagnostic and therapeutic paradigms that have been applied to the management of this disease, especially the application of rapidly emerging novel targeted therapies, the use of newer sensitive diagnostic tools and the use of large databases that challenge clinical wisdom (Garipour Salesi et al., 2013; Salehi et al., 2013a, b). It is thus not surprising that controversies swirl around the management of thyroid cancer (Fardiazar et al., 2013; Pacini et al., 2010; Salehi et al., 2013c; Soleimanpour et al., 2013). Well-differentiated thyroid cancers often have an indolent clinical course with low morbidity and mortality. With some exceptions, these are among the most curable of cancers (Daghigh et al., 2013; Nemati et al., 2013; Qadim et al., 2013). As a consequence, patients are sometimes advised that thyroid cancer is not a serious problem, an attitude that trivializes the importance of the disease and is certainly not the view of most patients. Nonetheless, this may lead some patients and physicians to forgo long-term follow-up that is an essential component of management (Goforoukhzhan et al., 2013; Rakotoarisona et al., 2010; Razi et al., 2013; Salehi et al., 2012; Yousefi et al., 2013). This study assessed trends in thyroid cancer incidence from 2000-2010 in the young population using the surveillance, epidemiology and end results database.

MATERIALS AND METHODS

In this descriptive-analytical study, we studied patients admitted for thyroid cancer and various other conditions to department of surgery, Imam Khomeyni hospital, Tabriz University of Medical Sciences from April 2000 to April 2010. Patients below the age of 25 with histologically confirmed thyroid cancer diagnosed within 1 year previously were considered. Total 242 cases (56 males and 186 females) aged 5-25 were interviewed. The local cancer registry was used to check recruitment of thyroid cancer cases. A standard questionnaire was used for information on demographic factors, general characteristics, personal and family history of thyroid diseases, relevant medical conditions (i.e., metabolic and immunological disorders), diagnostic and therapeutic procedures (X-rays and radiotherapy) and history of residence in endemic goiter areas. Patients were counted as having thyroid disease only if diagnosis had been made at least 1 year before cancer discovery. Five histological groups were considered. The large majority of the thyroid cancers were papillary (76%), the remainder was composed of follicular (12%), medullary (6%), other carcinomas (5.2%) and of anaplastic type (0.8%). Stages included local disease (tumor confined to the thyroid); regional disease (lymph node involvement); or distant disease (metastatic spread to distant organs). Operative therapies were defined as follows (1) Partial thyroidectomy included lobectomy and isthmusectomy, (2) Total thyroidectomy was restricted to cases in which the entire thyroid was removed or a near total thyroidectomy was performed, (3) Radical dissection+Total Thyroidectomy and (4) Complementary. SPSSSTM, version 16 is the used statistical software program. The association between 2 factor variables was estimated using $\chi^2$ analysis. Regression equations included terms for age, sex, area of current residence and history of residence in endemic goiter area.

RESULTS

We studied 242 patients: 56 (23/1%) male and 186 (76/9%) female. The age of the patients ranged from 5 to 25 years, with a mean (SD) age of 12.4 (7.2) years.

History of radiation: There was not a history of obvious radiation to any of the patients.

Family history: There was a family history of thyroid cancer in 30 (12.3%) patients that 25 (10.3%) were female and 5 (2%) of them were male. There was not a significant difference between two sexes ($p = 0.52$).

First patient's symptoms: Neck mass was the most prevalent symptom of the patients that exist in 200 (82.6) of the patients and disphonia was the less prevalent symptom that was exist in only 10 (4%) patients. Eight (3.3%) patients were symptom free (Table 1).

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<tr>
<th>Table 1: First patient's symptom between two sexes</th>
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<td>Male</td>
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<tr>
<td>Neck mass</td>
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<td>Dysphagia</td>
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<td>Diaphonia</td>
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<td>Pain</td>
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<td>Symptom free</td>
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<td>Others</td>
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2004
Lymph node metastases: The prevalence of lymph node metastases at initial surgery were seen in 24 (42.8%) of males and 72 (38.7%) females. Lymph node metastases exist only in PTC and there were not any lymph node metastases in FTC and MTC.

Para clinic study: In Fine Needle Aspiration (FNA) examination, the large majority of the thyroid cancers were papillary (76%), the remainder was composed of follicular (12%), medullary (6%), other carcinomas (5.2%) and of anaplastic type (0.8%) (Table 2).

In Isotope scan, 158 (64.3%) patients had cold nodules, 38 (15.7%) patients had hot nodules and 46 (19%) patients had normal nodules.

Extent of surgery: Most patients (62.8%) underwent radical dissection+total thyroidectomy and the remainder (37.2%) underwent other types of surgery. For tumors <1 cm, the extent of surgery did not affect recurrence rates or survival. On the other hand, patients with tumors ≥1 cm had a 20% higher risk of recurrence if lobectomy alone was carried out (p = 0.04) (Table 3).

Recurrence: The incidence of recurrence was observed in 30 (12.3%) patients that 24 (9.9%) of them female and 6 (2.4%) of them were male. Recurrence was observed in PTC and FTC and was not observed in MTC.

Survival: The 5-year survival of patients diagnosed with thyroid carcinoma in 2000-2010 was 96% in patients between 5-25 years old. No significant differences in survival were observed between boys and girls.

Mortality: Mortality records from 2000 to 2010 show relatively stable or slightly improved mortality rates for thyroid cancer patients. However, over the same period, mortality rates measured in terms of relative survival show an overall significant decline (p<0.05 for trend) in mortality rates in women and an increase in mortality rates in men (p<0.05 for trend).

Tumor size: Tumor size correlates with outcome in patients with PTC; larger tumors are more likely to present with loco regional and distant metastases.

Gender: Mortality rates were higher among men than women. Recurrence rates are also higher in men. Compared with women, men have greater likelihood of loco regional lymph node involvement (42.8% vs. 38.7%) and more than twice the rate of distant metastases.

DISCUSSION

We described the pattern of occurrence of thyroid cancer in Tabriz, Iran over the period 2000-2010, using the assembled database on childhood and adolescent cancer. Overall, this study confirms female predominance in thyroid cancer occurrence in children and adolescents, its increasing frequency with age, high proportion of papillary tumor type, growing incidence over time and low fatality from this cancer. Despite the steady worldwide increase in the incidence of thyroid cancer, the disease remains relatively uncommon, comprising only 1.18 per 100000 people around the world (Akslen and Livolsi, 2000; Al-Sheyyab et al., 1993). Thyroid cancer affects a wide spectrum of people, ranging from pre pubertal children to octogenarians. Children and adolescents (age <20 years) tend to present with higher-stage disease and greater likelihood of loco regional and distant metastases (Albores-Saavedra et al., 2007). Despite late-stage presentation of tumors, children generally have excellent survival rates; one study found 2% cause-specific mortality at 40 years of follow-up (Alessandri et al., 2000). The best indicator of outcome in this group is response to radioiodine therapy (Alessandri et al., 2000). The incidence of thyroid cancer in women remains steady at about 3-fold that of men. The incidence of PTC is significantly greater than that of FTC and the overall increase in incidence is greater in women than men. The epidemiological features of thyroid cancer are important to clinicians for several reasons. First, PTC is the main cause of the steadily increasing incidence of thyroid cancer, mainly because it comprises about 85% of all thyroid cancers. Second, during the same period, the incidences of FTC and MTC have remained relatively stable in some studies and the incidence of ATC has declined. Finally, perturbations of the incidence and mortality rates relate directly to decisions concerning the diagnosis and treatment of thyroid cancer (Ensami and
Mozaffari, 2001). In comparison to study the detection methods were not changed and this difference in prevalence could not be related to the methods of detection. Study of the SEER database by Mettler et al. (1992) found that the incidence of well-differentiated thyroid cancers of all sizes has been increasing in both men and women from 1988 to 2005 and that attributing this change to increased diagnostic activity. Rego-Iraeta et al. (2009) reached a similar conclusion in a study in Spain and reported that the increasing incidence of thyroid cancer is due to factors other than increased diagnostic scrutiny and the radiation because tumors of all sizes were increasing at an equal rate.

CONCLUSION

In conclusion, numerous factors affect outcome for patients with DTC, including age, gender, tumor histology and presence of extra capsular extension, tumor size, presence of lymph node or distant metastases and oncogene expression of the tumor. Mortality rates are significantly higher in men compared with women, largely due to late diagnosis and more advanced disease in men at the time of initial diagnosis.

REFERENCES