

Management of Papillary Thyroid Cancer at King Abdul-Aziz University Hospital between 2003 and 2012, Jeddah, Saudi Arabia

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Abstract: One of the leading causes of death worldwide is cancer. During the last few decades, we have observed an increase in the number of deaths due to cancer, and one of the most common types is thyroid cancer. According to the Saudi Registrar of Oncology, thyroid cancer is the second most common cancer in females and the fourth most common cancer in both genders [1]. Therefore, we aimed to identify the frequency of the commonest type of thyroid cancer, which is papillary thyroid cancer (PTC), and its clinical presentation, characteristics, and management. Our study took place at King Abdul-Aziz University Hospital (KAUH) in Jeddah, Saudi Arabia, which is one of the main tertiary care centers in the kingdom of Saudi Arabia. As a major teaching hospital, it attracts people of different nationalities, providing a large and varied sample size. This was a retrospective study that reviewed 76 files from KAUH medical records between the period from 2003 until 2012. The results showed a majority of female cases with a mean age of 41.45(± 15.8) years. Most of these were of multiple nationalities and presented with euthyroid status; the main complaint was a thyroid lump. Twenty-one cases had metastasis to regional lymph nodes. Almost 60% of the sample had a solitary nodule according to ultrasound, while the rest were multinodular, and only nine patients had calcifications. A thyroid scan showed a hot nodule in 44% of the sample. Regarding our diagnostic protocol, we used ultrasound guided fine-needle aspiration and frozen sections to make the diagnosis. For management, 92% of the patients underwent thyroidectomy and only 67% of the cases had postoperative radioactive iodine I-131 therapy. We hope that our results will benefit health workers in this field and improve the management and health care for these patients.

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Keywords: Papillary Carcinoma, Thyroid Cancer, KAUH.

1.Introduction

Cancer is one of the leading causes of death worldwide, accounting for 7.6 million deaths in 2008, which represent around 13% of all deaths annually [2]. There are about 56,000 new cases of thyroid cancer diagnosed in the United States each year [3]. In Saudi Arabia, the thyroid cancer incidence has increased at an alarming rate that is currently between 15% and 30%, while the incidence of thyroid cancer worldwide ranges from 5 to 15% [1, 4, 5]. During the last 20 years, the incidence of thyroid cancer has risen mainly due to the better identification of micro

papillary thyroid cancers [6], as the majority of papillary thyroid cancer (PTC) is sporadic [3]. According to the Saudi Registrar of Oncology, 586 cases were registered in 2007 with a male-to-female ratio of 24:100. Thyroid cancer represents the second commonest cancer in females and the fourth most common cancer in both males and females, and the most prevalent type in Saudi Arabia is PTC [1]. Some of the risk factors for papillary cancer include exposure to radiation and a family history of thyroid disorders, and the classic presentation of this cancer

is a thyroid nodule. To evaluate this nodule, physical examination and ultrasound can be done in addition to fine-needle aspiration (FNA)^[7]. In our study, we aimed to identify the incidence of the most common type of thyroid cancer, which is papillary cancer, and its clinical presentation and characteristics. We also searched for other associated risk factors and compared our results with existing local and international data. At the end of this study, we hope to identify a management protocol for PTC and compare it with the standard of care for PTC.

2. Materials and methods

Our study took place in Jeddah, which is the second largest city in the Kingdom of Saudi Arabia. As a major city, it attracts many people from different nationalities, which can provide a wide variety of people. Regarding sample size, we reviewed 114 files from KAUH medical records, and only 76 files from the period between 2003 and 2012 were included. The collected data from the medical records were reviewed to ensure that they met the exclusion and inclusion criteria, which were complete demographic data, a full follow-up history pre-operatively and post-operatively, and a complete investigation with available data. These parameters assured easier accessibility and more accurate data. To ensure quality, there were four groups responsible for quality control. The first one checked if the data were complete or not. The second was responsible for coding; these group members made sure that every code was relevant to the right question. The third group of people handled data entry; they entered the data into the computers in order to be processed. The final group carried out random checks by obtaining random samples and reviewing them completely to make sure that there were no mistakes.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 19 was used for our statistical analysis. The qualitative data were presented as numbers and percentages. Chi-square test was used as a test of significance for qualitative data; Yates correction was employed when the expected cell was less than 5. The quantitative data were expressed as the mean and standard deviation.

3. Results

Our results are based on 76 patients; 54 (71%) were females, and 22 (29%) were males, with a mean age of $41.45 (\pm 15.8)$ years. Only 29 (38%) were Saudis, while the rest were of a different nationality. Most patients had a history of euthyroid status 62 (81.6%). In regards to risk factors, there were 12 (15.8%) cases with a positive family history of papillary cancer; all of them were first-degree

relatives. Two (2.6%) cases had a history of radiation. Five (6.6%) participants were smokers, while 23 (30.3%) had associated chronic diseases like (rheumatoid arthritis (RA), irritable bowel disorder (IBD), and diabetes mellitus (DM)), which may be due to the increase in the number of chronic diseases in this country, and 3 (3.9%) cases had a history of other associated cancers. Sixty-four (84%) cases presented with a thyroid lump, and 12 (15.8%) of these patients complained of difficulty swallowing as a complication of the lump. Ten (13.2%) patients presented with hoarseness, and 9 (11.8%) complained of weight gain, while 7 (9.2) experienced weight loss. Seven (9.2%) patients reported dyspnea, and 6 (7.9%) had anxiety and palpitations. Few participants complained of fatigue, alopecia, heat intolerance, cold intolerance, or menstrual cycle disorders. Thirty-five (35.1%) cases had metastasis, and 21 (27.6%) of these cases were to regional lymph nodes.

Half of the patients (50.8%) had normal thyroid-stimulating hormone (TSH) levels (mean \pm SD = 6.7 ± 15.25), and most patients (84.1%, 63.5%) were normal regarding the T3 and T4. The mean \pm SD for T3 was 4.8 ± 1.55 , and the mean \pm SD for T4 is 17.1 ± 7.2 . Sixty-eight (89.5%) participants received ultrasound of the neck; 39 (57.3%) of them had a solitary nodule, and the others 29 (42.9%) were multinodular. Only 9 of these 68 patients who received an ultrasound examination had calcifications. In our sample, 23 (36.5%) patients went for a thyroid scan, and 10 (43.5%) of them had a hot nodule. Seventy (92%) patients had surgery, and the most common type of operation was a total thyroidectomy (64 patients, 84.2%); only 51 (67%) of the cases had postoperative radioactive iodine I-131 therapy. Few cases had complications after thyroidectomy 12 patients (17.1%), which included hypocalcemia in 10 patients (14.3%) and laryngeal nerve injury in 2 (2.9%).

4. Discussion

Thyroid cancer can be classified based on cell origin to follicular cell-derived cancer (FCDC), which includes papillary carcinoma, follicular carcinoma, Hürthle cell carcinoma, anaplastic carcinoma, and parafollicular C cell cancer, which is medullary carcinoma, "75% sporadic and 25% hereditary" ^[8]. A study was done in Mures County and board areas, where the increase in thyroid cancer incidence is mainly due to PTC (61.1%, 1990-1999 vs. 81.8%, 2000-2009), which represents the largest majority of thyroid carcinomas (78%)^[4]. Similar results also have been reported worldwide^[4, 9-12]. In our study, PTC cases made up 74 out of 109, which represent 67.8% of the patients. There has been much speculation about why the incidence of differentiated thyroid

carcinoma is rising. Some researchers have suggested that potential risk factors, including radiation exposure^[13, 14], iodine deficiency^[15], and head and neck radiation therapy^[16, 17], are more common nowadays. In our study, we found the most common risk factors were a positive family history (12 cases, 15.8%) and radiation (2 cases, 2.6%); others included smoking (5 patients, 6.6%) and a history of other cancers (3 patients, 3.9%). We also discovered that the number of chronic diseases (23 patients, 30.3%), such as rheumatoid arthritis (RA), irritable bowel disorder (IBD), and diabetes mellitus (DM), was high due to the rising number of diabetic patients in Saudi Arabia^[18]. Additionally, there was a female predominance in our population (54 patients, 71%); some studies have suggested that certain female hormonal and reproductive factors may play a role^[19-21] in the development of this malignancy, which could explain the net female predominance of thyroid carcinoma. Advances in the diagnosis of cancer in general and especially of its subclinical forms have significantly contributed to the detection of more tumors in the last 10 years as well^[22, 23].

Patients with PTC are usually asymptomatic and may present with a neck lump alone, which is usually palpable in 5 to 7% of the cases during a routine physical examination or discovered during an imaging study done for another reason, such as ultrasound, which identifies 40 to 50% of PTC^[24, 25]. In our study, we found that most patients presented with a history of euthyroid status (62 cases, 81.6%), and the only complaint was of a neck mass (64 patients, 84%) that led to difficulty in swallowing in 12 (15.8%) cases; other clinical presentations may be seen but are less likely. Even when patients present with occult lymph node metastases or invasion into surrounding neck structures, PTC is largely a localized disease; distant metastases are uncommon, occurring in fewer than 4% of patients at the time of the initial diagnosis, with the most common sites being the bone and lung^[26]. In our study, there were 26 (35%) cases with metastases, and 21 (27.6%) had metastases to the occult lymph node. The remaining cases had distal metastases, with 4 (5.3%) to the bone and 1 (1.3%) to the lung, a rate that is higher than those reported in other studies because of the late presentation to our tertiary center. The diagnostic investigation of a patient with PTC usually begins with the evaluation of a thyroid nodule, which includes measurement of serum TSH levels and ultrasonography of the thyroid gland, and the diagnosis is usually made by FNA biopsy. Although most patients with thyroid cancer are euthyroid, people with higher or normal TSH concentrations may be at increased risk of cancer in a thyroid nodule^[27]. Half of our patients (50.8%) had normal

TSH levels (mean \pm SD = 6.7 ± 15.25), and most patients even T3 and T4 (84.1%, 63.5%) of the cases were normal. The number of patients who received ultrasound of the neck was 68 (89.5%); 39 (57.3%) of them had a solitary nodule, and the other 29 (42.9%) patients were multinodular. Only 9 patients had calcification, and FNA was done to confirm the diagnosis. Because of the low mortality rate and the low incidence of operative and post-operative complications, thyroidectomy is considered the gold standard of care for treating patients with well-differentiated PTC^[28]. However, debate still exists regarding whether total or partial thyroidectomy is the best method for well-differentiated papillary thyroid cancer^[29, 30, 31]. Numerous studies have shown that surgical resection of all gross tumors offers the best outcome to patients with locally aggressive thyroid cancer. Hence, it is incumbent on the thyroid surgeon to determine the extent of local invasion prior to and during surgery and to make the appropriate intraoperative decision regarding the surgical extent^[32]. As there is a higher local recurrence rate, most patients with extensive extra-tracheal extension require adjuvant radioactive ablation or external beam radiotherapy in select patients^[33]. In our study, the number of patients who underwent surgery was 70 (92%), and most of them had total thyroidectomy (64, 84.2%); only 51 (67%) cases received postoperative iodine radiotherapy. Few participants experienced complications after thyroidectomy (12 patients, 17.1%), including hypocalcemia (10 cases, 14.3%) and laryngeal nerve injury (2 cases, 2.9%).

Conclusions and Recommendations

Among our 76 patients, 70% were female, and all patients had a mean age of $41.45 (\pm 15.8)$ years. Most patients presented with euthyroid status, and the main complaint was a thyroid lump in the neck. Thirty-five percent of the cases had metastasis, and most were to the lymph nodes. Almost 60% of the sample had a solitary nodule according to ultrasound, while the other patients were multinodular; only nine participants had calcifications. Thyroid scans showed a hot nodule in 44% of the sample. To manage the condition, 92% of patients received thyroidectomy, and only 67% of the cases had postoperative iodine radiotherapy. Greater awareness of the disease and early diagnosis and treatment using both surgical and medical management, such as I131 ablation, should change the disease and survival rates. Additionally, early detection of pathology in female patients with thyroid lumps by clinical or laboratory investigations are a must to improve the outcome of malignant thyroid disease.

Limitation of the research

Because our study was retrospective, the main limitation we faced was missing data. In addition, the Phoenix system only contained data from 2003 to the present; it did not include all the information we needed, so we had to review the archives to obtain additional information. The treatment approach for patients with thyroid disease can vary widely from one physician to another, so not all the investigations we were looking for had been done for all the patients. We also were not able to collect the data from different centers or hospitals.

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11/12/2013