



Pathological and clinical findings in a series of 22 cases of medullary carcinoma of the thyroid at the Korle-Bu teaching hospital (1994-2013)

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Abstract

There is paucity of published data on medullary thyroid cancer (MTC) as a single entity in Ghana and Africa as a whole despite its first description six decades ago. The aim of this study was to determine the proportions of thyroid malignancies diagnosed in the department of pathology of the Korle-Bu Teaching Hospital (KBTH) between 1994-2013 that were MTCs and the clinicopathological characteristics by a retrospective histopathological study.

Material and methods: This was a retrospective study in KBTH from 1994 to 2013.

Results: During the period under review, MTC was found to be the third common thyroid malignancy, accounting for 10.0% of all the cases. The mean age of patient was 38.4 years ($SD \pm 16.0$) with half (50.0%) being younger than 40 years of age. The male to female ratio was 1:1. The modal age of the males was 40-49 years (27.3%), but that for the females was 20-29 years (36.4%). Anterior neck swelling was the commonest presentation of MTCs (95.5%), particularly diffuse gland involvement (45.5%). Males with MTC presented relatively early within two years (50.0%), compared to females who commonly presented after 5 years (37.5%) with the disease. AMTCs were commonly diagnosed in lobectomy specimens (44.4%). Two of the females had neck dissection (18.2%). Extra-glandular spread at diagnosis was found in lymph nodes (22.7%), lymphovascular space (13.6%) and neck muscles (13.6%).

Conclusion: Medullary thyroid cancer was found to be the third common thyroid malignancy at KBTH with no significant sex differences in the clinical presentation. Patients commonly presented with large anterior neck swelling of variable duration. Approximately 59.1% of the patients had organ confirmed disease at diagnosis.

Keywords: Medullary thyroid cancer, neuroendocrine, Ghana, extra-glandular spread, anterior neck swelling

Introduction

Medullary thyroid cancer (MTC) is a neuroendocrine carcinoma, composed of malignant C-cells (parafollicular cells) [1]. MTC was first described by Hazard et al., in 1959 [2]. The majority of MTCs are sporadic, but approximately 20% of MTCs are as a result of a germline genetic mutation in the rearranged during transfection (*ret*) proto-oncogene. Hereditary MTC can be seen in isolation (familial medullary thyroid cancer [FMTC]) or as part of the multiple endocrine neoplasia (MEN) syndrome type 2 (2A or 2B) [3-6]. The associations of MTC and neuroendocrine

disorders was described by Steiner and colleagues in 1968 [7].

The relative proportion of MTC among thyroid malignancies varies across Africa [8-11] and globally [12-14]. For instance Sippel et al., in their study found that MTC accounts for approximately 10.0% of all thyroid malignancies [12], while Well et al., found 1-2% [14].

The age at diagnosis with MTC varies among studies [15,16]. MTC may show slight female preponderance [12,13], one study found male preponderance [17], while Grubbs et al., [18] found no sex differences. The commonest clinical presentation of MTC

from previous studies is an enlarged thyroid gland, especially at the poles [19,20].

The prognosis of MTC is worsened by advanced age (>65 years) at diagnosis, in patients diagnosed with the sporadic variant, cases with paucity of calcitonin immunostaining and rising serum carcinoembryonic antigen (CEA) level [21-26].

Medullary thyroid cancer has generally not been studied as a single entity in Africa, West Africa including Ghana. Similarly the relative proportion of thyroid malignancies that are MTCs and the clinical presentation have not been studied in Ghana. The aim of this study was to determine the proportions of histologically diagnosed thyroid malignancies and the associated clinicopathological characteristics from 1994-2013, in the department of pathology of the KBTH, by a retrospective histopathological study.

Materials and methods

Study design

This was a retrospective review from January 1994 to December 2013.

Study site

The study was conducted in the Department of Pathology, Korle-Bu Teaching Hospital (KBTH) the biggest referral hospital in Ghana. Surgical specimens are received from the Korle-Bu teaching hospital and other hospitals across the region and beyond.

Data collection and analysis

All clinical request forms, the histology reports and the corresponding histology slides of all thyroid malignancies diagnosed in the department institution from January 1994 to December 2013 were reviewed. Data were collected on the demographic features and the histopathological characteristics of MTCs diagnosed during the period of underreview. Data were entered into and analysed using SPSS software version 23.0 (Chicago).

The total number of thyroid malignancies diagnosed over the period of study was determined over the period 1994-2013.

The relative proportions of the subtypes of the TMs were determined: Papillary, follicular, anaplastic, medullary, and others were determined over the period 1994-2013.

The clinicopathological characteristics of patients diagnosed with MTCs including the types of surgical specimens were then determined separately as an entity.

Descriptive statistics of mean and standard deviation were used to describe the data. The results were presented in frequency tables and a histogram. The clinical presentations of MTC in males and females were compared using Chi-Square Test.

Availability of data

The data used to prepare this manuscript will be made available on demand.

Inclusion criteria

All histologically confirmed thyroid malignancies were included.

Exclusion criteria

All cases of poorly fixed specimens and those with incomplete records were excluded from the analysis.

Results

Age characteristics of patients diagnosed with MTC

During the period under review, a total of 220 thyroid malignancies were diagnosed. Of this number, 22 (10.0%) were MTCs, thus making it the third common TM, after papillary (52.7%) and follicular (35.0%) respectively. The ages of patients diagnosed with MTC range from 11 to 73 years with a mean age of 38.4 years (SD±16.0) and a modal age group of 40-49 years. There were equal numbers of males and females patients respectively. Approximately half (50.0%) of the patients were younger than 40 years. There were no significant age differences between males and females (p-value=0.530), (Tables 1 and 3).

Clinical presentation and laterality of symptoms

All the patients diagnosed of MTCs presented with neck swelling, of which 21 (95.5%) involved the thyroid gland. Only one patient presented with cervical lymphadenopathy (4.5%). Of those with thyroid gland enlargement, 45.5% presented with diffuse gland enlargement (Table 2).

Duration of symptoms at presentation of MTC

A total of 16 (72.7%) of the patients had stated duration of the symptoms at presentation (8 males and 8 females). Approximately half (50.0%) of the males presented within two years of noticing the swelling while 37.5% of females presented at 5 or more years of onset of the disease. There were no significant differences in duration at presentation between males and females (Tables 2 and 3).

Types of surgical specimens in which MTC was diagnosed

A total of 11 (44.4%) patients with MTCs were diagnosed in lobectomies. Majority of males had lobectomy (54.5%) compared to 45.4% of females (Table 2). Two of the female patients

Table 1. Age groups of male and female patients diagnosed with MTC.

	Whole group	Male	Female
Age group (years)	(n/%)	(n/%)	(n/%)
≤ 19	2(9.1)	2(18.2)	0 (0.00)
20-29	5(22.7)	1(9.0)	4(36.4)
30-39	4(18.2)	2(18.2)	2(18.2)
40-49	6(27.3)	3(27.3)	3 (27.3)
50-59	3(13.6)	2 (18.2)	1(9.0)
≥60	2(9.1)	1(9.0)	1(9.0)
Total	22(100.0)	11(100.0)	11(100.0)

Table 2. Clinical features and type of surgical specimens from which MTCs were diagnosed (1994-2013).

	Whole group (n/%)	Males (n/%)	Females (n/%)
Symptoms			
Diffuse gland enlargement	10(45.5)	4(36.4)	6 (54.5)
Left lobe enlargement	7(31.8)	4 (36.4)	3(27.3)
Right lobe enlargement	4(18.2)	2(18.2)	2(18.2)
Cervical lymphadenopathy	1(4.5)	1(9.0)	0(0.0)
Total	22(100.0)	11(100.0)	11(100.0)
Duration of symptoms at presentation (years)			
1	5(31.2)	3(37.5)	2(25.0)
2	4(25.0)	4(50.0)	0(0.0)
3	3(18.8)	0(0.0)	3(37.5)
4	1 (6.2)	1(12.5)	0(0.0)
≥5	3(18.8)	0(0.0)	3(37.5)
Total	16(100.0)	8(100.0)	8(100.0)
Type of surgical specimens			
Total thyroidectomy	6(27.3)	2(18.2)	4(36.4)
Neck dissection	2(9.0)	0(0.0)	2(18.2)
Lobectomy	11(50.0)	6(54.5)	5(45.4)
Incision biopsy	3(13.7)	3(27.3)	0(0.0)

had neck dissection (18.2%).

Invasion of surrounding structures

At the time of histological diagnosis 5 (22.7%) patients had nodal involvement, 3(13.6%) with vascular invasions and one with invasion of the neck muscles (4.5%) at the time of

histological diagnosis.

Discussion

In our institution patients diagnosed with medullary thyroid cancer (MTC) were not categorised into sporadic and familial cases [3-7] and thus not grouped as such in this review. We found that MTC was the third common thyroid malignancy. This is similar to previous studies in Ghana [8] and Nigeria [9]. The current rank of MTC however differs from other studies in Africa that found it to be the fourth common type of thyroid malignancy [10,11]. The relative proportion of MTC in this current study was 10.0%. This rate is comparable to those reported by Sippel et al., [12] and Williams et al., [13], but much higher than the 1-2% and 4.0% reported by Well et al., study [14] and Hundahl et al., [15] respectively.

MTC was commonly diagnosed in younger patients with a mean age of 38.4 years. Although the study did not categorise patients into hereditary and sporadic forms of MTC, this value is closer to the mean age of 38.0 years previously reported by Kebebew et al., [16] who did not group their patients into the two forms. Furthermore, the current mean age of patients with MTCs lies between the mean age of 35.0 years for familial variant [6] and 46.7 years for patients with sporadic variant [13,17].

There were equal numbers of males and females diagnosed with MTC in the present study. This finding differs from those reported by Saral et al., [17] who found the disease to be twice as common in men as in women. This finding is also different from the studies of Sippel et al., [12] and Williams et al., [13] that found female predominance, but similar to the study of Grubbs et al., [18] that found no difference in incidence

Table 3. Comparing the clinical presentation of MTC between males and females using Chi-Square Test.

Age groups (Years) cross tabulation						
	≤29	30-39	40 - 49	≥50	Total	P-value
Sex: Female	4	2	3	2	11	0.530
Male	3	2	3	3	11	
Total	7	4	6	5	22	--
Part of thyroid involved cross tabulation						
	Whole	Left lobe	Right lobe	Lymph node	Total	P-value
Sex:Female	6	4	1	0	11	0.630
Male	4	4	2	1	11	
Total	10	8	3	1	22	--
Type of surgical specimens cross tabulation						
	Neck dissection	Excision/ incision biopsy	Thyroidectomy	Lobectomy	Total	P-value
Sex: Female	2	0	4	5	11	0.169
Male	0	5	2	4	11	
Total	2	5	6	9	22	--
Duration of symptoms at presentation cross tabulation						
	1	2	3	≥4	Total	P-value
Sex: Female	2	0	3	3	8	0.111
Male	3	4	0	1	8	
Total	5	4	3	4	16	--

bet-ween males and females.

The majority of patients diagnosed with MTC presented with thyroid gland enlargement, as found in previous publications [17-20]. In this current study, 27.3% of the patients with MTC had nodal involvement at histological diagnosis. This rate is lower than the 35%-50% reported in the study by Sipple [12] and 80.0% in the study of Moley et al., [20]. There is no apparent reason for the low extra nodal involvement by MTC in this study. It may however be due to the fact that only 27.2% and 9.0% of the patient with MTC had total thyroidectomy and neck dissection respectively.

Studies published in the last decade found MTC to have relatively good 5-year and 10-year survival rates [21-23]. In the current study approximately 77.2% of patients diagnosed with MTCs were younger than 50 years of age and a significant number (59.1%) were organ confined. Although 22.7% of the patients had nodal involvement it has been found that the presence of cervical lymph node metastases does not affect the survival adversely [22,23]. Direct invasion of the surrounding neck structures by MTC has been shown to be a bad prognostic factor [23]. But the current study found neck muscle invasion in just one case. In view of the younger age at diagnosis, organ confined cancer and the lack of invasion of surrounding neck structures, the author opines that the outcome of the disease in these patients will be favourable as suggested in the literature [24-26].

Conclusion

Medullary thyroid cancer was found to be the third common thyroid malignancy in the current study with no significant sex differences in the clinical presentation. Patients were relatively younger and presented late with large anterior neck swelling. Majority of the patients had organ confined disease at diagnosis.

Competing interests

The author declares that he has no competing interests.

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