

Original article

Medullary thyroid carcinoma in King Chulalongkorn Memorial Hospital: Natural history, management, and outcome

Natawat Narueponjirakul, Pasurachate Samorn*

Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Background: Medullary thyroid carcinoma (MTC) is rare and a diagnosis difficulty disease. In term of natural history, management, and outcomes among Thai patients, the data were scarce.

Objectives: We aimed to review natural history, management, and clinical outcome of MTC patients in the tertiary care hospital.

Methods: Retrospective study of medullary thyroid carcinoma patient was performed in our hospital from January 1, 2002 to December 31, 2011. Medical records has been carefully reviewed. Demographic data, clinical presentation, investigation, management and outcomes has been collected.

Results: Sixteen MTC patients were taken into account for 1.1% of all thyroid carcinoma of the hospital, 12 were women. Mean age was 51.9 years. All of them were sporadic cases. 75.0% of cases present with thyroid nodule. 87.5% underwent fine needle aspiration (FNA). Preoperative diagnosis was made only 25.0% by FNA. Preoperative serum calcitonin levels and CEA levels were measured in 4 and 5 patients; the levels were increased in all cases. Regarding mode of treatment, total thyroidectomy, near total thyroidectomy and subtotal thyroidectomy were applied for 11, 2 and 2 patients respectively. In patients with advance disease, cervical lymphadenectomy was adopted (2 prophylactic central neck dissection, 4 prophylactic ipsilateral neck dissection, 6 therapeutic ipsilateral neck dissection and 1 contralateral neck dissection). Median follow up period was 41 months. There was no mortality observed.

Conclusions: Since, lack of an accurate preoperative diagnosis, the treatment varies especially in cervical lymphadenectomy procedures, depending on surgeon's preferences. However, favorable outcomes have been achieved.

Keywords: Medullary thyroid carcinoma, outcome, management.

Medullary thyroid carcinoma (MTC) is rare, about 5.0 – 8.0% of thyroid cancer. Most of them are sporadic type. About 20.0% - 30.0% is hereditary⁽¹⁾ (e.g. multiple endocrine neoplasia type 2 (MEN 2) and familial medullary thyroid carcinoma). The poor prognostic factors are age > 65 years, extent of disease, and surgical treatment.⁽²⁾

Most of the patients present with thyroid mass. Cervical lymph node metastases have been found in 35.0 – 50.0% of the patients and distant metastases have been found in 10.0 -15.0% at the time of

diagnosis. The common sites of metastases are mediastinum, liver, lung, and bone.⁽³⁾

Although there are improvement in the investigation and treatment, survival rates are not increased. Surgery is the main treatment of MTC.⁽⁴⁾ Even, there are some controversies about the extent of surgery; National Comprehensive Cancer Network (NCCN) guideline suggests that total thyroidectomy is the treatment of choice for MTC patients. About the lymphadenectomy NCCN suggests prophylactic central neck dissection and therapeutic lateral neck dissection.⁽⁵⁾ Neither lymph node positive nor negative MTC patients, there is evidence that increasing in lymph node yield from lymphadenectomy has no impact on survival.⁽⁶⁾ The other treatments (e.g. chemotherapy, radiotherapy) are not improving the outcomes. The purpose of this study was to review natural history, management, and clinical outcome of medullary thyroid carcinoma.

* **Correspondence to: Pasurachate Samorn**, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

E-mail: Pasurachate.s@chula.ac.th

Received: November 5, 2019

Revised: January 23, 2020

Accepted: March 10, 2020

Materials and methods

This study was approved by the institute review board committee. Inform consent was waiving. Retrospective study of medullary thyroid carcinoma patient in King Chulalongkorn Memorial Hospital (KCMH) from January 1st, 2002 to December 31st, 2011 was conducted. Medical records were carefully reviewed for demographic data, clinical presentation, investigation, management, and outcomes. Demographic data (e.g. age, sex), clinical presentations, tumor markers (e.g. calcitonin, CEA), histopathological data (e.g. fine needle aspiration, tumor size), treatment, thyroidectomy procedures (e.g. total thyroidectomy, near total thyroidectomy, and subtotal thyroidectomy), lymphadenectomy procedures (e.g. central lymphadenectomy (cervical lymph node group VI), lateral lymphadenectomy (cervical lymph node group II-V), prophylactic lymphadenectomy (no evidence of suspected metastatic lymph node), therapeutic lymphadenectomy (suspected metastatic lymph node)), and outcome were collected. Descriptive statistic was analyzed.

Results

In our hospital, there are 1,500 thyroid cancer patients from January 1st, 2002 to December 31st, 2011. Sixteen (1.1%) MTC patients were included.

All of them are sporadic but 2 of them were co-incident with papillary carcinoma and follicular carcinoma. Female was 12 (75.0%), mean age was 51.9 years (27 - 77 years). Neck mass was the most common presentation (75.0%). Abnormal serum CEA level was presented in 4 patients (25.0%). Cervical lymphadenopathy was found in 1 patient (6.3%).

Fine needle aspiration biopsies were performed in 14 of 16 MTC patients (87.5%). The results shown MTC 3 cases, malignancy 2 cases, follicular neoplasm 2 cases, and data no available for 2 cases. Serum calcitonin and CEA level were investigated in 4 cases and 5 cases, respectively.

Unifocal lesions were found in 10 cases and multifocal lesions were found in 2 cases. The mean size of tumor was 2.81 cm. Lymph node metastases were found in 6 cases (37.5%) and bone metastasis in 1 case (6.3%).

Total thyroidectomy procedures were performed in 11 cases, Near total thyroidectomy in 2 cases, and subtotal thyroidectomy in 2 cases. Prophylactic central neck dissections were performed in 2 cases. About lymphadenectomy, ipsilateral prophylactic neck dissections were performed in 4 cases, ipsilateral therapeutic neck dissections in 6 cases, and contralateral prophylactic neck dissection in 1 case.

Table 1. Medullary thyroid carcinoma patients in KCMH.

Male : female (cases)	4:12	Lymphadenectomy (cases)	
Age (years)	Mean 51.9 (27 - 77)	Central neck dissection	2
Presentation (cases)		Ipsilateral lateral neck dissection	
Thyroid nodule	12	Prophylactic	4
CEA rising	2	Therapeutic	6
Lateral neck mass	1	Contralateral lateral neck dissection	1
Unknown	1	Node metastases (+/all)	
FNA (cases)		Central	0/2
Benign (colloid + benign fat cell)	2	Prophylactic	0/2
Follicular neoplasm	6	Ipsilateral	6/10
MTC	4	Prophylactic	0/4
Malignant	2	Therapeutic	6/6
Not available	2	Contralateral	0/1
Baseline calcitonin (pg/ml, 4 cases)	627, 3, 386, 3, 745, 4, 257	Distant metastases (cases)	1/16
Baseline CEA (ng/ml, 5 cases)	30.3, 284.0, 224.3, 189.0, >210.0	Biological cure (cure/data available)	6/11
Size (cm., 12 cases)	Mean 2.8 (0.7 - 7)	Clinical cure (cure/data available)	11/12
Unifocal	10/12	Morbidity	
Multifocal	2/12	Chyle leak	1
Surgery (cases)		Vocal cord paralysis	1
Total or completion thyroidectomy	11	Seroma	1
Near total thyroidectomy	2	Mortality	0/12
Subtotal thyroidectomy	2	Median follow up (months)	41(9 - 90)
Unknown	1	Loss follow up (cases)	4

Table 2. Data of Medullary thyroid carcinoma patients in KCMH.

No.	Sex	Age (years)	Presentation	CT (pg/ml)	CEA (ng/ml)	FNA	Patho	Size (cm.)	Thyroid Surgery	Lymph node Surgery	
										Ind.	site
1	M	36	Thyroid nodule	-	-	colloid	MTC	2.8	TTD	P	IL
2	F	55	Thyroid nodule	-	-	-	MTC	NA	TTD	T	IL
3	F	54	Thyroid nodule	-	-	benign	FTC+	2.7	TTD	-	-
4	F	48	Thyroid nodule	-	-	MTC	MTC	NA	STD	T	IL
5	F	69	NA	-	-	-	MTC	NA	TTD	-	-
6	F	43	Thyroid nodule	-	-	Follicular neoplasm	MTC	7.0	NTD	T, P	IL,CL
7	F	41	Thyroid nodule	3,386	> 210.0	MTC	MTC	1.9	STD	T	IL
8	F	47	Thyroid nodule	-	-	Follicular neoplasm	MTC	0.8	TTD	-	-
9	M	61	Thyroid nodule	-	-	Follicular neoplasm	MTC	0.7	TTD	-	-
10	F	77	Thyroid nodule	4,257	189.0	MTC	MTC	3.5	TTD	P	C+IL
11	F	49	Thyroid nodule	-	-	Follicular neoplasm	MTC	2.5	TTD	P	IL
12	M	49	Thyroid nodule	3,745	224.3	MTC	MTC	5.0	TTD	T	IL
13	F	27	Thyroid nodule	-	-	Follicular neoplasm	MTC	3.0	TTD	P	C
14	M	42	Lateral neck mass	-	-	malignancy	MTC	-	NA	T	IL
15	F	64	CEA rising	-	284.0	malignancy	MTC	3.0	NTD	P	IL
16	F	69	CEA rising	627	30.3	Follicular neoplasm	MTC+ PTC	0.9	TTD	-	-

CT: calcitonin, CEA: carcinoembryonic antigen, FNA: fine needle aspiration, NA: not available, MTC: medullary thyroid carcinoma, PTC: papillary thyroid carcinoma, FTC: follicular thyroid carcinoma, TTD: total thyroidectomy, NTD: near total thyroidectomy, STD: subtotal thyroidectomy, P: prophylactic, T: therapeutic, C: central group, IL: ipsilateral group, CL: contralateral group

Biological cure was achieved in 6 patients and also clinical cure in 11 patients. However, there were 4 patients that loss follows, so the data were not available.

There were 3 cases of morbidity in our hospital chyle leakage 1 case, vocal cord paralysis 1 case, and seroma 1 case. There was no mortality in our patients. Median time to follow up was 41 months.

Discussion

Medullary thyroid carcinoma (MTC) is a rare thyroid cancer. In ten-year period at our hospital, we found that MTC patients were 1.1% of all thyroid cancer. All our MTC patients were sporadic, that is comparable to other series, those shown MTC incidence was 5.0 – 8.0% of all thyroid cancer and most of them are sporadic. It is difficult to diagnose MTC by FNA biopsy, only 4 cases in our institution

received diagnosis by FNA biopsy before treatment. There was the literature studied in 245 MTC patients, its result shown that about 45.7% received the diagnosis by FNA biopsy.⁽⁷⁾ There was a study that reviewed effectiveness of screening serum calcitonin level in the patients with thyroid nodules but it was not cost and effectiveness because MTC prevalence was only 0.4% of all patients with thyroid nodule and the evidence shown that screening serum calcitonin increased the rate of unnecessary thyroidectomy.⁽⁸⁾

In our study, total and near total thyroidectomy were performed in 81.3% of our patients and 12.5% of patients were underwent subtotal thyroidectomy. There is evidence that survival rate was poor in the MTC patients that received the surgery less than total thyroidectomy⁽²⁾, so the recommended surgery for the MTC patients that do not have local invasion or distant metastases is total thyroidectomy.^(5, 9)

About the extent of lymphadenectomy in our hospital, it was depended on surgeons' evaluation. Our study showed prophylactic central neck dissection 12.5%, prophylactic ipsilateral neck dissection 25.0%, therapeutic ipsilateral neck dissection 37.5%, and contralateral neck dissection 6.3% of the patients. Up to date, prophylactic central neck dissection is recommended^(5, 9) because there was a study showed the better survival in the groups of MTC patients that received total thyroidectomy and central lymphadenectomy than only total thyroidectomy.⁽¹⁰⁾ The prophylactic lateral neck dissection is still controversial. Furthermore, increased lymph node yield was not improved survival in both positive and negative node patients.⁽⁶⁾ Serum calcitonin and CEA were used in follow up in 68.8% of our patients.

This study showed some limitation. First, low number of the patients limited possibility to find prognostic factors of disease or compare treatment options. Second, retrospective study design that can cause some missing data. Last, high percentage of loss follow up rate (25.0%). Further study may aim to study how to increase the preoperative diagnostic rate, compare treatment options either in thyroidectomy or lymphadenectomy.

Conclusion

In this study, the MTC patient was 1.1% of all thyroid cancer patients in our hospital. Only 25.0% of patients were diagnoses before the treatment. Despite the treatment options were depended on the surgeons' decision, good outcome was accomplished.

Conflict of interest

The authors, hereby, declare no conflict of interest.

References

1. Pacini F, Castagna MG, Cipri C, Schlumberger M. Medullary thyroid carcinoma. *Clin Oncol (R Coll Radiol)* 2010;22:475-85.
2. Roman S, Lin R, Sosa JA. Prognosis of medullary thyroid carcinoma: demographic, clinical, and pathologic predictors of survival in 1,252 cases. *Cancer* 2006;107:2134-42.
3. Sippel RS, Kunnimalaiyaan M, Chen H. Current management of medullary thyroid cancer. *Oncologist* 2008;13:539-47.
4. Shepet K, Alhefdhi A, Lai N, Mazeh H, Sippel R, Chen H. Hereditary medullary thyroid cancer: age-appropriate thyroidectomy improves disease-free survival. *Ann Surg Oncol* 2013;20:1451-5.
5. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN guidelines™) thyroid carcinoma version 2.2013. Pennsylvania: NCCN; 2013.
6. Kandil E, Gilson MM, Alabbas HH, Tufaro AP, Dackiw A, Tufano RP. Survival implications of cervical lymphadenectomy in patients with medullary thyroid cancer. *Ann Surg Oncol* 2011;18:1028-34.
7. Essig GF Jr, Porter K, Schneider D, Debora A, Lindsey SC, Busonero G, et al. Fine needle aspiration and medullary thyroid carcinoma: the risk of inadequate preoperative evaluation and initial surgery when relying upon FNAB cytology alone. *Endocr Pract* 2013;19:920-7.
8. Daniels GH. Screening for medullary thyroid carcinoma with serum calcitonin measurements in patients with thyroid nodules in the United States and Canada. *Thyroid* 2011;21:1199-207.
9. Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, Gharib H, et al. Medullary thyroid cancer: management guidelines of the American Thyroid Association. *Thyroid* 2009;19:565-612.
10. Greenblatt DY, Elson D, Mack E, Chen H. Initial lymph node dissection increases cure rates in patients with medullary thyroid cancer. *Asian J Surg* 2007;30:108-12.