Endocrine Malignancies: A Five-Year Retrospective Analysis in a Tertiary Hospital

Celeste C. Ong-Ramos, M.D.*; Leila Sawadjaan, M.D.*; Michael L. Villa, M.D.*

Abstract

Background: Endocrine malignancy in the Filipino population has not been well documented particularly on the incidence, prevalence, demographic profile and survival rate. It is the aim of this study to determine the prevalence rate and demographic profile of all endocrine malignancies diagnosed at a tertiary hospital.

Materials and Methods: This is a retrospective study from March 2003 to March 2008. Data were obtained from the Tumour Registry of St. Luke's Medical Center Cancer Institute (SLMC-CI) and from the Annual Report of the Diabetes, Thyroid and Endocrinology Center (DTEC) Section of SLMC-Quezon City. Only individuals with retrievable histopathology at this institution were included in the study.

Statistical Analysis: Data were calculated using percentages and proportions.

Results: There were a total of 855 cases of endocrine malignancies documented in five years of which, 833 were cases of thyroid malignancies (97.4%). Fourteen cases of adrenal cancer (1.60%), seven cases of neuroendocrine carcinoma (0.79%), and one case of parathyroid carcinoma (0.14%). There was no note of pituitary cancer.

There were a total of 833 newly diagnosed thyroid cancer: 652 papillary carcinoma (78.2%), 157 follicular carcinoma (18.8%), 11 anaplastic carcinoma (1.32%); nine medullary thyroid cancer (1.08%); two thyroid lymphoma (0.28%), one poorly differentiated carcinoma (0.14%) and one metastatic to the thyroid (0.14%).

Among the 14 adrenal cancers, seven cases were due to adrenal cortical carcinoma, one case was due to adrenal neuroblastoma and six cases were due to adrenal metastases. Among the neuroendocrine carcinomas, four were pancreatic neuroendocrine carcinoma which included two malignant insulinoma and three patients were extra pancreatic neuroendocrine carcinoma.

Keywords: endocrine malignancies, thyroid cancer, adrenal cancer, parathyroid cancer, pancreatic cancer

Introduction

Endocrine cancers are a mixed group of diseases in which cancer cells are found in tissues of the endocrine system which includes the thyroid, adrenal, pancreas, parathyroid and pituitary gland (Figure 1).

To date, the occurrence of endocrine malignancies in the Filipino population has not been well-documented. Prevalence of different cancers is based on foreign literatures. Since genetic mutation varies geographically worldwide, it is therefore important to establish our own cancer prevalence. It is the aim of this study to present the prevalence of endocrine malignancies in Filipino patients based on a five-year record from March 2003 to February 2008, from a tertiary hospital.

This is a retrospective study that looked into all endocrine malignancies among patients in St. Luke's Medical Center, Quezon City (SLMC-QC).

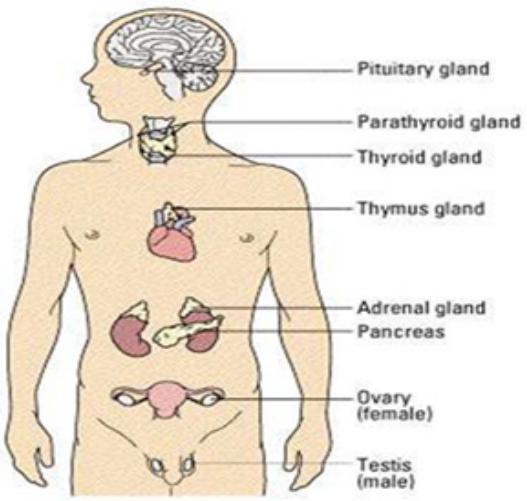

Figure 1: **Endocrine glands**

*Section of Endocrinology, Diabetes and Metabolism, St. Luke's Medical Center, Quezon City, Philippines

Reprint request to: Celeste C. Ong-Ramos, M.D., St. Luke's Medical Center, 279 E. Rodriguez Sr. Boulevard Quezon City, Philippines
Email: celesteongramos@yahoo.com

Methodology

The data is obtained from the Tumour Registry of St. Luke's Medical Center Cancer Institute (SLMC- CI) and from the Annual Report of the Diabetes, Thyroid and Endocrinology Section of SLMC-QC (DTEC) from March 2003 to February 2008, which reflects patients being seen by the Endocrinology fellows both in the pay and social service inpatient setting. Only patients who have histopathology report retrievable at this institution were included.

Statistical Analysis

Data gathered were calculated using percentages and proportions.

Results

There were a total of 873 cases of endocrine malignancies encountered in five years, however only 855 cases were documented. Eighteen cases were excluded due to unavailability of histopathology result at our institution. There were 833 cases of thyroid malignancies, accounting for 97.4%; 14 cases of adrenal, 1.6%; seven cases of neuroendocrine cancers accounting for 0.8%; and one case of parathyroid cancer, accounting for 0.1% (Figure 2). There was no note of pituitary cancer.

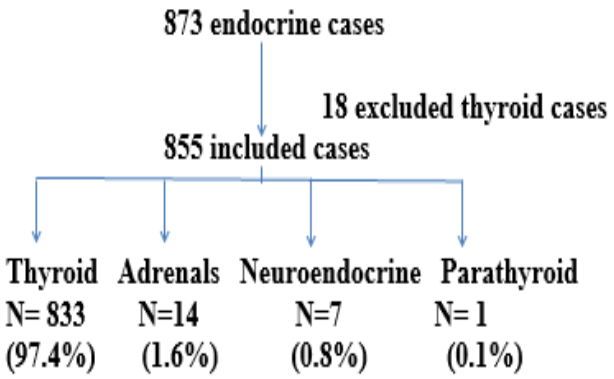

Figure 2: **Distribution of endocrine malignancies**

In this five-year data collection, the 833 confirmed thyroid cancer were divided as follows: 652 papillary carcinoma (78.2%), 157 follicular carcinoma (18.8%), 11 anaplastic carcinoma (1.32%); nine medullary thyroid cancer (1.08%); two lymphoma (0.24%), one poorly differentiated carcinoma (0.12%) and one metastatic to the thyroid (0.12%) (Figure 3).

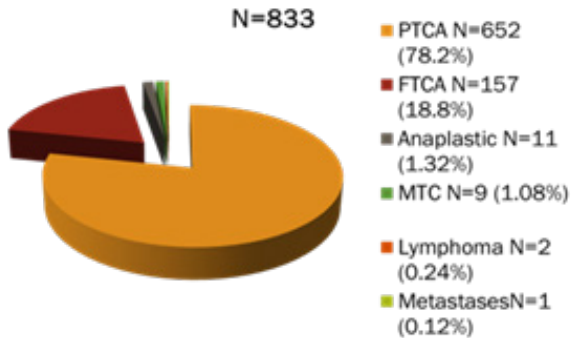

Figure 3: **Distribution of thyroid malignancies**

There were 14 cases of adrenal cancers encountered in five years. These were as follows: seven adrenocortical carcinoma, six adrenal metastases and one central adrenal neuroblastoma (Figure 4). Table I shows the demographic profile of the different adrenal cancers.

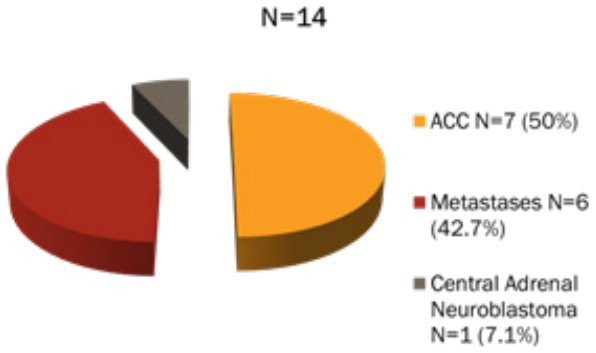

Figure 4: **Distribution of adrenal cancers**

Table I: **Demographic profile of the different adrenal cancers**

	Adrenocortical Cancer N=7	Adrenal Metastases N=6	Adrenal Neuroblastoma N=1
% in the study	50%	42.7%	7%
Mean Age	44.5	65.3	4
Age Range	50-57	56-75	4
Female	2	2	1
Male	5	4	0
F:M	1:2.5	1:2	1:0
Largest diameter	17.5 x 11 x 14 cm	6.5 x 6 x 4 cm	

Discussion

Thyroid Cancer

Among the endocrine malignancies, thyroid carcinoma is the most common. The high incidence of thyroid carcinoma is likely due to improvement in

early diagnosis, with the rampant use of ultrasound-guided fine-needle aspiration biopsy, and thus, in case reporting. Thyroid carcinomas that were encountered were mostly papillary in nature. Included in this category were the micro papillary carcinoma and those patients with mixed thyroid cancers (papillary and follicular at the same time) while the 10 hurthle cell carcinoma cases were included in the follicular thyroid cancer category.

The incidence of thyroid cancer in the Philippines is increased with 6.6 cases reported per 100,000 population in all ages, making it the ninth most common cancer among Filipinos, both sexes.[2]

Table II shows the demographic profile of the different thyroid malignancies, their percentage and Western prevalence.[3]

different treatment modalities. The mortality rate of anaplastic cancer is over 90% with a mean survival of six months after diagnosis.[9,10] The poor prognosis of UTC is mainly due to its aggressive behavior and resistance to cancer treatment.[11]

Medullary thyroid carcinoma (MTC) accounted for only 1.0% of all thyroid malignancies seen in five years. Among the nine MTC patients encountered, four (44%) were part of MEN2A. Two were siblings and both had concomitant hyperparathyroidism. The other two had concomitant pheochromocytoma.

Primary thyroid gland lymphomas accounted for only 0.24% of all thyroid malignancies. In two cases of thyroid lymphoma encountered, they had diffuse large B cell type and underwent surgery. One patient had infiltration of adjacent skeletal muscles and

Table II: **Comparison of demographic profile of the different thyroid malignancies**

	PTCA	FTCA	Anaplastic	Poorly Differentiated	MTC	Lymphoma	Metastases
% in Western[3]	50-90%	10-15%	1-2%	5%	5-10%	5%	
% in our study	78.2%	18.8%	1.32%	0.12%	1.08%	0.24%	0.12%
Age range (mean age) in Western	30-50 (45)	(50)	(60)	(55)		7th decade	
Age range (mean age) in our study	10-79	19-81	32-92 (63.7)	55 (55)	33-75 (51)	57-65 (61)	64 (64)
Female	535	131	7	1	5	1	
Male	117	26	4	0	4	1	
F:M	4.5:1	5:1	1.75:1	1:0	1.25:1	1:1	

The prevalence of undifferentiated (anaplastic) thyroid carcinoma (UTC) in our study is only 1.4% of all thyroid malignancies. The percentage would have been higher had the nine cases without retrievable biopsy were included formally in the study. However, we only included 11 patients who have official biopsy result. It is said that UTC occurs mainly in the elderly with a female to male ratio of 1.5:1.[3] This observation was also seen in our study; about 72.7% of the affected patients were more than 60 years old with a female to male ratio of 1.75:1. It is interesting to note that the youngest patient was 32 years old and the oldest patient was 92 years old. At the time of diagnosis, the tumors were already large, ranging from 4.5 to 6.7cm which is probably due to the rapid growth of the tumor. Three out of 11 cases (27%) were with documented metastasis at the initial presentation; two metastasised to the lymph nodes, and one to the lung. Of the 11 patients, four had surgery alone, three had surgery combined with chemotherapy and one had surgery and radiotherapy. Two patients had purely chemotherapy alone. Among the five out of 11 patients who died in our institution, the duration of survival was only 26 days to four months. The survival rate is poor despite fibrous fatty tissue while the other had oesophageal involvement and eventually underwent concomitant chemotherapy, who, unfortunately expired in two months. Patients who have large B-cell lymphoma are said to have poor prognosis.[14]

The thyroid gland is a richly vascularized structure, and as such, would be expected to harbour metastases with a relatively high frequency.[15,16] In this study, it accounted for only 0.14% of all thyroid malignancies. Only one case was identified, a metastatic adenosquamous carcinoma with supraclavicular lymph node involvement. In the literature, most tumors involving the thyroid by direct extension are squamous cell carcinoma or malignant lymphomas.[3] Although prognosis of patients with metastases to the thyroid gland is generally poor, surgical resection of solitary thyroid metastatic disease is recommended. This approach may lead to prolonged survival, particularly in patients with renal cell carcinoma.[3]

Parathyroid Carcinoma

Parathyroid carcinoma is a rare disease accounting for less than 1.0% of all patients with primary hyperparathyroidism in Western countries.[3] In

this study, we have only encountered one female patient, aged 67 years old. The tumor size measured 4.5cm in its widest diameter and is found in the left inferior parathyroid gland. The etiology of parathyroid carcinoma is unknown, with no associated risk seen in patients with prior head and neck irradiation, or prior iodine 131 exposures.[3]

Adrenal Cancers

In our study, half of the adrenal cancers were due to adrenocortical carcinoma followed by metastases to the adrenals and adrenal neuroblastoma.

Adrenal cortical carcinomas (ACC) are rare tumors with an incidence of one per million population per year, accounting for about 3.0% of endocrine malignancies.[3] In this study, we encountered seven patients with ACC. Other studies have revealed that there are more women than men (2.5:1) with ACC, however in this study, finding is different. The mean age of onset is 40-50 years, which was in accordance with our finding with mean age of diagnosis at 44.5 years old. Adrenal cortical carcinomas tend to be large tumors (greater than 5.0–6.0 cm); the largest ACC noted in this study was 17.5 x 14 x 11.5 cm and weighed 1,695 grams.

Adrenal Neuroblastoma is the most common cancer in infants less than one year old and it accounts for about 7.0% of all cancers in children and there are about 700 new cases of neuroblastoma being discovered each year in the United States, according to American Cancer Society.[25] In our case, our patient was diagnosed at four years old and underwent chemotherapy. The very low number of reported cases in this study is because pediatric patients are being referred to pediatric oncologist and pediatric endocrinologist and not to the adult endocrinologist.

Secondary tumors of the adrenal gland increase in frequency with advancing age, and are most commonly diagnosed in the sixth to eighth decades.[26,27] In our institution, Primary Adrenal Carcinoma was more common than Adrenal metastases which is contrary to several studies. We had only four documented cases of adrenal metastases and seven cases of primary adrenal carcinoma. Adrenal Metastases is the fourth most common site for distant metastases following lungs, liver and bone.[28] In a more recent series, the most common primary sites of malignancy that metastasised to the adrenal gland involve the lung, stomach, oesophagus, liver/bile duct.[27] In our study, two cases of adrenal metastases came from a primary lung cancer, and one case came from pancreatic cancer and another case from renal carcinoma. The mean diameter of adrenal metastases was 2.0 cm in one series.[27] The largest adrenal metastases from our study measured 6.5 x 6.0 x 4.0 cm.

Neuroendocrine Tumors

Neuroendocrine tumors (NET) are solid malignant tumors that arise from dispersed neuroendocrine cells found throughout the body.[29,30] It is divided into two groups: pancreatic neuroendocrine tumors (PNETs, also known as pancreatic islet cell tumors) and other NETS that generally arise from the gut (excluding the pancreas) and the bronchopulmonary system.

Of the seven patients encountered, four are due to PNET and the rest belongs to other NETS. Pancreatic endocrine tumors are uncommon and represent 1.0-2.0% of all pancreatic neoplasms. In this study, there were a total of 117 pancreatic cancers admitted and treated at our institution in five years, and four of them belong to neuroendocrine carcinoma representing 3.4%. The tumors show no significant gender predilection and occur at all ages, with a peak incidence between 30-60 years.

The reported overall incidence of tumors of the endocrine pancreas has increased during the recent years which are probably due to the application of more sensitive diagnostic approaches such as imaging techniques, reliable laboratory test and careful "morphofunctional" analysis by immunohistochemical and molecular biological techniques.[31]

Pancreatic endocrine tumors are separated based on their clinical manifestation into functioning and non-functioning. Among the functioning tumors, we only encountered two malignant insulinomas. In the literature, it usually occurs in older age group[32] and males are more frequently affected than females.[33] This is contrary to our study; the two affected patients were females with mean age of 53.5 years.

Malignant insulinomas are usually large (average size 6.2cm). In this study, the tumor ranges from 1.4 cm up to 8.0 cm. Half of the cases have no metastases while the other half have metastasized to the inferior mesenteric lymph nodes and liver. The median survival in metastatic disease to the liver ranges from 16-26 months. The five year survival probability for certain NET patients (well to moderately differentiated NETs) with distant metastases: NET colon, 14%; NET lung or pancreas, 27%.[30]

Conclusion

This study shows that thyroid malignancy, particularly papillary thyroid carcinoma, is the most common endocrine malignancy; whereas, parathyroid carcinoma is the least common endocrine cancer. In our population, there was more primary adrenal carcinoma than adrenal metastasis.

Recommendation

A follow up study is recommended to determine the survival rate of these different endocrine malignancies.

Acknowledgment

The authors would like to thank Dr. Archie Brian Ramos for his help in data collection.

References

1. **Ngelangel C, Wang, E.** Cancer and the Philippine Cancer Control Program. Japanese Journal of Clinical Oncology, 32 (suppl 1): S52-S61, 2001.
2. **Department of Health.** www.doh. gov.ph. [November 4, 2013].
3. **Ronald A. DeLellis, Ricardo V. Lloyd, Philipp U. Heitz, CharisEng:** World Health Organization Classification of Tumors. Pathology and Genetics, Tumors of Endocrine Organs.77, 2004.
4. **Randolph GW:** Follicular Carcinoma of the Thyroid, Saunders, Philadelphia, 2003.
5. **Shaha AR, Loree TR, Shah JP.** Prognostic Factor and Risk Group Analysis in Follicular Carcinoma of the Thyroid. Surgery 118: 1131-1136, 1995.
6. **Carcangui ML, Zampi G,Rosai J.** Poorly Differentiated ("insular") Thyroid Carcinoma, A Reinterpretation of Langhan's "wucherndestruma". Am JSurgPathol 8: 655-668,1984.
7. **Sabrinho-Simoes M.** Tumors of the Thyroid: a Brief Overview with Emphasis on the Most Controversial Issues. Current Diagnostic Pathology 2: 15-22, 1995.
8. **Sobrinho-Simoes M, Sambade C. Fonseca E. Soares.** Poorly Differentiated Carcinomas of the Thyroid Gland: a Review of the Clinicopathologic Features of a Series of 28 cases of a Heterogenous, Clinically Aggressive Group of Thyroid Tumors. Int J SurgPathol 10; 123-131, 2002.
9. **Giuffrida D, Gharib H.** Anaplastic Thyroid Carcinoma: Current Diagnosis and Treatment. AnnOncol 11; 1083-1089, 2000.
10. **Karavitaki N, Viassopoulou V, TzanelaM, Tzavara I, Thalassinos N.** Rucurrent and/ or Metastatic Thyroid Cancer: Therapeutic Options. Expert OpinPharmacother 3; 939-947, 2002.
11. **Liu AH, Vassilopoulou-Sellin R.** Anaplastic Thyroid Cancer with Uncommon Long Term Survival. J Chin Med Assoc69 (10):489-91, 2006.
12. **Aozasa K, Tsujimoto M, Sakurai M, Honda M, Yamashita K, Hanada M, Sugimoto A.** Non hodgkin's Lymphoma in Osaka Japan. Eur J Cancer ClinOncol 21; 487-492,1985.
13. **Freeman C, Berg JW.** Occurrence and Prognosis of Extranodal Lymphomas.Cancer.29: 252-260, 1972.
14. **Aozasa K, Inoue A, Tajima K, Miyauchi A, Matsuzuka F, Kuma K.** Malignant Lymphomas of the Thyroid Gland. Analysis of 79 patients with Emphasis on Histologic Prognostic Factors.Cancer 58; 100-104, 1986.
15. **Nakhjavani MK, Gharib H, Goellner JR, Van Heerden JA.** Metastases to the Thyroid Gland. A report of 43 Cases.Cancer 79; 574-578, 1997.
16. **Willis RA.** Metastatic Tumors in the Thyroid Gland. Am J Pathol 7; 187-208,1931.
17. **Heffess CS, Wenig BM, Thompson LD.** Metastatic Renal Cell Carcinoma to the Thyroid Gland: a Clinicopathologic Study of 36 Cases. Cancer 95; 1869-1878, 2002.
18. **Shane E.** Clinical Review 122: Parathyroid Carcinoma. J ClinEndocrinolMetab 86(2): 485-93, 2001.
19. **Hamill J, Maoate K, Beasley SW, Corbett R, Evans J.** Familial Parathyroid Carcinoma in a Child. J Paediatr Child Health 38; 314-317, 2002.
20. **Hundahl SA, Fleming ID, Fremgen AM, Menck HR.** Two Hundred Eighty Six Cases of Parathyroid Carcinoma Treated in the U.S. Between 1985-1995: a National Cancer Data Base Report. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 86; 538-544, 1999.
21. **Sandelin K, Auer G,Bonderson L, Grimelius L, Farnebo LO.** Prognostic Factors in Parathyroid Cancer: a Review of 95 cases. World J Surg 16; 724-731, 1992.
22. **Stewart PM. The Adrenal Cortex.** Williams Textbook of Endocrinology, Larsen PR, Krokenberg HM, Melmed, Polonsky KS, 10th ed. Saunders: Philadelphia, pp. 491-551, 2002.
23. **Lack EE.** Pathology of Adrenal Glands.Churchill Livingstone: New York, 1990.
24. **Wieneke JA, Thompson LD, Heffess CS.** Adrenal Cortical Neoplasms in the Pediatric Population: a Clinicopathologic and Immunophenotypic Analysis of 83 Patients. Am J SurgPathol 27; 867-881, 2003.
25. **American Cancer Society.** Cancer Facts and Figures 2012. Atlanta.www.cancer.org. [November 5, 2012].
26. **Glomset DA.** The Incidence of Metastases of Malignant Tumors to the Adrenals.Am J Cancer 32; 57-61, 1938.
27. **Lam KY, Lo CY.** Metastatic Tumors of the Adrenal Glands: a 30-year Experience in a Teaching Hospital. ClinEndocrinol (Oxf) 56; 95-101, 2002.
28. **Willis RV.** The Spread of Tumors in the Human Body. 3rd ed. Butterworth: London, 1973.
29. **Vinik Al, Renar IP.** Neuroendocrine Tumors of Carcinoid Variety. In: De Groot L, ed. Endocrinology. 3rd ed. Philadelphia, PA: WB Saunders; 1995: 2803-14.
30. **Yao JC.** One hundred years after Carcinoid: Epidemiology of and Prognostic Factors for Neuroendocrine Tumors in 35,825 Cases in the United States. J ClinOncol 26: 3063-72, 2008.
31. **Solcia E, Kloppel G, Sobin LH.** World Health Organization Histological Classification of Tumors. Histological Typing of Endocrine Tumors.2nd Ed. New York. Geneva,2000.
32. **Stringel G, Dalpe-Scott M, Perelman AH, Heick HM.** The Occult Insulinoma Operative Localization by Quick Insulin Radioimmunoassay.J PediatrSurg 20; 734-736, 1985.
33. **Danforth DNJr, Gorden P, Brennan MF.** Metastatic Insulin Secreting Carcinoma of the Pancreas: Clinical Course and Role of Surgery. Surgery 96; 1027-1037, 1984