

Incidental Diagnosis of Rectal Cancer in a Patient with Papillary Thyroid Cancer

Tom Edward N. Lo, M.D.*; Myrna Buenaluz-Sedurante, M.D.*; Mara Teresa T. Panlilio, M.D.**

Abstract

Background: Differentiated thyroid cancer is a common endocrine malignancy with an indolent course and a high overall survival rate. With more cases diagnosed early, survivors of this cancer live longer and hence are at risk of second primary cancers. In patients with known primary malignancy, work-up often focuses on the primary disease, so that coexistence of another primary malignant lesion can be missed.

Case Presentation: We report a case of a 78 year-old Filipino male diagnosed to have papillary thyroid cancer with nodal metastases presenting with an incidental rectosigmoid cancer on pre-operative workup.

Treatment and Outcome: Patient eventually underwent

complete surgical removal of both malignancies. He is currently on levothyroxine suppression therapy with no evidence of tumor recurrence for both malignancy and is on close follow-up for cancer recurrence surveillance.

Conclusion: Clinical vigilance for cancer screening and surveillance is mandatory for patients diagnosed with any type of primary malignancy to reduce the rate of missing secondary primary malignancy simultaneously present in the same patient. Early cancer detection might improve cancer patient's overall prognosis and eventually proved to be life-saving.

Keywords: Multiple Primary Malignant Neoplasms, Papillary Thyroid Cancer, Colon Cancer

Introduction

Differentiated thyroid cancer (DTC) is the most frequent endocrine gland malignancy accounting for approximately 0.5–1.5% of all malignancies.¹ The incidence is increasing in most populations.² This increase may be due to evolution in clinical practice and/or changes in histological criteria but may also be due to changing environmental and hormonal factors³. The overall survival rate is high and currently even close to 99% in papillary carcinomas.⁴ With more and more cancers diagnosed early, survivors of this cancer live longer and hence are at risk of second primary cancers.⁵

Multiple primary malignant neoplasms (MPMN) occurring in a patient's lifetime are not uncommon. Moreover, the number of cancer survivors is growing by two percent each year and a second cancer could represent a leading cause of death.⁶ The proportion of MPMN in clinical and autopsy series reported since 1932 ranges from 0.8% to 16%. The

population-based systematic studies carried out by long standing Cancer Registries have reported a proportion of MPMN ranging from 2.1 to 6.6% of all incident cases registered from 1935 up to 1995⁷. The definition of a second primary cancer is a cancer that is detected in another organ of an individual patient, either synchronously or metachronously. Each tumor has to have a definite histological picture of malignancy, be distinctly separated, and clearly not metastatic from the other tumor.⁸

Several studies have reported a consensus increase in the risk of second primary cancers among thyroid cancer primary patients. The largest Surveillance, Epidemiology, and End Results (SEER)-based analysis from 30,278 patients with thyroid cancer showed a significantly increased risk for second primary cancers of the brain, breast, prostate, kidney, and salivary glands, Hodgkin lymphoma, leukemia, and myeloma as well as a significantly decreased risk for cancers of the head and neck (excluding thyroid and salivary gland), lung, esophagus, and bladder⁹.

In patients with known thyroid malignancy, work-up often focuses on the thyroid disease, so that coexistence of another primary malignant lesion can be missed. This paper will highlight a case of an incidental secondary primary malignancy in a patient with papillary thyroid cancer during a preoperative evaluation.

*University of the Philippines- Philippine General Hospital- Department of Medicine- Section of Endocrinology and Metabolism

**University of the Philippines- Philippine General Hospital- Department of Medicine- Section of Gastroenterology

Corresponding Author: Tom Edward N. Lo, M.D., University of the Philippines-Philippine General Hospital, Taft, Manila, Philippines
Email: tomedwardlo@yahoo.com

Case Presentation

This is a case of a 78-year-old Filipino male farmer from Samar, Philippines presenting with a two-year history of gradually enlarging goiter associated with multiple cervical nodal enlargement. He had no prior co-morbidities and had a good functional capacity spending most of his time planting and farming in the rice field. Patient did not have family history of malignancy. He did not have any prior history of radiation exposure, chemotherapy session. He also did not have a history in smoking and excessive alcohol intake.

Patient was barely asymptomatic except for the grossly enlarged neck masses that eventually caused limited neck flexion. He did not complain of difficulty of breathing and swallowing, hoarseness or weight loss. On physical examination, patient had a 4x5 cm nodular non-tender goiter with multiple bilateral cervical lymphadenopathies (right larger than left). No other masses were palpated throughout the thoracic and abdominal area. Persistence of the mass prompted consult at our institution where initial fine needle aspiration biopsy revealed suspicion for papillary thyroid cancer. On physical examination, patient had a 4x5 cm nodular non-tender goiter with multiple bilateral cervical lymphadenopathies (right larger than left). No other masses were palpated throughout the thoracic and abdominal area. Neck CT scan done revealed multiple deep cervical lymph nodes with the largest located in the right upper posterior jugular area (4.2x3.3x4.4 cm) and a complex predominantly solid mass (3.5x3.0x2.5 cm) at the right thyroid lobe with irregular wall calcifications (Figure 1). Patient was initially assessed to have stage 4A papillary thyroid cancer hence advised total thyroidectomy and bilateral neck dissection.

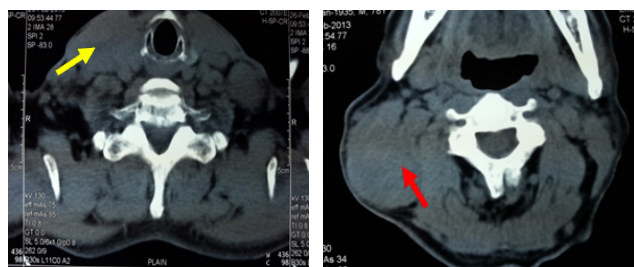


Figure 1: Neck CT scan revealing complex solid right Thyroid mass (Yellow Arrow) and multiple deep cervical Lymphadenopathies with the largest at the right (Red Arrow)

Upon admission, several work ups were done as routine requirements for preoperative assessment. All laboratory tests done showed unremarkable results except for an incidental finding of hypereosinophilia on routine complete blood count (Table I). Search for the cause of hypereosinophilia was done. Fecalalysis

came out positive for Ascariasis and Hookworm infection. Liver ultrasound revealed a characteristic lace-like pattern consistent with chronic schistosomiasis. Hepatitis profile was negative.

Table I: Preoperative diagnostic tests

Test Done	Result	Comments
12L ECG	Regular sinus rhythm, normal axis	Normal ECG finding
Fasting Blood Sugar	83.45 mg/dl	Normal
Complete Blood Count	Hemoglobin 125 g/L WBC 6.11 x 10 ⁹ /L (Neutrophils 39%; Lymphocytes 23%; Eosinophils 33%; Basophils 4%) Platelet 191 x 10 ⁹ /L	Hypereosinophilia
Serum Electrolytes	Sodium 142 mmol/L; Potassium 3.7 mmol/L; Calcium 2.29 mmol/L; Magnesium 0.82 mmol/L	Normal
Renal Function	BUN 4.5 mmol/L; Creatinine 71 umol/L	Normal
Urinalysis	Specific Gravity 1.030; pH 5.5; Negative for hematuria, pyuria, glucosuria and proteinuria	Normal
Liver Function	AST 28 IU/L; ALT 21 IU/L; Alkaline phosphatase 52 IU/L; Albumin 40 g/L	Normal
Thyroid Function	Free T4 14.0 pmol/L; TSH 5.9 mIU/L	Normal

To fully document the presence of schistosomiasis a rectal imprint and proctosigmoidoscopy was done. Rectal imprint eventually revealed schistosome eggs (Figure 2) but proctosigmoidoscopy incidentally showed a 3x3 cm polypoid pedunculated rectal lesion at two to three centimeters from the anal verge and four millimeter sigmoid polyp. Total polypectomy and complete removal of the lesions were done leaving clean margins. Biopsy of the sigmoid polyp turned out to be a benign tubular adenoma (Figure 3A) while the rectal polyp surprisingly showed well-differentiated adenocarcinoma (Figure 3B). Immediate completion colonoscopy done showed a 0.2 mm sessile colonic polyp at the hepatic flexure which was negative for malignancy (Figure 3C). Carcinoembryonic antigen CEA done showed normal baseline result. Abdominal CT scan done did not show any gross mass lesions or lymph node involvement.

Patient was eventually treated with mebendazole 500mg per day for three days and praziquantel 60mg/kg divided into three doses for ascariasis, hookworm infection and schistosomiasis respectively. After further histopathologic examination of excised polyps, diagnosis of stage I colorectal cancer with complete tumor removal was made. Patient however did undergo total thyroidectomy with bilateral neck dissection which finally turned out to be papillary thyroid cancer with nodal metastases on final histopathology result (Figure 4). Patient was then given high dose radioactive iodine therapy (150 mci) to ensure ultimate eradication of any residual thyroid tissue and started on high dose levothyroxine (150 mcg/day) to suppress thyroid stimulating hormone (TSH) thereby

lowering the risk for tumor recurrence. Patient is currently on follow up for cancer surveillance and monitoring.

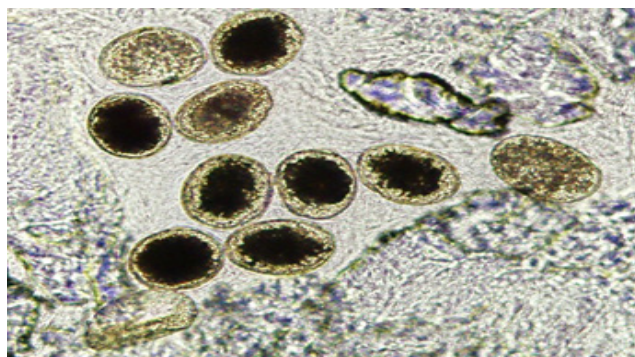


Figure 2: Rectal imprint showing schistosome eggs consistent for schistosomiasis

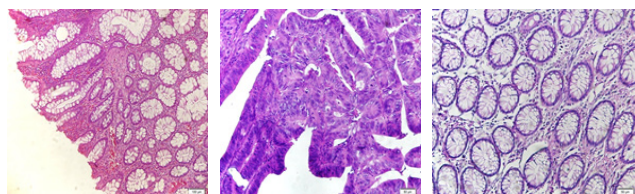


**Figure 3: A. Sigmoid polyp revealing tubular adenoma on histology
B. Rectal Polyp revealing well-differentiated adenocarcinoma on histology
C. Hepatic flexure sessile polyp revealing hyperplastic changes**

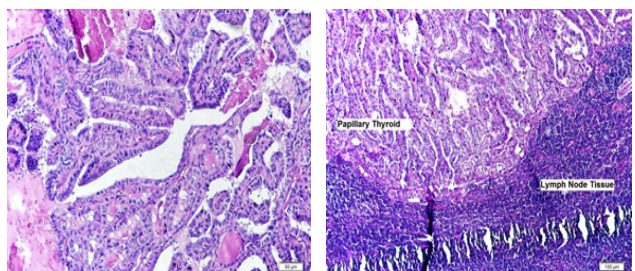


Figure 4: Final histopathologic result revealing papillary thyroid cancer with nodal metastases

Diagnosis

Papillary Thyroid Cancer (T4N1M0) Stage IVA
s/p Total Thyroidectomy and Bilateral Neck Dissection
s/p Radioactive Iodine Therapy (150 mci)
Colorectal Adenocarcinoma Stage I
s/p Complete Polypectomy
Chronic Schistosomiasis - Treated
Ascariasis and Hookworm Infection - Treated

Discussion

Multiple primary tumours were first described by

Billroth in 1889.¹⁰ In 1932, Warren and Gates, proposed three criteria for the diagnosis of a second primary cancer: each tumour should show specific malignant findings; the tumours should differ in site and one tumour should not be a metastatic focus from another.¹¹ In 1977, Moertel proposed new definitions, including the term "multicentric" if tumours occurring simultaneously in the same anatomical site shared the same histology and "metachronous" if the second tumour was diagnosed more than six months after the diagnosis of the first primary.¹²

Data collected from Italian Cancer Registries revealed that patients affected by cancer had an approximately ten percent statistically significant increase in the risk of cancer of all sites in comparison with the general population.¹³ A 1/3 rule has been hypothesized regarding the incidence and prevalence of secondary primary tumors, which means that approximately 33% of the patients with a malignancy will develop a second primary malignancy, 33% of these patients with second primary malignancy will develop a third malignancy, and so on.¹⁴ A well described phenomenon, in this respect, is the field cancerization concept, which states that organ systems exposed to the same carcinogenic agents have a greater chance of transforming into a malignancy.¹⁵ Another explanation for secondary primary tumor may be the presence of a genetic base for multiorgan cancer.¹⁶ Generally, the prevalence of additional primary neoplasms in epithelial cancers is substantial. Dong et al. reported that 8.5% of 633,964 patients with known cancers were subsequently proven to have other and previously unrecognized types of second primary cancers.¹⁷ Ueno et al. reported that 5.2% of 24,498 cancer patients had multiple, simultaneous, nonrelated cancers.¹⁸

Patients with papillary thyroid cancer have generally a very good prognosis due to its insidious course, well-established curative treatment options and highly sensitive monitoring tests. Due to the prolonged survival of patients with papillary thyroid cancer, incidence of a secondary primary malignancy is increased. In a multinational record linkage study by Sandeep, patients with primary thyroid cancer had a 30% increased risk of developing a second primary cancer in comparison with the general population. On the other hand, there was a reciprocal increased risk of thyroid cancer development in patients with other primary malignancies. In particular, patients with primary thyroid cancer had 27% increase risk of developing colorectal cancer while patients with colorectal cancer had 52% increase risk of developing thyroid cancer. This risk seems to increase with the duration of follow-up, with no substantial differences in risk being associated with age at the time of diagnosis of thyroid cancer, the sex of the patient, or the calendar period of diagnosis.⁵

A study by Kim et al., showed that even thyroid

microcarcinomas have increased risk of developing second primary cancers in all body sites.¹⁹ Based on the large population-based study in Taiwan, 3.38% developed second primary cancer among patients diagnosed with thyroid cancer. The risk of developing a secondary malignancy was observed to be as high as 33% which also negatively impacted survival. In contrast to the results of the European population, there was no significant risk noted for developing colon cancer.²⁰ This might be incidental cancer provided that our patient is an elderly.

A meta-analysis done by Subramanian et al. revealed a significant risk of second primary malignancy for thyroid cancer patient survivors regardless of the radioactive treatment status. In their analysis of data from several studies, they have shown an increased incidence of colorectal cancer as a second primary malignancy.²¹ This finding was also shown in the nationwide study done in Korea where there was elevated risk of second malignancy in all sites except stomach and cervix.²²

Technical advances in the diagnosis of cancer have increased the reported incidence of multiple primary cancers simultaneously diagnosed at the time of detection of a primary malignancy. However, the true incidence and prevalence of colorectal cancer combined with primary thyroid cancer is difficult to estimate⁸. Cancers develop because of accumulated mutations of multiple responsible genes, which increase the risk of developing cancers in other organs.²³ Therefore, the detection of a primary cancer should alert the treating team to exclude or effectively detect second cancers.

Conclusion and Recommendation

Clinical vigilance for cancer screening and surveillance is mandatory for patients diagnosed with any type of primary malignancy to reduce the rate of missing concomitant second primary malignancy simultaneously present in the same patient. Early cancer detection might improve cancer patient's overall prognosis and eventually proved to be life-saving.

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