

Synchronous Papillary Thyroid Carcinoma with Metastatic Nasopharyngeal Carcinoma Issues Regarding its Diagnosis and Management

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A 46-year old female presented with a one-year history of a right lateral neck mass which gradually increased in size and subsequently involved bilateral cervical nodes. Diagnosed as Papillary Thyroid Carcinoma Stage I (T1N2M0), she underwent Total Thyroidectomy, Central Neck Dissection, Modified Radical Neck Dissection, Type I, right and Modified Radical Neck Dissection Type III, left. Histopathology revealed papillary thyroid carcinoma with no lymphovascular and capsular invasion, and metastatic undifferentiated carcinoma in 15 out of 16 lymph nodes, probably nasopharyngeal in origin. Work up uncovered an erythematous, friable nasopharyngeal mass. Its histopathology was nasopharyngeal cancer, a second primary malignancy. The malignancies were treated as separate entities. The patient underwent chemoradiotherapy first for the nasopharyngeal cancer. Radioactive Iodine for the thyroid malignancy was given six months after completion of radiotherapy. Double primary malignancies deserve aggressive treatment. The sequence of therapy should be based on the severity of the malignancy.

Keywords: Case report, double primary head and neck malignancy, papillary thyroid, nasopharyngeal cancer

Although cervical lymphadenopathy is a common complaint of patients with head and neck malignancies, a double primary in the said region with such presentation is a rare entity. This condition is different from multiple head and neck cancers which refers to mucosal squamous cell cancer and whose incidence is increasing due to field cancerization.^{1,2} The incidence of double primary with different histopathologies occurs infrequently worldwide, more so, in the Philippines. There has not been much information which can be utilized to guide

the diagnosis and management of such conditions. Well-differentiated cancer of the thyroid gland remains to be the most common endocrine malignancy. The incidence of thyroid cancer has increased more than twofold to 8.7 cases/100,000 in 2002, a rise attributable almost entirely to papillary thyroid cancer, according to a study by Burke, et al.³ Among nationalities and population subgroups, Filipino patients have a significantly higher risk of thyroid cancer compared with non-Filipino patients as noted by a study done by Lukas H, et al.⁴ With regards to nasopharyngeal cancer (NPCA), Wei-Hua and Hai-De⁵ discussed that although it can be considered to be a rare cancer globally, there are populations in high-risk areas with high incidence rates. In a study done by Sarmiento and Mejia in 2014, the Philippines was found to have an increase in the incidence of 2.07 per 100,000 from 1.2 in 2002.⁶

Although both Papillary Thyroid Carcinoma and NPCA were noted to be relatively more common in Asia compared to Western countries, with significant prevalence rates in the Philippines, there has not been any reported case of these malignancies being diagnosed in one patient.

This paper aimed to present and document a case of a Filipina presenting with an anterior neck mass with cervical lymphadenopathies which was eventually diagnosed and treated for synchronous thyroid and nasopharyngeal malignancies.

This report presents and discusses the clinical presentation, diagnostic and therapeutic management of a case of synchronous, double primary malignancies of the head and neck.

The Case

A 46-year old female presented with a 1-year history of gradually-enlarging right lateral neck mass with subsequent tumor growth on the contralateral neck region. Persistence of bilateral neck tumors, associated with occasional dyspnea as well as dysphagia prompted consult at the Jose R. Reyes Memorial Medical Center. On physical examination, the patient was noted to have palpable fixed, hard, lobular masses on the right lateral neck region from the submandibular area to the inferior border of the angle of the mandible. Largest mass was 3 cm in its widest diameter. There were also multiple, non-movable, well-circumscribed masses on the left lateral neck, the largest measuring 2 cm in its widest diameter. Upon physical examination of the thyroid, both lobes were enlarged. There was a 2 cm hard nodule on the anterior neck area that moved with deglutition. (Figure 1).

Subsequent diagnostic work up included neck ultrasound and fine needle cytology which was consistent with papillary thyroid cancer. A clinical impression of

Papillary Thyroid Carcinoma Stage 1 (T1, N2, M0) was made. Total thyroidectomy, central neck dissection, modified radical neck dissection, type I, right with and modified radical neck dissection type III, left via en-bloc resection was performed. The intraoperative findings showed an enlarged thyroid gland with cut section revealing an inhomogeneous parenchyma with a 2 cm admixed yellow and white, hard gritty, irregular nodule situated in the mid-section of the right lobe. The parenchyma of the left lobe was noted to be homogenous, with multiple subcentimeter calcifications. (Figure 2). Centrally-located, the right paratracheal and tracheoesophageal lymph nodes were also removed.

There were also multiple enlarged bilateral antero-lateral lymph nodes. Levels I-IV jugular chain nodes on the right were noted to be hard, with conglomerated levels Ib to III lymph nodes encasing and invading the internal jugular vein and spinal accessory nerve. (Figure 3). Levels II to V jugular chain nodes on the left, were noted to be hard to rubbery lymph nodes with inhomogenous parenchyma on cut section. (Figure 4).

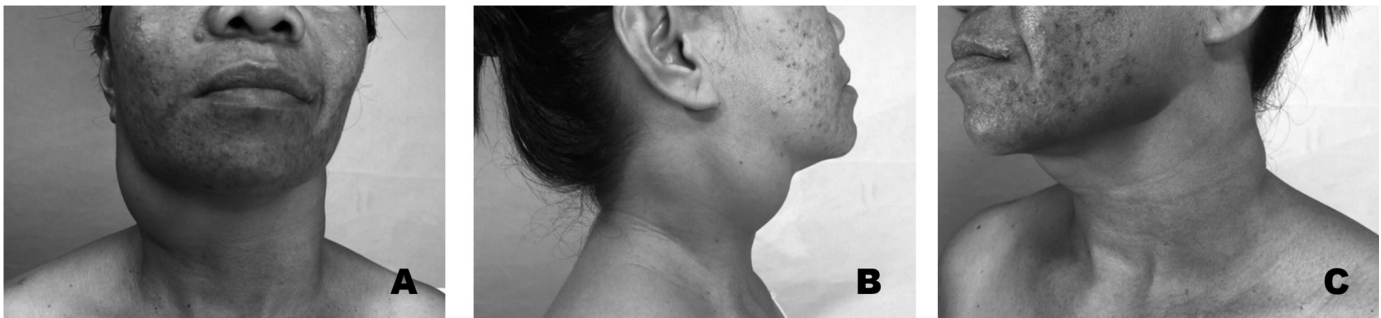


Figure 1. A. Anterior view. B. Lateral view, right. C. Oblique view, left.

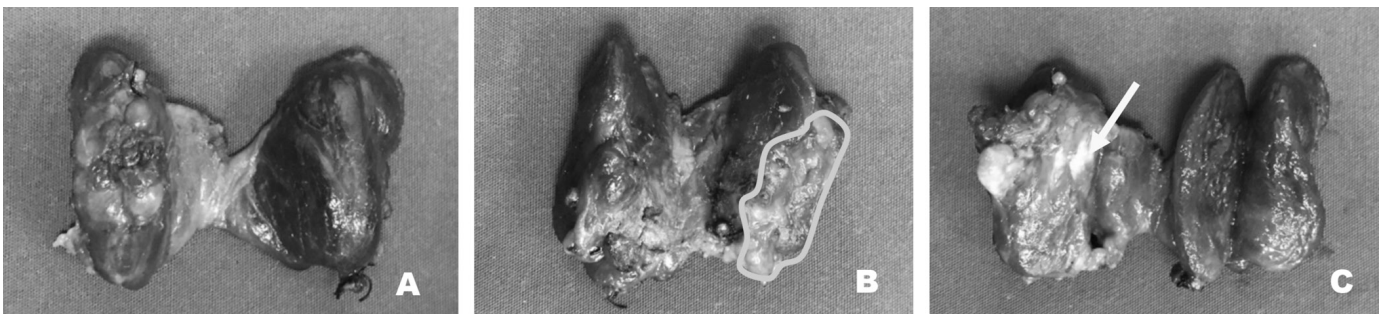


Figure 2. A. Anterior view of the bilateral thyroid lobes, including the isthmus. B. Posterior view. Outlined: central nodes, right. C. Cut-section of the bilateral thyroid lobes. Arrow: 2 cm calcified nodule on the mid-portion of the right thyroid lobe.

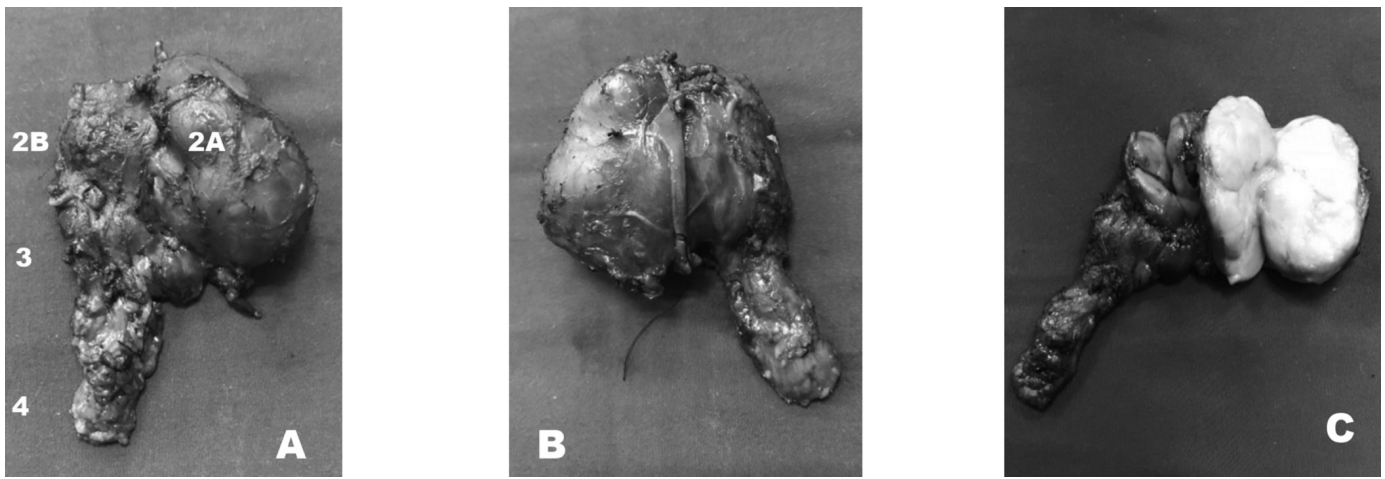


Figure 3. A. Anterior view of the right jugular chain nodes. Numbers indicate the lymph node level. B. Posterior view of the right jugular chain lymph nodes. C. Cut-section of the right jugular chain, level I lymph node.

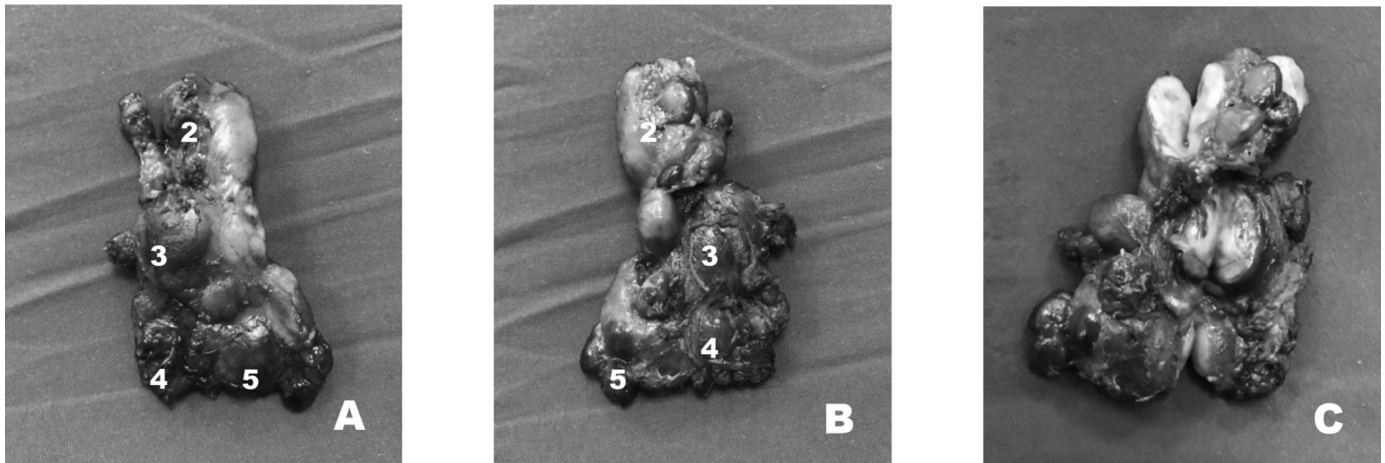


Figure 4. A. Anterior view of the left jugular chain nodes. Numbers indicate lymph node level. B. Posterior view of the left jugular chain lymph nodes. Numbers indicate lymph node level. C. Cut-section of the left jugular chain lymph nodes.

The final histopathology report revealed papillary thyroid carcinoma with no lymphovascular and capsular invasion. (Figure 5). A metastatic undifferentiated carcinoma was also noted in 15 out of 16 lymph nodes, probably nasopharyngeal in origin. The patient was referred to the Department of Otorhinolaryngology for nasal endoscopy and biopsy. On endoscopy, there was an erythematous, friable, mass on the right nasopharyngeal area. Biopsy of the mass was done, which revealed nasopharyngeal carcinoma, undifferentiated, with similar

histologic features to the metastatic lymph node tumor. (Figures 6 & 7). Given the final histopathological findings, the final diagnosis was Papillary thyroid cancer Stage I (T1N0M0) and Nasopharyngeal carcinoma, undifferentiated type Stage III (T1N2M0).

The patient was referred to radiation oncology and nuclear medicine for further management of the nasopharyngeal cancer and papillary thyroid carcinoma, respectively. The patient underwent concurrent chemoradiotherapy with Cisplatin 100 mg/m² and 35

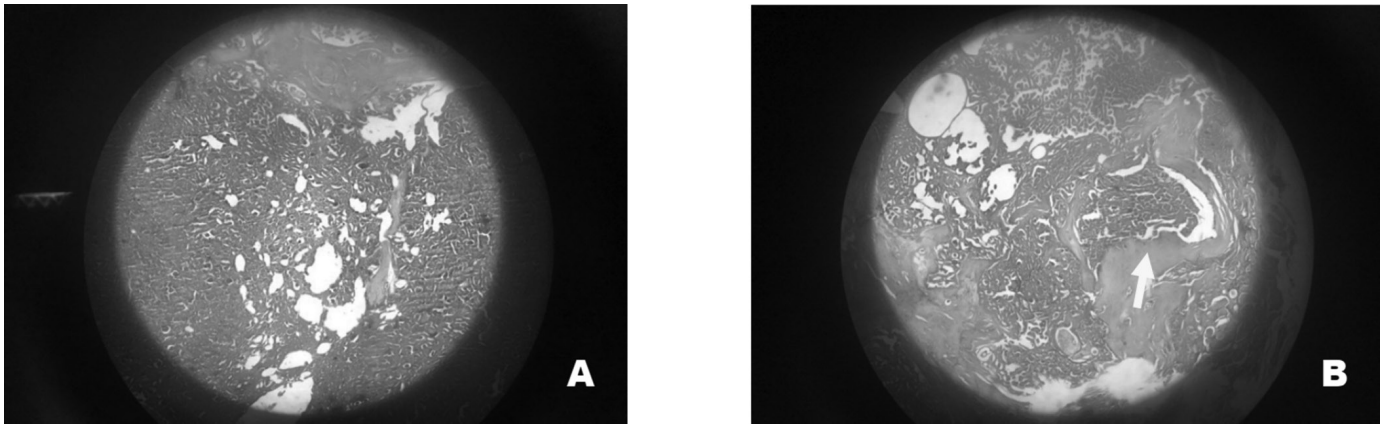


Figure 5. A. Low power microscopic view of thyroid nodule, showing malignant features. B. Shows no capsular invasion. (arrow-capsule)

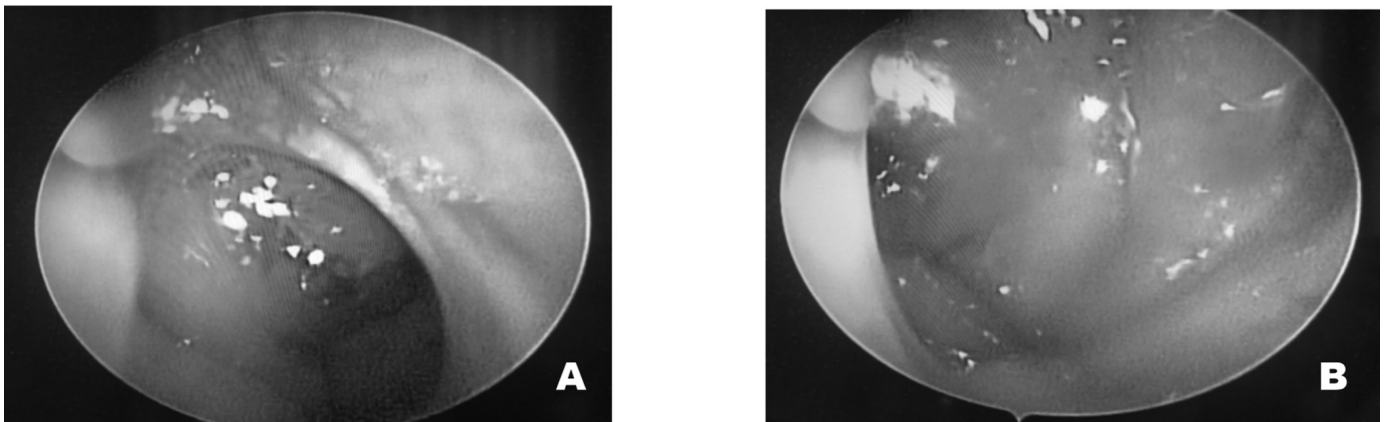


Figure 6. Endoscopic views of the nasopharyngeal mass. A. View from the right nostril. B. View from the left nostril.

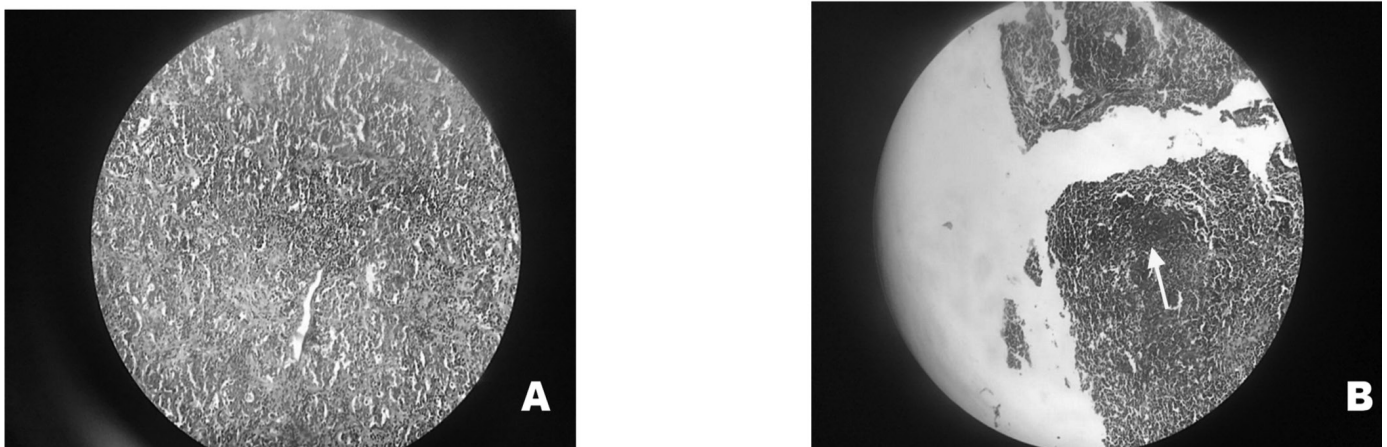


Figure 7. A. Low power microscopic view, lymph node, right. Arrow indicates the malignant metastatic tumor most likely nasopharyngeal in origin. B. Nasopharyngeal mass biopsy showing similar features with picture A. Arrow indicates the malignant tumor.

fractions of EBRT at 200 cGy/fraction with a total absorbed dose of 7000 cGy targeted at the fasciocervical area, and 30 fractions at 200 cGy/fraction with a total dose of 6000 cGy targeted at the anterior low neck area. Figures 8 and 9a & 9b show the isodose distribution and mapping for the radiotherapy given to the patient. Radioactive iodine ablation was done six months after the completion of the concurrent chemoradiotherapy. 100 mCi (3,700 MBq) of radioactive iodine-131 was administered. Whole body scan done on the 9th day post ablation showed multiple foci of functioning thyroid tissue remnants in the anterior neck. There was no functioning thyroid tissue elsewhere.

Discussion

Although multiple primary mucosal squamous head and neck cancers are not that rare.^{1,2,7,8} review of the literature on the incidence of double primary head and neck cancers specifically the co-occurrence of second primary malignancy with thyroid cancer yielded only a few studies including autopsy material. In the study by Tislavicz involving 37,504 autopsies performed in a span of 30 years, it was noted that thyroid cancers were seen most frequently with lung, breast and gastrointestinal system malignancies with no recognizable association with other cancers.⁹ In another study by Hsu, et al.

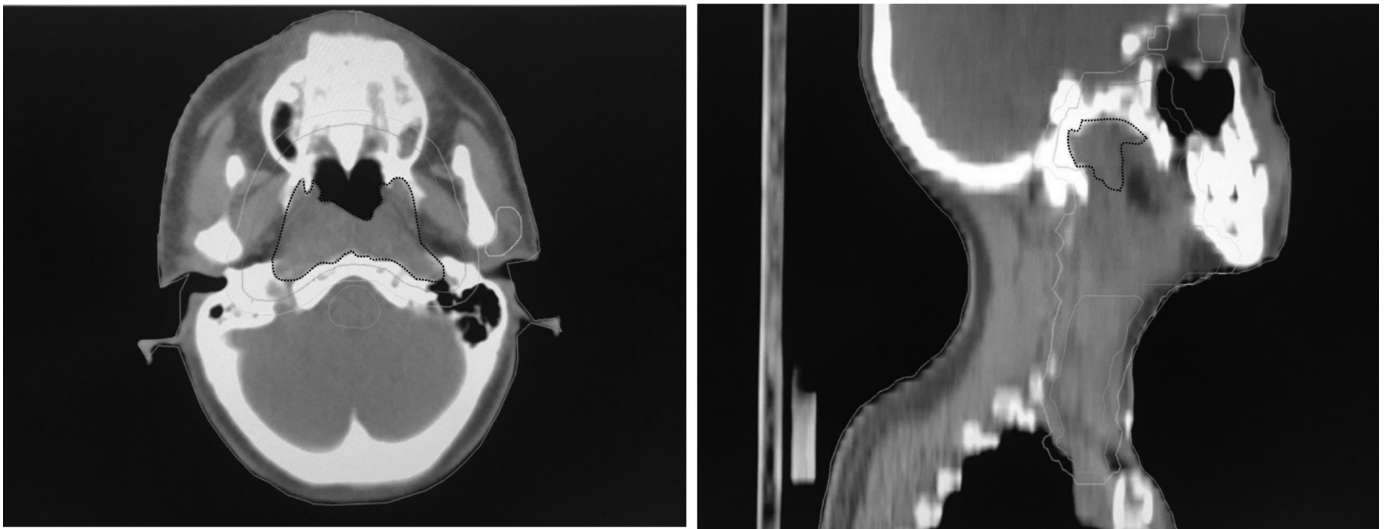


Figure 8. Digital images showing the nasopharyngeal mass contoured for radiotherapy. Dotted line indicates the bulk of the tumor.

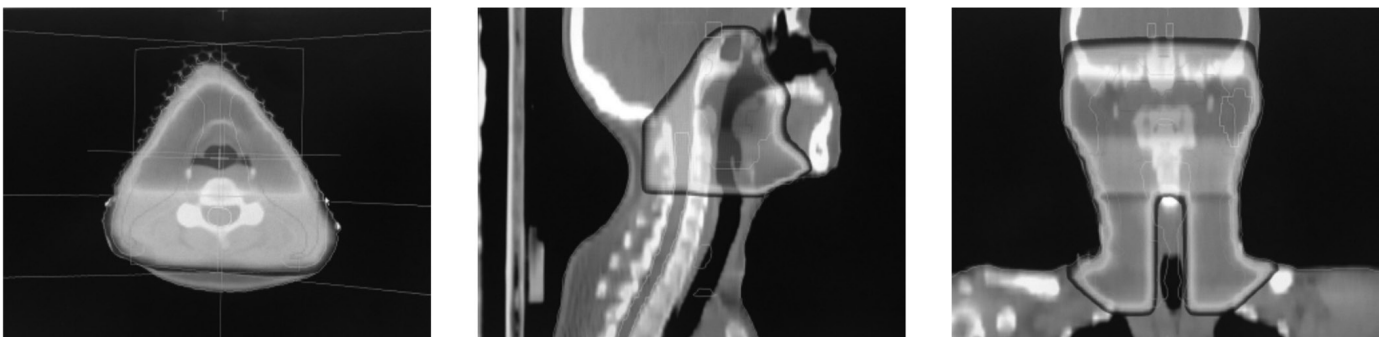


Figure 9.

involving 9,423 cases of thyroid cancer, there were 861 recorded co-occurrences with the following sites and the corresponding incidence rate: head and neck, 1.93%; breast, 1.59%; digestive system, 1.44% and lung, 1.18%, respectively.¹⁰ In a population-based study of 19,608 subjects by Chang-Hsien Lu on second primary malignancies following thyroid cancer, it was noted that there is a 33 % risk increase for patients with thyroid cancers to have a second primary cancer. In this same study, there was higher risk of developing cancer in the salivary glands, nasopharynx, lung, thymus, breast(females), bladder, brain, and leukemia and lymphoma. The risk was highest within 5 years of diagnosis with a standardized incidence ratio of 5.29.¹¹

With regards to nasopharyngeal cancer and the occurrence of secondary primary malignancy (SPM), an epidemiology study by Ooft, et al. utilizing the Dutch Pathology registry for NPC revealed that patients with nasopharyngeal cancer have increased risk for second head and neck cancer (SPM) (SIR 4.795% 3.3-6.5) regardless of its EBV status. The incidence of SPM, however, is higher in keratinizing compared to the non-keratinizing type and the most common second primary cancers are the squamous cell cancer type.¹²

With limited information on the clinical aspects of double primary head neck cancers specifically the thyroid and nasopharynx, the diagnostic work up and subsequent management may pose a challenge in patients such as the present case.

Preoperatively, the patient presented with a classical presentation of well-differentiated thyroid malignancy – an anterior neck mass with bilateral cervical lymphadenopathies, something that would not make a clinician suspect a different etiology for the cervical lymphadenopathy. The patient had nasal congestion and intermittent epistaxis but these were not recognized.

With a more detailed history and physical examination, the team might have considered the possibility of a double primary cancer. A triple endoscopy should have been done to detect the NPCA.

The initial management, total thyroidectomy with neck dissection, was tailored for a thyroid malignancy with cervical node metastasis. Had NPCA been diagnosed preoperatively and had the team known the cervical nodes were metastatic from the NPCA, chemoradiation

therapy would have been done first. The thyroidectomy would have been performed subsequently without the need for lymph node dissection.

Given this rare clinical presentation, the team relied on understanding the epidemiology, course and prognosis of the individual malignancies to decide on the subsequent treatment options after the initial surgery. As of this writing, there have not been any literature on how two malignancies presenting like this should be managed. Standard treatment strategies are available for each malignancy but not when they occur simultaneously. Graff, et al. in 2011, described management strategies and the outcome of head and neck patients presenting with a synchronous cancer from another anatomic site.¹³ In general, the treatment of these conditions were complex and involved multiple modalities done consecutively over a mean duration of 4.6 months. When the malignancies differed in severity, locoregional treatment targeted only one tumor (85%) and priority was given to the most advanced one (76.5%). In the presented case, the authors followed this treatment philosophy.

The overall management given for this patient can be considered as a “sandwich type” where initial management done was for thyroid cancer followed by management for the nasopharyngeal cancer and followed later on with radioactive iodine ablation for the papillary cancer. At this point, it is uncertain how this sequence of treatment modalities will influence locoregional control and overall survival.

Conclusion

There is a paucity of information on double primary head and neck malignancies involving the thyroid and nasopharynx. In this female Filipino patient presenting with an anterior neck mass with cervical lymphadenopathy, the index of suspicion for a secondary nasopharyngeal cancer was low. A detailed history and physical examination may have been able to detect the occurrence of a second primary tumor and the corresponding diagnostic work up and treatment strategy followed. In the presence of double primary malignancy, aggressive treatment should be given and the sequence should be based on the severity of the malignancy.

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