A case report of synchronous primary malignancy: Papillary thyroid carcinoma and non-Hodgkin's lymphoma

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ABSTRACT

Multiple primary malignancies involving papillary thyroid carcinoma and non-Hodgkin's lymphoma (NHL) is an extremely unusual event. Here, we report the case of a 70-year-old man presented with high-grade fevers and abdominal discomfort and were found to have pancytopenia. He had generalized lymphadenopathy, hepatosplenomegaly, goiter, and tracheal shift. Biopsy of the left cervical lymph node was positive for papillary carcinoma of the thyroid. He underwent excision biopsy of axillary lymph node which was suggestive of high-grade NHL. The patient was started on chemotherapy (R-CHOP) and his fevers resolved promptly. He then underwent total thyroidectomy and the histopathology of the thyroid gland post-operative showed papillary carcinoma. The second primary malignancy is a second malignant neoplasm occurring in a patient with known cancer. This case highlights the unusual synchronous occurrence of the papillary carcinoma of thyroid and NHL and the diagnostic challenges involved in such cases.

Key words: *Double primary malignancy, Metachronous, Second malignancy, Synchronous*

The occurrence of multiple neoplasms is not uncommon in present times with the advent of advanced diagnostic imaging modalities as well as the increased efficacy of cancer therapy. The incidence of multiple primary cancers is reported to be between 0.734% and 11.7% [1]. Papillary thyroid carcinoma is the most common thyroid malignancy. Pure papillary (and mixed papillary-follicular) carcinoma comprises about 80% of all thyroid cancers. About 10% of cases present with palpable cervical lymph node metastases from small cancer. Non-Hodgkin's lymphomas (NHLs) can be divided into aggressive and indolent cell types. Aggressive NHLs comprise a large number of cell types, the most common of which is large-cell lymphoma. They most frequently arise from lymph nodes, but an extranodal site can be the primary source in approximately 30% of cases [2].

Multiple primary malignancies involving papillary thyroid carcinoma and NHL is an extremely unusual event. No such cases have been reported so far in medical literature. We report the case of a 70-year-old male patient who presented with pyrexia of unknown origin, generalized lymphadenopathy, splenomegaly, and thyroid swelling.

CASE REPORT

A 70-year-old man presented with high-grade fever, abdominal discomfort, and loss of appetite and malaise of 10 days duration. He had no other comorbidities and no significant family history. On physical examination, he had pallor and cachectic. He had bilateral cervical and axillary lymphadenopathy; he was febrile (101F) and tachycardic (110/min) and BP was 100/70 mmHg. His trachea was deviated to the right and had marked splenomegaly (spleen palpable 7 cm below the left costal margin).

The patient hemogram revealed mild anemia, normocytic and normochromic with moderate anisocytosis, mild leukopenia with monocytosis (23%), and moderate thrombocytopenia (Hb - 9.5 g/dl, white blood cell count - 3900/mm^3, and platelet count of 65,000/mm^3). Chest X-ray (Fig. 1) showed a tracheal shift to the right with an indentation on the left side. Ultrasound of the neck showed grossly enlarged thyroid with the heteroechoic lesion and cervical lymphadenopathy with calcific cystic degeneration, suggestive of papillary carcinoma of the thyroid. Ultrasound of abdomen revealed hepatomegaly, massive splenomegaly, peripancreatic, and mesenteric lymphadenopathy.

Contrast-enhanced computed tomography scan of the chest and abdomen (Fig. 2) showed extensive cervical, bilateral axillary, mediastinal, retroperitoneal, pelvic, and mesenteric lymphadenopathy. Thyroid gland showed multiple heterogeneous nodules with an exophytic nodule extending into the superior mediastinum and causing mass effect on the trachea, suggestive of multinodular goiter. He also had symptoms of mild stridor and dysphagia. His general condition was deteriorating. His cultures, Mantoux and HIV (human immunodeficiency virus) serology, were all negative. Lymphoma was suspected in view of his widespread lymphadenopathy and hepatosplenomegaly. He underwent biopsy of the left cervical lymph node and to our

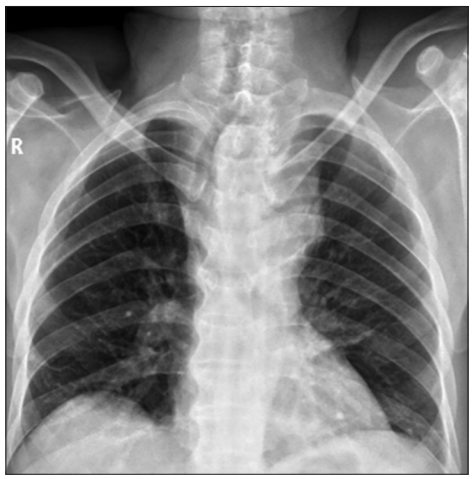

Figure 1: Chest X-ray showing tracheal shift to the right with indentation on the left side and mediastinal widening

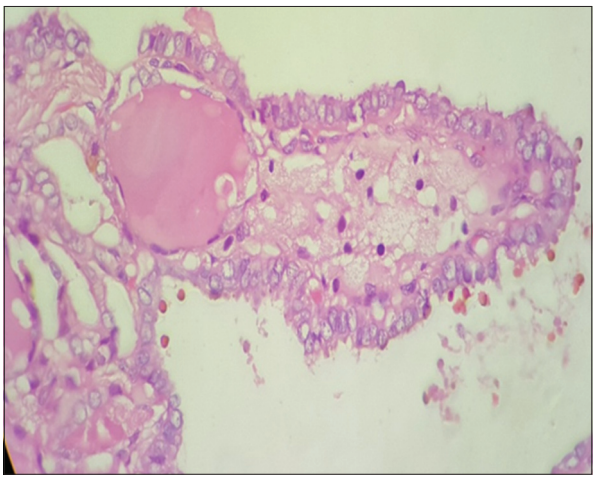

Figure 3: Histopathology of cervical lymph node showing papillary thyroid carcinoma

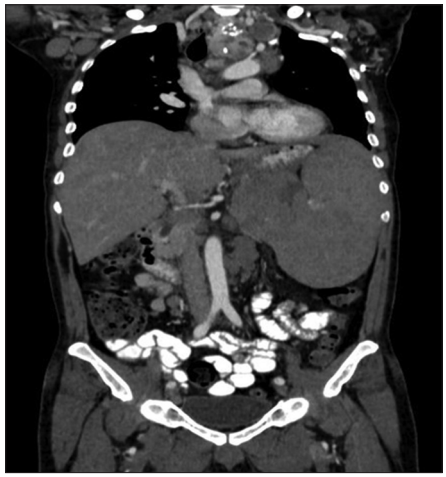

Figure 2: Contrast-enhanced computed tomography chest and abdomen showing extensive bilateral axillary, mediastinal, paracaval lymphadenopathy, and massive splenomegaly

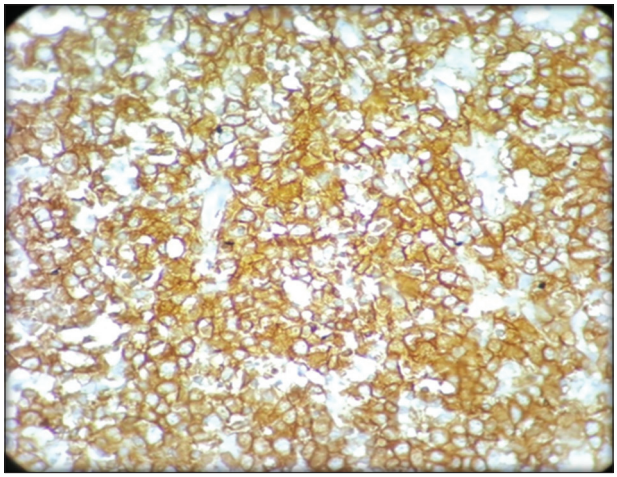

Figure 4: Immunohistochemistry of axillary lymph node with CD 20 as marker

surprise; the report was positive for papillary carcinoma of the thyroid (Fig. 3), which was unlikely to explain his high-grade fevers and other clinical findings. He underwent bone marrow biopsy which showed reactive hyperplasia in the marrow with erythroid prominence.

Clinically, only lymphoma could explain his symptoms, but the results so far had not confirmed our suspicion. Therefore, we went ahead with a second excision biopsy, this time with the right axillary lymph node. Finally, we got the diagnosis which correlated with our clinical suspicion. It was suggestive of high-grade NHL. Immunohistochemistry (Fig. 4) was consistent with diffuse large B cell lymphoma Stage IIIB CD 20+.

The patient was started on chemotherapy with R-CHOP (rituximab, doxorubicin, vincristine, and cyclophosphamide) and his fevers resolved promptly. His lymphadenopathy and hepatosplenomegaly also showed marked regression. He underwent 6 cycles of chemotherapy and went into remission following the chemotherapy. He then underwent total thyroidectomy and the histopathology of the thyroid gland post-operative showed papillary carcinoma (largest focus 2 cm × 1 cm) in the background of multinodular goiter with an extrathyroidal extension and metastasis to the right lymph nodes, central lymph nodes, and superior mediastinal nodes. Concomitant follicular adenoma was also seen in the background of multinodular goiter. Subsequently, radioactive iodine ablation was planned, but he was lost to follow-up.

DISCUSSION

The second primary malignancy (SPM) is a second *de novo* malignant neoplasm occurring in a patient with known cancer. The criteria for classifying a tumor as SPM have remained consistent since it was first proposed in 1932. Warren and Gates criteria for diagnosis of multiple primary malignancies include the following: (a) Each of the tumors must be malignancy confirmed by histology, (b) each must be geographically separate and distinct; the lesions should be separated by normal mucosa, and (c) probability of one being the metastasis of the other must be excluded [3].

SPM can arise either synchronously or metachronously [2]. This is based on their temporal relationship to the primary or index tumor. The term “metachronous” is used when the second

primary malignancy is diagnosed >6 months after the diagnosis of the index tumor and "synchronous" designates SPM diagnosed within 6 months of the index tumor.

The pathophysiology behind the occurrence of multiple primary malignancies has been theorized to be common carcinogen-induced multiple cancers in an exposed epithelial surface, called "field cancerization" as seen in head-neck tumors, as a late side effect of treatment used to treat the first tumor and a genetic predisposition to neoplasia [4]. Other possible causal factors include persistent carcinogen exposure from environment, progressive ozone depletion and effects of ionizing radiation, increased use of organ transplant, and the increasing use of newer treatment modalities such as hormonal manipulation, target therapies, genetic manipulation, and immunomodulators [5].

The patient described in our case had all the clinical findings suggestive of lymphoma, but we were surprised to find papillary carcinoma of thyroid on cervical lymph node biopsy. Bone marrow examination was also not helpful. However, we persisted with our clinical suspicion and got a second lymph node biopsy (this time from axilla) which diagnosed NHL in the patient, the cause of his persistent high-grade fevers, generalized lymphadenopathy, and hepatosplenomegaly. NHLs most frequently arise from lymph nodes, but an extranodal site can be the primary source in approximately 30% of cases, and the thyroid gland is among the most common of these extranodal sites. However, in our case, there was no evidence of primary thyroid lymphoma, lymphoid infiltration, or metastasis within the gland. Therefore, we can assume that papillary carcinoma of thyroid and lymphoma in our patient was two different primary malignancies occurring synchronously. This assumption is also in agreement with NAACCR definition that "multiple lesions of different histologic types occurring in different sites are considered as separate primaries whether occurring simultaneously or at different times" [2].

A study analyzing the SEER Program database has revealed that the incidence of multiple primaries varies from 1% (initial liver primary) to as high as 16% (initial bladder primary); if the initial primary is the breast, the percentage of patients expected to develop multiple primaries is 10% and for the lung it is 4% [6]. In a recent Indian study, most diagnosed synchronous malignancies were carcinoma breast, while in metachronous malignancies, carcinoma breast and gynecological cancers were most common [7]. Preetam *et al*. reported a double primary cancer of infiltrating ductal carcinoma of the breast and small-cell carcinoma of the lung [8]. An online search for synchronous malignancy involving papillary thyroid carcinoma and lymphoma failed to yield any results. Therefore, the case that we have presented may be the first case documenting this to the best of our knowledge.

A high index of suspicion of the second malignancy should prompt a thorough and aggressive workup for early detection and treatment for improved outcomes. Importance of clinical assessment to direct further workup cannot be overemphasized.

CONCLUSION

This case highlights the unusual synchronous occurrence of the papillary carcinoma of thyroid and NHL and the diagnostic challenges involved in such cases.

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