Case Report

Cytodiagnosis of Primary Thyroid Lymphoma Coincident with Unnoticed Papillary Thyroid Carcinoma: A Case Report and Review of the Literature

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Abstract

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, whereas primary thyroid lymphoma is very rare. Here, we report a case in which a right-sided nodule measuring 4.3 × 2.2 cm was examined using fine-needle aspiration biopsy. This revealed abundant monomorphic non-cohesive large lymphoid cells without thyroid follicular cells, on which basis cytodiagnosis of lymphoma coincident with lymphocytic thyroiditis was made. Subsequent histologic examination revealed CD45−, CD20+, and Bcl-6+ and cytokeratin-, CD3-, CD5-, and CD30-negative tumor cells arranged diffusely in the whole thyroid coexisting with a separate PTC nodule sized 1.3 × 1.0 cm in the right lobe. The key point exemplified by this case is that a cytodiagnosis of this extremely rare coexistence of PTC and lymphoma can be made by adequate sampling of both nodules preoperatively. In our case, only one nodule formation was sampled, and therefore the coexisting PTC was not detected with cytology preoperatively.

Keywords: Coexistence, papillary thyroid carcinoma, primary thyroid lymphoma

INTRODUCTION

Although the risk of papillary thyroid carcinoma (PTC) is higher in patients with lymphocytic thyroiditis, there have been very few reports of these malignancies coexisting in the same patient.[1-10] Here, we report a case of diffuse large B-cell lymphoma (DLBCL) of the thyroid coexisting with PTC in an elderly female patient diagnosed initially with high-grade non-Hodgkin’s lymphoma (NHL). A differential diagnosis of lymphocytic thyroiditis was made using a fine-needle aspiration biopsy (FNAB) and was subsequently confirmed by histologic examination.

CASE REPORT

A 77-year-old female patient had had a progressively enlarging thyroid gland for 24 months. Ultrasonography (USG) revealed diffuse bilobate enlargement of the thyroid with a poorly defined boundary and heterogeneous nodularity. FNAB was used to examine a 4.3-×-2.2-cm-sized nodule in the right lobe without sampling a concomitant 1.3-cm nodule formation in the same lobe.

FNAB was performed under ultrasound guidance using 27-gauge needles and 10-mL syringes. The material was air-dried and fixed in alcohol, and then stained with May–Grunwald–Giemsa and Papanicolaou stains. Part of the aspirated material was fixed in alcohol and 10% formalin, and embedded in paraffin. Sections (3–4 μm) prepared from cell blocks were stained for immunohistochemical studies on an automated immunostainer (Ventana ES, Ventana Medical Systems, Tucson, AZ, USA) using the biotin–avidin technique.

FNAB material revealed a prominent population of monotonous non-cohesive large lymphoid cells without thyroid follicular cells, on which basis acytodiagnosis of lymphoma coincident with lymphocytic thyroiditis was made. Subsequent histologic examination revealed CD45−, CD20+, and Bcl-6+ and cytokeratin-, CD3-, CD5-, and CD30-negative tumor cells arranged diffusely in the whole thyroid coexisting with a separate PTC nodule sized 1.3 × 1.0 cm in the right lobe. No granuloma, thyroid follicular, or Hurthle cells were observed, and no oncocytic changes were detected. Immunohistochemistry

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was performed on the cell block and it was confirmed that the atypical cells had a lymphoid origin, as they were positive for CD45 and that they had a B-cell lineage, as they were positive for CD20. A cytodiagnosis of high-grade NHL with a differential diagnosis of lymphocytic thyroiditis was established. Imaging studies and bone marrow examination did not reveal other areas of involvement. Hematologic parameters and thyroid function tests were normal, but no anti-thyroid peroxidase antibodies were detected. Based on the cytologic diagnosis, the surgeon performed a bilateral total thyroidectomy. Grossly, the right thyroid lobe measured 4.5 × 3.5 × 2.0 cm and the left lobe measured 4.5 × 3.0 × 1.5 cm. Cut sections showed a firm, pinkish-white fleshy mass. There was a discrete 1.3–m sized nodule formation in the right thyroid lobe that had not been sampled by FNAB previously, even though preoperative USG-guided needle aspiration biopsy is currently the mainstay diagnostic approach for these lesions and should be performed for every suspected nodule.

Sections of the thyroid demonstrated a prominent lymphocytic thyroiditis with reactive secondary follicles, and a proliferation of large monomorphic lymphocytes in diffuse sheets. The cells had prominent single or multiple nucleoli, and there was a high mitotic count. Immunohistochemical analysis revealed that the tumor cells were positive for CD45, CD20, and Bcl-6 and negative for pancytokeratin, CD3, CD5, and CD30. The proliferative index (Ki-67) was high (75%). A whole body scan did not reveal any other organ involvement or lymphadenopathy. Thus, a final diagnosis of diffuse large B-cell subtype primary NHL in the thyroid was established. The thyroid had almost completely been replaced by lymphoma. Microscopic examination of the nodule on the right side revealed a 1.3 × 1-cm-sized PTC [Figure 1b]. There was no extrathyroidal extension, and all surgical resection margins were negative. The patient was treated with cyclophosphamide, daunorubicin, vincristine, and prednisolone (CHOP)-based chemotherapy and radiiodine. There was no evidence of recurrence or metastases at the 2-year follow-up examination.

**Discussion**

The coexistence of both malignancies in the same patient has only rarely been reported. Although there have been numerous reports of lymphoma involving the thyroid gland, there are only a few case reports of primary thyroid lymphoma (PTL) diagnosed by FNAB due to the diagnostic difficulty. Unfortunately, many of these cases were misdiagnosed on cytology. Such errors have significant clinical implications, as they can result in unnecessary surgical intervention and/or radiation therapy. Even in the present case there was no definitive diagnosis of PTC on FNAB and it is not correct to allege that others misdiagnosed it on FNAB. In addition, there are very few reports on the diagnosis of simultaneous PTL and PTC by FNAB. To the best of our knowledge, only 11 cases of PTC concomitant with thyroid lymphoma have been reported previously, and only in three of these were both malignancies diagnosed on the basis of cytology [Table 1]. In the present case, we did not diagnose PTC by FNAB. In addition, our literature review of co-occurrence of primary thyroid lymphoma and PTC has revealed that only in our case a cell block was prepared and immunohistochemistry was applied on it to use. As in our case, a cell block preparation facilitates to apply immunohistochemistry and approach definitive diagnosis. It is important to perform FNAB for each separate nodule in multinodular goiter in conjunction with lymphocytic thyroiditis. In our case, FNAB was performed for the 4.3-cm sized but not the 1.3-cm-sized nodule in the right lobe, and consequently the concomitant PTC was overlooked. Therefore, we want to emphasize the necessity of adequate sampling of all nodules to exclude a coincident second malignancy. It is

**Table 1: Literature review of co-occurrence of primary thyroid lymphoma and papillary thyroid carcinoma**

| Author            | Case no. | Thyroidectomy/lobectomy | Cell block | Immunohistochemistry on cell block/immunocytochemistry | Co-occurrence with PTC | Cytodiagnosis of lymphoma | Cytodiagnosis of PTC |
|-------------------|----------|--------------------------|------------|--------------------------------------------------------|------------------------|---------------------------|----------------------|
| Reid-Nicholson et al.,[1] 2008 | 1        | Yes                      | None       | None                                                   | Yes                    | Yes                       | Yes                  |
| Melo et al.,[2] 2010 | 1        | Yes                      | None       | None                                                   | Yes                    | None                      | None                 |
| Panayiotides et al.[3], 2010 | 1        | Yes                      | None       | None                                                   | Yes                    | None                      | Yes                  |
| Vassilatou et al.,[4] 2011 | 2        | 2 cases                  | None       | 2 cases                                                | None                   | 1 case                    | None                 |
| Cheng et al.,[5] 2012 | 1        | Yes                      | None       | Yes                                                    | Yes                    | Yes                       | Yes                  |
| Cakir et al.,[6] 2013 | 1        | Yes                      | None       | Yes                                                    | Yes                    | Yes                       | None                 |
| Nam et al.,[7] 2013 | 1        | yes                      | None       | Yes                                                    | Yes                    | None                      | Yes                  |
| Jayaprakash et al.,[8] 2014 | 1        | Yes                      | None       | Yes                                                    | Yes                    | None                      | Yes                  |
| Tarui et al.,[9] 2014 | 1        | Yes                      | None       | Yes                                                    | Yes                    | Yes                       | Yes                  |
| Xie et al.,[10] 2015 | 1        | Yes                      | None       | Yes                                                    | Yes                    | None                      | None                 |
| Kir, Sarbay, 2015 | 1        | Yes                      | Immunohistochemistry on cell block | Yes | Yes | Yes |

PTC: Papillary thyroid carcinoma
also noteworthy that a cytodiagnosis of high-grade NHL with a differential diagnosis of lymphocytic thyroiditis was established. A subsequent total bilateral thyroidectomy allowed a definitive tissue diagnosis using confirmatory immunohistochemistry: DLBCL of the thyroid with an incidental finding of PTC in the right lobe. For patients with aggressive DLBCL, the most frequent histologic subtype of PTL treatment is based on CHOP chemotherapy. The combination of chemotherapy and radiotherapy is the gold standard for localized high-grade NHL. PTC is the most common type of thyroid malignancy with an excellent prognosis. Postoperative management depends on the patient’s general medical condition. In cases of DLBCL comorbid with PTC, the recommended management is to provide the optimal treatment for both malignancies.

This case emphasizes the necessity of adequate sampling of all separate nodules of PTL in order not to overlook concomitant PTC.

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**Conflicts of interest**
There are no conflicts of interest.

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