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Case Report

Primary Burkitt Lymphoma of the Thyroid Associated With Hashimoto Thyroiditis Masquerading as Post-COVID Thyroiditis

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Abstract

Primary thyroid lymphoma accounts for only 2% to 5% of all thyroid tumors, and Burkitt lymphoma of the thyroid is even rarer than other types of B-cell lymphoma. It is a highly aggressive non-Hodgkin lymphoma characterized by intermediate-sized lymphoid cells with a "starry sky" appearance and exhibits chromosomal translocations that activate the *MYC* oncogene. A male predominance and an aggressive clinical course with a high risk of central nervous system involvement and tumor lysis syndrome are all well-recognized features of Burkitt lymphoma. We present a case of a 28-year-old man with primary Burkitt lymphoma of the thyroid initially misdiagnosed as post-COVID thyroiditis. Core needle biopsy showed round, intermediate-sized lymphoid cells admixed with scattered tingible body macrophages displaying a "starry sky" appearance. Following the final histological diagnosis of primary thyroid Burkitt lymphoma, the patient received intensive chemotherapy. Six months after the diagnosis, the patient succumbed to disease progression, causing upper airway obstruction. Primary Burkitt lymphoma of the thyroid can cause pain and other symptoms due to the rapidly growing mass in the neck. Adequate pathological diagnosis with core needle biopsy rather than fine needle aspiration is essential for treatment planning and outcome improvement.

Key Words: primary thyroid lymphoma, Burkitt lymphoma, post-COVID thyroiditis

Abbreviations: CNS, central nervous system; COVID-19, coronavirus disease 2019; PTL, primary thyroid lymphoma.

Introduction

Primary thyroid lymphoma (PTL) is 1 of the rarest forms of all thyroid cancers, predominantly affecting elderly women with a history of long-standing Hashimoto thyroiditis [1]. Since the normal thyroid gland lacks native lymphoid tissue, individuals with Hashimoto thyroiditis are at an elevated risk of developing PTL due to chronic antigenic stimulation and clonal B-cell lymphocytosis [2]. Diffuse large B-cell lymphoma and extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue are the most frequently encountered histological subtypes of PTL [3, 4]. However, this entity is a heterogeneous disease with diverse clinical presentations.

Primary Burkitt lymphoma of the thyroid, a highly aggressive non-Hodgkin lymphoma, is exceptionally rare, with fewer than 30 reported cases worldwide to date [5-10]. It displays a unique histologic feature characterized by intermediate-sized lymphoid cells with a "starry sky" appearance and exhibits chromosomal translocations that activate the *MYC* oncogene. Historically, Burkitt lymphoma is a highly aggressive disease that is endemic in Africa and sporadic in other parts of the world [11]. The endemic variant is associated with Epstein-Barr virus. It is more aggressive than the other types of non-Hodgkin lymphoma and requires aggressive chemotherapy for better outcomes. Primary Burkitt lymphoma of the thyroid has clinicopathologic features similar to sporadic Burkitt lymphoma at other anatomic sites (mainly at the jaw and facial bones, nasopharynx, and terminal ileum) and develops predominantly in children and young individuals [9]. In this report, we present a patient who was initially misdiagnosed as post-coronavirus disease 2019 (COVID-19) thyroiditis but was ultimately found to have primary Burkitt lymphoma of the thyroid.

Case Presentation

A 28-year-old Thai male presented with anterior neck pain and a rapidly enlarging neck mass that developed over 2 months, shortly after a mild COVID-19 infection. He denied systemic symptoms, such as weight loss, fever, or abdominal pain. The patient had a history of mild autism spectrum disorder. He displayed difficulties with social interaction, communication, and repetitive behaviors since childhood but otherwise achieved normal developmental milestones with no history of recurrent infections. He had no history of radiation exposure and no family history of thyroid-related

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disorders or malignancy. Initially, he was evaluated at a local clinic, where a multinodular goiter was noted, estimated to weigh 45 grams. Based on his clinical presentation, a diagnosis of post-COVID subacute thyroiditis was made, and he was treated with oral prednisolone 20 mg per day, which resulted in a slight improvement in thyroid tenderness.

However, the patient later presented to our hospital with a rapidly enlarging neck mass with an estimated thyroid size of 60 grams. Physical examination revealed a visibly swollen neck with multiple thyroid nodules in both thyroid lobes. The masses had a hard consistency without signs of local inflammation. Multiple enlarged cervical lymph nodes were also noted. The rest of the systemic examination was unremarkable.

Diagnostic Assessment

Initial laboratory investigations showed a normal complete blood count but a significantly elevated erythrocyte sedimentation rate of 70 millimeters per hour (normal ≤ 20 millimeters per hour). Thyroid function test results were within normal ranges; serum TSH level was 2.95 μIU/mL (normal range 0.27-4.20 μIU/mL). The thyroid peroxidase antibody test was negative, while anti-thyroglobulin antibody was elevated at 325 IU/mL (normal 0-115 IU/mL). Serologic testing for HIV was negative.

Neck ultrasonography demonstrated multiple homogeneous hypoechoic areas involving both thyroid lobes, measuring 2.6 by 9.3 cm as shown in Fig. 1A and 1B. No calcifications or necrosis were found. The ultrasound also revealed heterogeneous parenchymal echotexture in both thyroid lobes, consistent with thyroiditis. Additionally, sonographic features of malignant cervical lymph nodes in regions IV and V on the right side of the neck were present (hypoechoic, round, and loss of central fatty hilum) as shown in Fig. 1C. The patient underwent core needle biopsy of the thyroid gland due to the presumptive diagnosis of PTL from these ultrasonographic features.

Histological examination of the core needle biopsy revealed monomorphic, intermediate-sized neoplastic lymphoid cells with round nuclei, dispersed chromatin, and scant cytoplasm, as shown in Fig. 2A and 2B. Scattered tingible body type macrophages creating a "starry sky" appearance were also present, as depicted in Fig. 2B. Immunohistochemical staining was then performed, and the tumor cells were positive for cluster of differentiation (CD) 20, CD10, B-cell lymphoma 6, and cellular myelocytomatosis oncogene as shown in Fig. 3. The antigen Kiel 67 showed a proliferation index greater than 95%, indicating a highly proliferative tumor. The tumor cells were negative for B-cell lymphoma 2, CD3, and cyclin D1. Epstein-Barr virus-encoded RNA in situ hybridization showed a negative result. Fluorescence in situ hybridization staining for *MYC* gene translocation analysis revealed *MYC* gene rearrangement. Burkitt lymphoma of the thyroid was diagnosed based on these morphologic, immunophenotypic features, and molecular studies.

Treatment

The patient was subsequently referred to the hematology department at a tertiary care center for further cancer staging and initiation of intensive chemotherapy. Further investigations with the computed tomography scan of the chest, abdomen, and pelvis showed no evidence of distant metastasis. Bone marrow examination was within normal limits. However, lymphoma cells were found in cerebrospinal fluid through lumbar puncture. The patient was diagnosed with

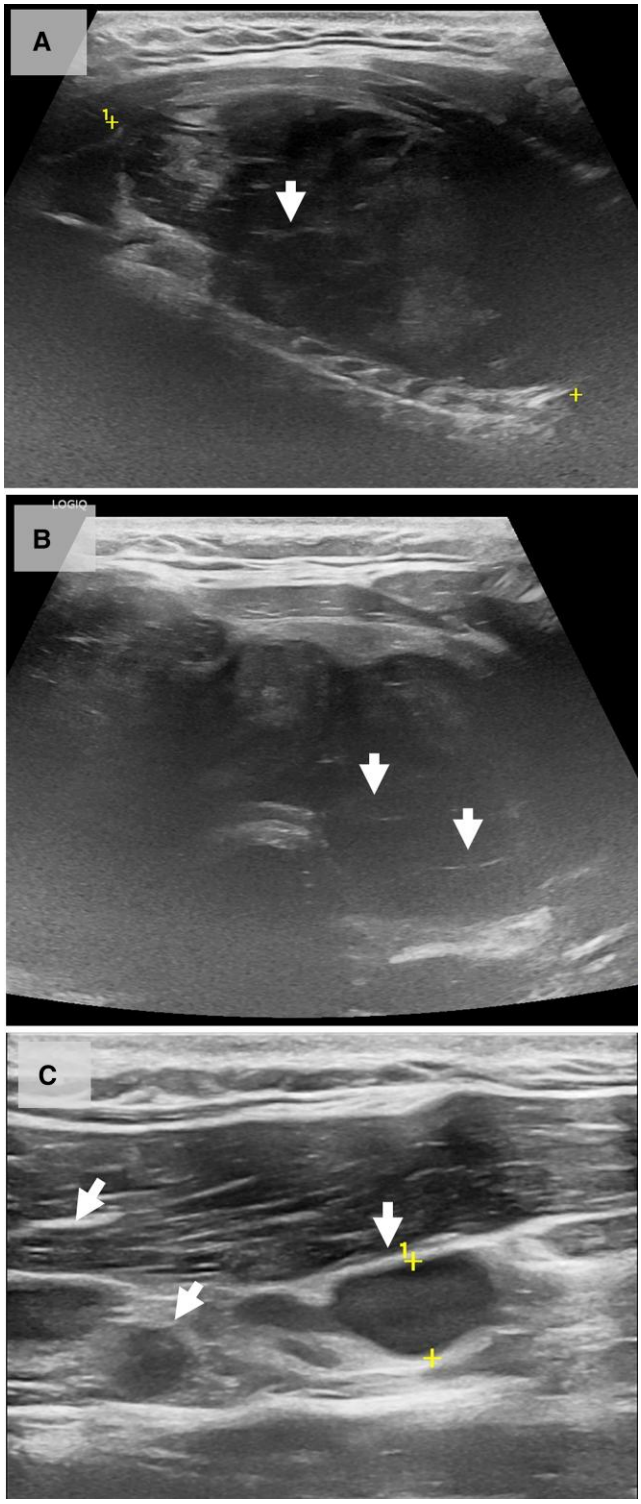

Figure 1. Ultrasonographic findings of neck at initial evaluation revealed typical findings of some suspicious signs of ultrasonography. (A, B) Enlarged thyroid gland, almost replaced by large, markedly hypoechoic mass (no internal calcification or necrosis) involving both lobes and isthmus of thyroid (arrow indicates echogenic fibrous strands); (C) multiple enlarged hypoechoic cervical lymph nodes were found; pathologically proven lymphomatous involvement.

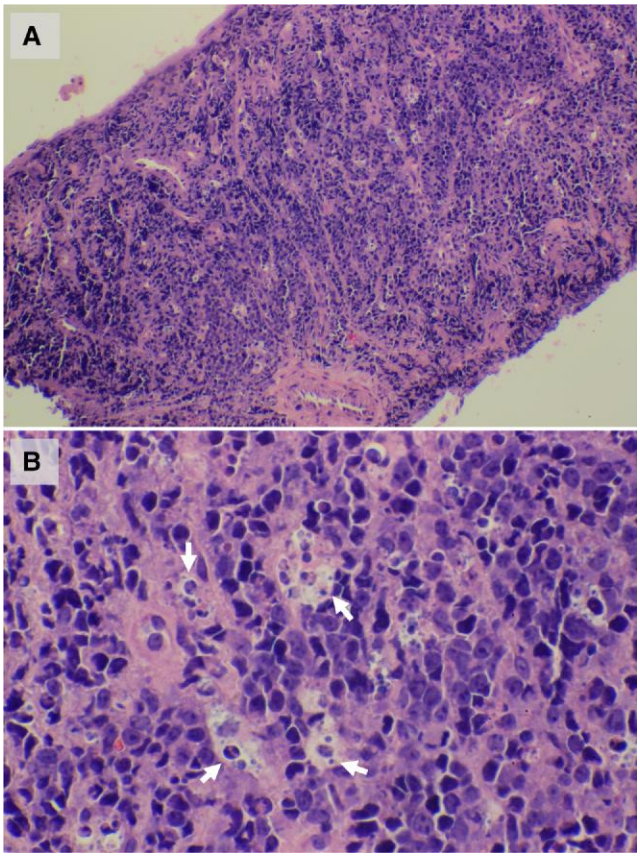

Figure 2. Histopathologic findings of the right thyroid mass from ultrasound-guided core needle biopsy showing monomorphic, intermediate-sized neoplastic lymphoid cells with round nuclei. Scattered tingible body macrophages are present among these tumor cells displaying a "starry sky" appearance (arrows) (hematoxylin and eosin stain) (A x100, B x200).

primary thyroidal Burkitt lymphoma with central nervous system (CNS) involvement. He was started on multiple cycles of high-intensity chemotherapy (rituximab, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, R-Hyper-CVAD regimen) and intrathecal chemotherapy with methotrexate as part of CNS-directed therapy.

Outcome and Follow-up

After 6 months of treatment, the patient's dysphagia and dyspnea rapidly worsened, despite high-dose corticosteroids and intensive chemotherapy. Ultimately, he succumbed 7 months postdiagnosis due to rapid deterioration from airway obstruction and tumor-related bleeding at the primary thyroid mass.

Discussion

PTL is a rare malignancy, accounting for less than 5% of all thyroid tumors, with primary Burkitt lymphoma of the thyroid representing an exceptionally rare subset [5-7]. Unlike other more common subtypes of PTL, Burkitt lymphoma exhibits a distinct clinicopathologic profile, including a male predominance, rapid disease progression, and a high propensity for CNS involvement at the initial presentation. Our case underscores the importance of maintaining a broad differential diagnosis in patients presenting with thyroid tenderness and a rapidly enlarging thyroid mass. Post-COVID thyroiditis can have a clinical course and outcomes similar to those of postviral subacute thyroiditis [12]. Although subacute thyroiditis is the most common cause of thyroid tenderness, other conditions such as hemorrhage within a thyroid nodule, Riedel thyroiditis, suppurative thyroiditis, infiltrative diseases, and rapidly growing anaplastic carcinoma should also be considered and appropriately ruled out [13].

Although often nonspecific, certain ultrasonographic features can assist clinicians in distinguishing thyroid lymphoma from other conditions. Clinically, PTL can closely mimic anaplastic thyroid carcinoma, as both present with rapid growth, potentially leading to compression symptoms such as dyspnea, dysphagia, pain, and hoarseness of voice. Ultrasonographic findings characteristic of lymphoma include large, extremely hypoechoic solid masses with enhanced posterior echoes and homogeneous texture, typical without calcification of necrosis. Identifying echogenic fibrous strands that are typical features of thyroid lymphoma could be the key feature for differentiating this identity from anaplastic thyroid cancer [14]. It is important to emphasize that the diagnosis of PTL requires adequate tissue sampling, with percutaneous ultrasound-guided core needle biopsy preferred over fine-needle aspiration [15, 16]. Due to the heterogeneous nature of thyroid malignant lymphomas, the prognosis and treatments vary depending on the histological diagnosis of the lymphoma. Immunohistochemistry and cytogenetics are often required to confirm the accurate diagnosis.

Despite its extremely low incidence, accounting for less than 1% of all PTL, the diagnosis of Burkitt lymphoma within the thyroid gland is relatively straightforward compared with other types of malignant lymphomas [9]. The presence of a monomorphic population of intermediate-sized atypical lymphocytes with a starry sky appearance, expression of CD10 and pan B-cell markers, as well as the presence of *MYC* gene rearrangement detected by fluorescence in situ hybridization, are defining pathogenetic features of Burkitt lymphoma [17]. Several published cases of primary Burkitt thyroid lymphoma have demonstrated an association with Hashimoto thyroiditis [9, 18]. A previously published meta-analysis of 21 cases with primary Burkitt thyroid lymphoma demonstrated that it mostly occurred in adult patients at a median age of 39.3 years with a male predominance [9]. Primary Burkitt thyroid lymphoma has a significantly better overall survival rate and more favorable response to intensive chemotherapy compared to extrathyroidal Burkitt lymphoma [9]. Therefore, an accurate pathological diagnosis is crucial for treatment planning and achieving favorable outcomes in patients with primary Burkitt thyroid lymphoma. The management of Burkitt lymphoma requires the urgent initiation of intensive chemotherapy due to its highly aggressive nature. Initial cytoreduction with cyclophosphamide, prednisolone, and vincristine, followed by more intensive combination chemotherapy regimens that include agents such as doxorubicin, alkylating agents, vincristine, and etoposide is essential for achieving better outcomes [19]. A thorough clinical tumor staging before the initiation of treatments should be considered because of the frequent presence of disseminated disease at presentation in patients with primary Burkitt thyroid lymphoma. Surgical intervention plays a limited role and should be reserved for obtaining diagnostic tissue samples or for urgent management of upper airway obstruction [20]. Similar to malignant lymphoma at other locations, chemotherapy alone had a more effective complete remission than those undergoing surgical debulking followed by adjuvant therapy. Patients with

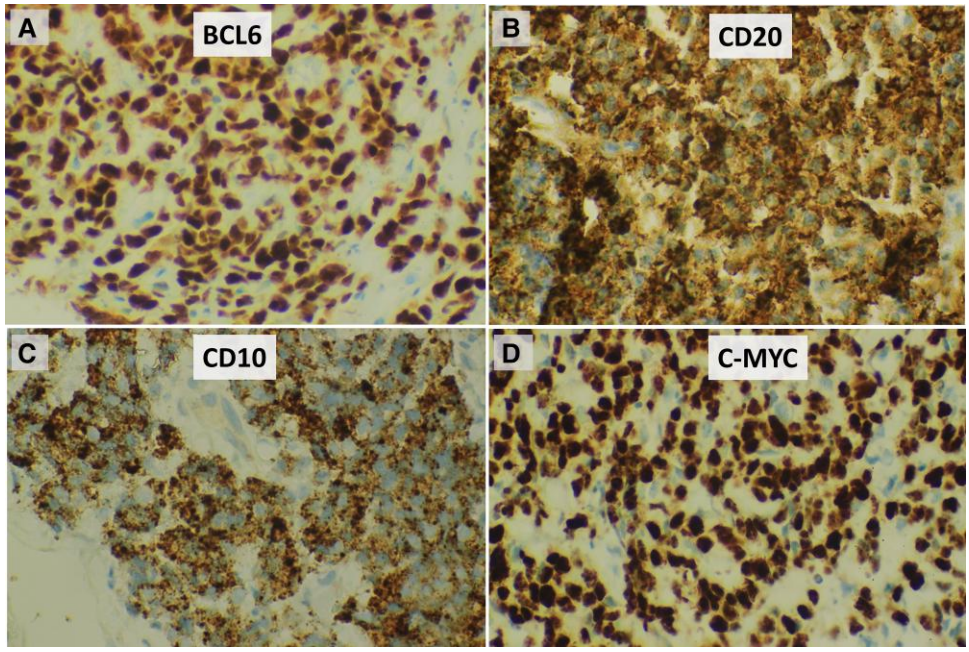

Figure 3. Immunohistochemical staining revealed (A) the expression of B-cell lymphoma 6, suggesting a germinal center origin (x200); (B) CD20 (x200); (C) CD10, suggesting B-cell lymphoma (x200); (D) C-MYC positivity in tumor cells, a hallmark of Burkitt lymphoma (x200).

Abbreviation: CD, cluster of differentiation.

chemotherapy-refractory disease have limited salvage options and a median survival of less than 3 months. Supportive care is essential in all steps of treatment, particularly for managing upper airway obstruction and tumor lysis syndrome.

In conclusion, rapidly enlarging neck masses accompanied by thyroid tenderness should raise suspicion for aggressive thyroid malignancies. Obtaining a definitive histological diagnosis through biopsy is crucial to differentiate PTL from other thyroid cancers. When PLT is suspected based on ultrasonographic findings, a core needle biopsy should be performed as the initial diagnosis procedure. Primary Burkitt lymphoma of the thyroid is a highly aggressive non-Hodgkin lymphoma characterized by a monomorphic population of intermediate-sized lymphoid cells displaying a starry sky appearance and harboring chromosomal translocations that activate the *MYC* oncogene. Early diagnosis and accurate staging are vital for implementing appropriate treatment strategies and achieving the best possible patient outcomes.

Learning Points

- Aggressive thyroid cancer should be considered in patients presenting with a rapidly enlarging neck mass and thyroid tenderness.
- Although the features are often nonspecific, clinicians should be attentive to certain suspicious signs on thyroid ultrasonography, as these can provide critical clues in distinguishing thyroid lymphoma from other conditions. Identifying marked hypoechoic areas without calcification or necrosis may be a key feature in differentiating thyroid lymphoma from anaplastic thyroid cancer.
- Core needle biopsy is preferred over fine-needle aspiration to maximize diagnostic yield and enable the rapid initiation of appropriate therapy in patients suspected of having PTL.
- Primary Burkitt lymphoma of the thyroid is a highly aggressive non-Hodgkin lymphoma and should be promptly recognized because its management is different from the treatment of other neoplasms of the thyroid.

Contributors

Y.T. contributed to data interpretation, study design, manuscript preparation, and submission. W.C. contributed to the graphic preparation and discussions. V.V. and S.K. contributed to the manuscript and graphic preparation. E.W. contributed to the diagnosis and management of the patient and manuscript preparation. T.H. contributed to the discussions. All authors reviewed and approved the final draft.

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Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient's relatives or guardians.

Data Availability Statement

Data sharing is not applicable to this article as no data sets were generated or analyzed during the present study.

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