Papillary thyroid carcinoma in a patient with long-standing chronic lymphocytic leukemia: A case report

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Abstract. The synchronous occurrence of papillary thyroid carcinoma (PTC) and chronic lymphocytic leukemia (CLL) is rare and poses diagnostic challenges, particularly in distinguishing metastatic thyroid disease from hematological lymphadenopathy. The present report documents the case of a 64-year-old female patient with long-standing CLL who presented with a malignant thyroid nodule accompanied by multiple enlarged cervical lymph nodes. A diagnosis was established through integrated immunohistochemistry, flow cytometry and multimodal imaging. After the diagnosis of synchronous PTC and CLL/SLL was confirmed, the patient underwent a total thyroidectomy with central compartment lymph node dissection. In addition, a focused review of the literature was conducted to contextualize the clinical presentation, diagnostic strategies and management approaches. Treatment and follow-up were guided by a multidisciplinary team. No adverse events occurred during follow-up. At the latest follow-up in November 2025, the patient remained clinically stable, with no evidence of PTC recurrence or CLL progression, and thyroid function test results showed decreased T3, elevated T4 and free T4, mildly elevated thyroid-stimulating hormone, and free T3 within the reference range. The present case highlights the importance of a comprehensive diagnostic work-up and provides practical guidance for the diagnostic and therapeutic management of patients with dual malignancies.

Introduction

Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy worldwide, accounting for 70-80% of all thyroid cancer cases (1). Over the past decades, the incidence of PTC has risen markedly, increasing from 4.8 to 14.9 per 100,000 individuals from 1975 to 2012, largely due to increased detection rather than carcinogenic effects of diagnostic procedures. In particular, the widespread use of high-resolution thyroid ultrasonography, ultrasound-guided fine-needle aspiration biopsy and more sensitive cytopathological assessment has improved the detection of small, asymptomatic or subclinical papillary thyroid lesions that may not have been identified by conventional diagnostic approaches, such as symptom-based clinical assessment and palpation-based neck examination (2). PTC primarily affects middle-aged women, 40-60 years of age, with a median age at presentation of ~50 years (female-to-male ratio, ~3:1) (3) and typically follows an indolent course. Metastasis occurs mainly through the lymphatic system, with cervical lymph node involvement serving as an important predictor of recurrence and poor outcomes (4,5). The coexistence of PTC with hematological malignancies is exceedingly rare. A focused literature search identified five directly comparable case reports of PTC coexisting with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL). Reid-Nicholson *et al* (6) reported a case of PTC with concurrent CLL/SLL involving the thyroid gland, while Ahmed and Salih (7) described a case of PTC and SLL within the thyroid gland diagnosed by cytohistological correlation. Sezer *et al* (8) reported a case of metastatic well-differentiated thyroid carcinoma and CLL in the same lymph node, accompanied by internal jugular vein thrombus. Furthermore, Rejeb *et al* (9) described a case of synchronous cervical lymph node involvement by metastatic PTC and SLL, and Farnin *et al* (10) reported a case of synchronous papillary thyroid microcarcinoma and CLL in a patient presenting with cervical lymphadenopathy. Collectively, these reports show that the main challenge in diagnosing and managing concurrent PTC and CLL/SLL is the diagnostic and therapeutic ambiguity caused by overlapping lymphadenopathy. Cervical lymph nodes may represent metastatic PTC, CLL/SLL involvement or coexistence of both lesions, whereas imaging and laboratory findings are often non-specific and fine-needle aspiration may sample only one component. This uncertainty can affect tumor staging, the extent of lymph node dissection and subsequent hematological management. Therefore, integrated assessment using imaging, cytology or

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histopathology, immunohistochemistry and flow cytometry is essential for an accurate diagnosis. The present case attempts to contribute to the literature by describing a rare case of the synchronous occurrence of PTC and CLL with the leukemic manifestation of SLL, emphasizing the diagnostic challenges and multidisciplinary management required.

Case report

Presentation. In October 2023, a 64-year-old female patient was admitted to the Second Hospital of Lanzhou University (Lanzhou, China) with complaints of a thyroid nodule. Specifically, the nodule had gradually enlarged over the past 4 years, accompanied by multiple enlarged lymph nodes in the bilateral axillae, inguinal regions and abdominal cavity. The patient had experienced no neck pain, hoarseness, dysphagia or dyspnea. Systemic symptoms, such as fever, palpitations, diarrhea and facial flushing, were also absent. On admission, the physical examination revealed multiple enlarged lymph nodes palpable in the bilateral cervical, axillary and inguinal regions. Baseline contrast-enhanced neck CT showed that the largest node in the right cervical region measured ~2.0x1.0 cm, whilst the largest on the left side measured ~1.0x1.0 cm (Fig. 1A and B). No hepatomegaly or splenomegaly was detected on abdominal palpation.

Past medical history. The patient had a 30-year history of hypertension and was receiving irbesartan/hydrochlorothiazide tablets (150/12.5 mg), one tablet orally once daily. Blood pressure measured at admission was 162/78 mmHg. The patient had undergone a cholecystectomy 15 years prior for gallstones with acute cholecystitis. In addition, 7 years before the present admission, the patient had been diagnosed with CLL and had since been followed up regularly, with no clear evidence of clinical progression. The patient was resident in an urban district of Lanzhou, China, and no specific environmental or occupational carcinogenic exposure was identified. The patient also had no prior exposure to ionizing radiation, radioactive materials or hazardous chemicals, with no history of smoking, alcohol consumption or known chronic infectious disease.

Laboratory tests. A complete blood count revealed a white blood cell count of $8.1x10^9$/l (reference range, 3.5-9.5x10^9/l), a lymphocyte count of $3.14x10^9$/l (reference range, 1.1-3.2x10^9/l), a hemoglobin level of 139 g/l (reference range, 115-150 g/l) and a platelet count of $185x10^9$/l (reference range, 125-350x10^9/l). Biochemistry showed elevated levels of β_2-microglobulin and uric acid at 6.44 mg/l (reference range, 0.8-2.2 mg/l) and 558 μmol/l (reference range, 155-357 μmol/l), respectively. Immunological analysis demonstrated the following results: Immunoglobulin (Ig)A, 0.29 g/l (reference range, 0.7-4.0 g/l); IgG, 3.32 g/l (reference range, 7.0-16.0 g/l); IgM, 0.26 g/l (reference range, 0.4-2.3 g/l); complement (C)3, 0.88 g/l (reference range, 0.9-1.8 g/l); and C4, 0.03 g/l (reference range, 0.1-0.4 g/l), with a κ/λ light chain ratio of 1.81 (reference range, 1.35-2.65). Thyroid function tests showed the following results: Triiodothyronine (T3), 1.5 nmol/l (reference range, 1.3-3.1 nmol/l); thyroxine (T4), 161.10 nmol/l (reference range, 66-181 nmol/l); free (F)T3, 4.57 pmol/l (reference range, 3.1-6.8 pmol/l); FT4, 16.62 pmol/l (reference range, 12.0-22.0 pmol/l); thyroid-stimulating hormone (TSH), 4.954 μIU/ml (reference range, 0.27-4.20 μIU/ml); calcitonin, 4.47 pg/ml (reference range, 0-8.4 pg/ml); vitamin D, 7.0 ng/ml (reference range, 30-100 ng/ml); and parathyroid hormone, 42.90 pg/ml (reference range, 15-65 pg/ml).

Peripheral blood flow cytometry was performed using ethylenediaminetetraacetic acid-anticoagulated peripheral blood as part of the routine clinical hematopathological work-up. After erythrocyte lysis, nucleated cells were stained with fluorochrome-conjugated antibody panels. Detailed antibody combinations and brief method details are provided in Data S1. Lymphocytes were gated according to CD45/side-scatter characteristics, followed by analysis of the CD19-positive B-cell population, light-chain restriction and CLL/SLL-associated markers. Representative dot plots/histograms with population frequencies are shown in Fig. 2. Flow cytometry identified an abnormal mature B-cell population accounting for 80.06% of the parent population, with κ light-chain restriction. The immunophenotype was characterized as CD5 (+), CD19 (+), CD20 (partial+), CD22 (partial+), CD23 (partial+), CD200 (weak+), CD10 (-) and FMC7 (-). These findings support a clonal mature B-cell lymphoproliferative disorder compatible with CLL/SLL.

Bone marrow cytomorphological examination showed active hematopoiesis with an increased proportion of lymphocytes, including certain immature forms. Fine-needle aspiration (FNA) of the left supraclavicular lymph node indicated an indolent small B-cell lymphoma (Fig. 3). Laryngoscopy showed no abnormalities.

Pathology examination. In November 2023, FNA of the right thyroid nodule revealed PTC. Cytological and immunohistochemical evaluation was performed according to routine clinical diagnostic pathology procedures. Briefly, the available cytopathological material was processed for immunohistochemical staining, followed by incubation with antibodies against cytokeratin (CK)19, galectin-3, Hector Battifora mesothelial-1 (HBME-1), CD56 and Ki-67. Appropriate positive and negative controls were used. Immunohistochemical staining demonstrated strong positivity for CK19, galectin-3 and HMBE1, absence of CD56 expression and a Ki-67 proliferation index of ~3% (Fig. 4). Other thyroid lesions were excluded based on the combined cytological, immunohistochemical and laboratory findings. Strong CK19, galectin-3 and HBME-1 positivity with loss of CD56 supported PTC rather than benign nodular disease. Medullary thyroid carcinoma was unlikely as the serum calcitonin level was within the reference range and no medullary carcinoma morphology was identified. Lymphoid involvement of the thyroid nodule was also not supported as the tumor cells showed an epithelial rather than lymphoid immunophenotype. The detailed pathological and immunohistochemical staining protocol is provided in Data S1.

FNA biopsy of the right supraclavicular lymph node suggested an indolent lymphoma of small B-cell origin. Immunohistochemistry (Data S1) showed positivity for CD20, CD79a, BCL-2, lymphoid enhancer-binding factor 1 (LEF-1; focal), and multiple myeloma oncogene-1 (MUM-1; focal). CD5 expression was partially positive, CD23 was weakly positive, and Cyclin D1, SOX11, CD2, CD3, CD10, CD21, CD30,

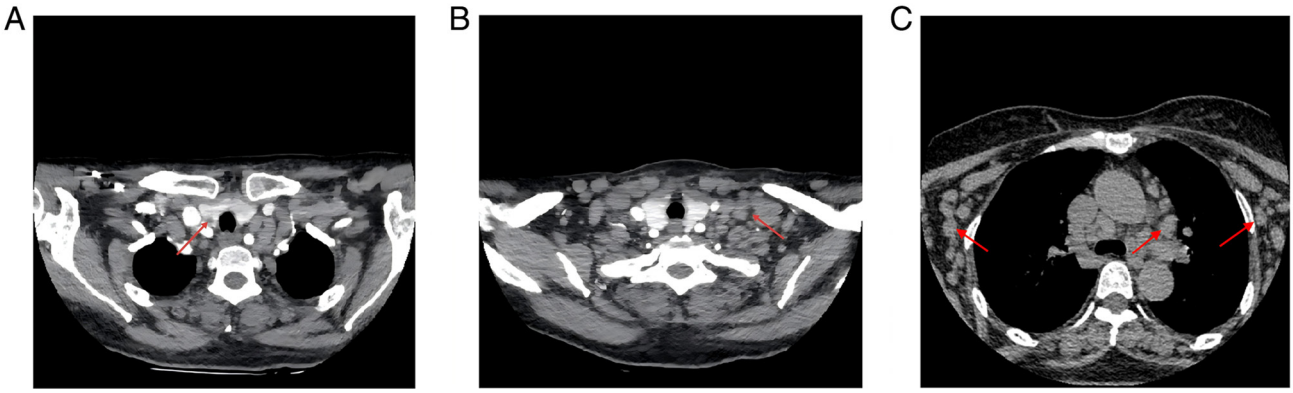

Figure 1. Baseline CT findings obtained during the initial diagnostic work-up at the index admission, showing multiple enlarged lymph nodes. (A) Contrast-enhanced neck CT scan at the level of the lung apices showing enlarged right cervical lymph nodes (red arrows), with the largest node measuring ~2.0x1.0 cm. (B) Contrast-enhanced neck CT scan at the root of the neck showing enlarged left cervical lymph nodes (red arrows), with the largest node measuring ~1.0x1.0 cm. (C) Chest CT scan showing multiple enlarged lymph nodes in the bilateral axillae and mediastinum (red arrows). CT, computed tomography.

c-Myc, BCL-6, myeloperoxidase, terminal deoxynucleotidyl transferase, anaplastic lymphoma kinase and Epstein-Barr virus (EBV)-encoded small RNA results were negative. The Ki-67 proliferation index was ~20% (Figs. 5 and 6).

Taken together, the immunophenotypic profile of the lymph node tissue, namely positivity for CD20, CD79a, LEF-1 (focal), BCL-2 and MUM-1 (focal), with partially positive expression of CD5 and CD23, was consistent with CLL. Other hematological malignancies were excluded based on the immunohistochemical profile. Negative cyclin D1 and SOX11 results argued against mantle cell lymphoma, the absence of CD10 and BCL-6 excluded germinal center-derived B-cell lymphomas, and negative CD3, terminal deoxynucleotidyl transferase and myeloperoxidase results did not support T-cell, lymphoblastic or myeloid neoplasms. Negativity for CD30, anaplastic lymphoma kinase and EBV-encoded small RNA further excluded CD30-positive, ALK-positive or EBV-associated lymphoid neoplasms.

Imaging examination. In November 2023, neck ultrasonography revealed a 0.38x0.31-cm hypoechoic nodule in the mid-portion of the right thyroid lobe [Thyroid Imaging Reporting and Data System (TI-RADS) 4a], a 1.0x0.8-cm hypoechoic nodule in the lower pole of the right lobe (TI-RADS 3) and a 0.5x0.3-cm mixed-echoic nodule in the left lobe (TI-RADS 3), according to the Chinese TI-RADS classification (11). Multiple enlarged lymph nodes were detected in cervical regions I-V bilaterally, the largest measuring ~3.1x1.0 cm on the right and 1.5x1.0 cm on the left (Fig. 7).

During the same initial diagnostic work-up at the index admission, contrast-enhanced CT of the neck demonstrated a 0.9-cm hypodense nodule in the right thyroid lobe, along with multiple enlarged lymph nodes in the bilateral cervical and supraclavicular regions (Fig. 1A and B). Chest CT revealed multiple enlarged lymph nodes in the bilateral axillae and mediastinum, suggestive of lymphoma (Fig. 1C).

Contrast-enhanced abdominal CT showed multiple enlarged lymph nodes in the abdominal and pelvic cavities, the largest measuring ~4.7x2.4 cm, with mild enhancement (Fig. 8). The chronological sequence of patient clinical presentation, diagnostic evaluations, interventions and outcomes is summarized in Table I.

The initial suspected diagnosis was a solitary thyroid malignancy. However, the presence of persistent and generalized lymphadenopathy raised suspicion for a concurrent hematological disorder, prompting further hematological evaluation, including flow cytometry and bone marrow cytomorphological examination, which confirmed CLL.

Diagnosis and treatment. In November 2023, the patient underwent a total thyroidectomy with right central compartment lymph node dissection under general anesthesia at the Second Hospital of Lanzhou University. The surgical thyroid specimens were fixed in 10% neutral buffered formalin at room temperature for 12-36 h, embedded in paraffin, sectioned at 4 μm, stained with hematoxylin and eosin at room temperature 20-25˚C for 45-50 min, and examined and imaged using an Olympus CX43 light microscope at x100 or x200 magnification. Postoperative histopathological examination of hematoxylin and eosin-stained sections revealed a micropapillary carcinoma of the right lobe and isthmus, with the largest focus measuring 0.3 cm in diameter, accompanied by nodular goiter (Fig. 9A). The left lobe showed a nodular goiter with adenomatoid hyperplasia (Fig. 9B). No metastatic carcinoma was identified in the dissected right central compartment and level 6B lymph nodes.

According to the American Joint Committee on Cancer 8th edition staging system (12), the diagnosis was papillary thyroid microcarcinoma, stage pT1aN0M0. The staging was supported by the largest tumor focus measuring 0.3 cm in diameter, consistent with T1a disease, no metastatic carcinoma being identified in the dissected lymph nodes, supporting N0 status, and no distant metastasis being suggested by the available examinations, supporting M0 status. The patient had an uneventful postoperative recovery and was discharged on postoperative day 7 without complications.

The subsequent treatment plan included lifelong oral endocrine suppressive therapy with levothyroxine (50 μg daily, taken in the morning on an empty stomach), along with dynamic follow-up of thyroid function and cervical ultrasonography.

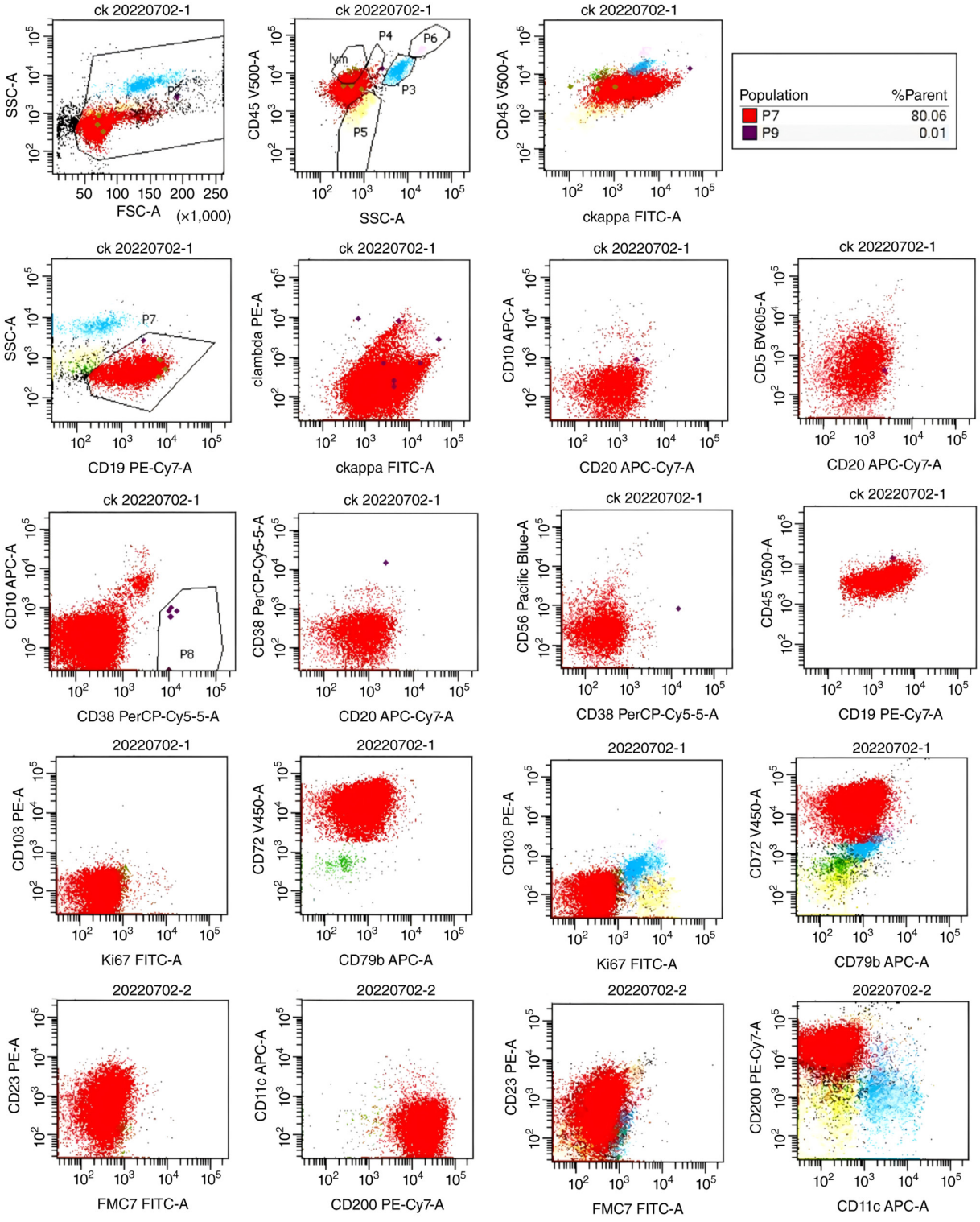

Figure 2. Peripheral blood flow cytometry analysis. In total, ~80.06% abnormal mature B lymphocytes were identified, showing κ light chain restriction. The immunophenotypic profile was characterized by positivity for CD5 and CD19, partial expression of CD20, CD22 and CD23, positivity for CD200, and negativity for CD10 and FMC7.

Given the indolent course of CLL and the absence of treatment indications, a watch-and-wait strategy was adopted in consultation with the hematology team.

At a 2-year postoperative follow-up in November 2025, the patient remained asymptomatic. The thyroid function test results were as follows: T3, 1.09 nmol/l; T4, 207.50 nmol/l; FT3, 4.06 pmol/l; FT4, 23.95 pmol/l; and TSH, 6.107 μIU/ml. Compared with the baseline values, T3 was lower, T4 and FT4 were higher, FT3 remained within the reference range and TSH remained mildly elevated. Follow-up cervical CT showed no thyroid-bed lesion after the thyroidectomy. Multiple soft-tissue nodules in the bilateral cervical, supraclavicular/infraclavicular and mediastinal regions were considered to be lymphoma-related lymphadenopathy in the context of known

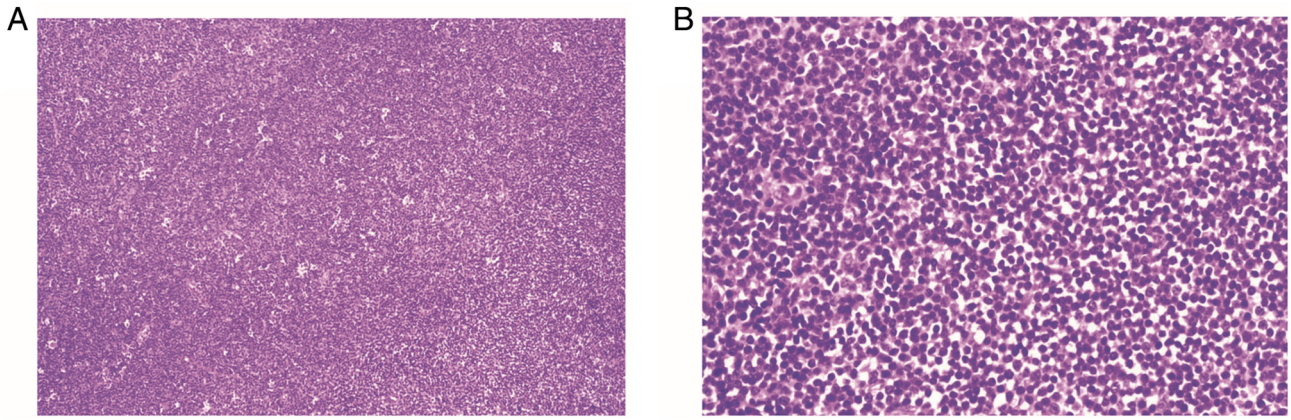

Figure 3. Fine-needle aspiration findings of the left supraclavicular lymph node. (A) Hematoxylin and eosin-stained section showing diffuse lymphoid cell proliferation (x100 magnification). (B) High-power view showing predominantly small lymphoid cells (x400 magnification).

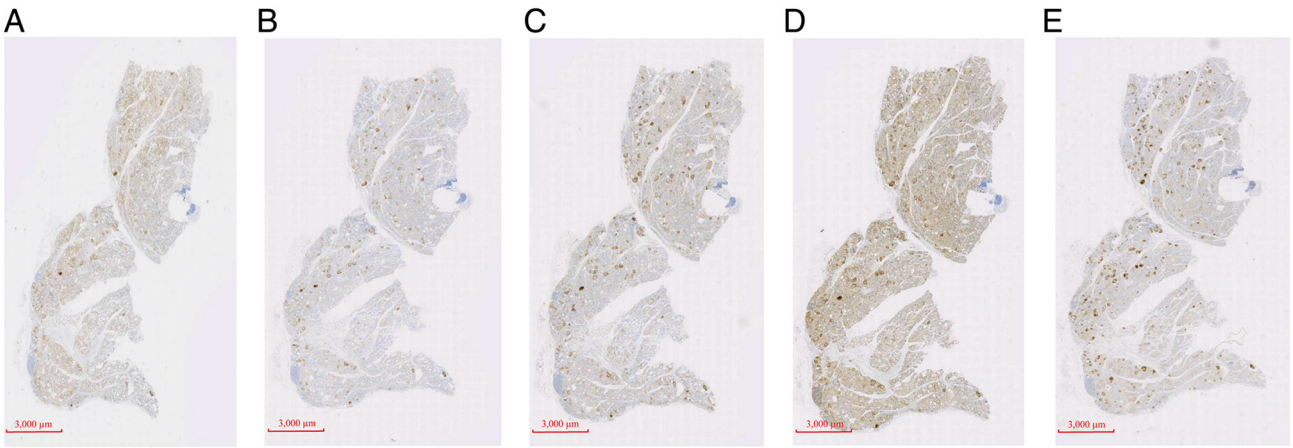

Figure 4. Immunohistochemical staining of the thyroid nodule confirming papillary thyroid carcinoma. (A) Cytokeratin 19 shows strong cytoplasmic and membranous positivity. (B) Galectin-3 demonstrates diffuse positivity. (C) Hector Battifora mesothelial-1 shows positive membranous staining. (D) CD56 expression is absent in the tumor cells; the apparent brown staining in the whole-section scanned image is mainly located in non-tumor thyroid tissue/background areas. (E) The Ki-67 proliferation index is ~3%. All panels are whole-section scanned images; conventional microscopic magnification is not applicable. Scale bars, 3,000 μm.

CLL/SLL. The patient was followed every 3 months during the first postoperative year and every 6 months during the second postoperative year, and remains under regular hematology follow-up.

Discussion

PTC originates from the thyroid follicular epithelium and is the most common and well-differentiated thyroid malignancy, accounting for ~85% all thyroid cancer cases (4,13). Over the past decade, the incidence of PTC has risen markedly with advances in diagnostic techniques. PTC predominantly affects middle-aged women, and the disease typically follows an indolent course (4). The typical histopathological features include complex papillary structures and the characteristic ground-glass ('Orphan Annie-eye') nuclear appearance (3). FNA cytology under ultrasound guidance remains the cornerstone of preoperative diagnosis, providing high accuracy in identifying PTC (14). Immunohistochemistry serves as an adjunct in difficult cases, with PTC tumor cells frequently expressing thyroid-specific markers [such as thyroid transcription factor-1 and thyroglobulin (Tg)] and CKs (CK19, HBME-1 and galectin-3) (3,15). CLL, by contrast, is an indolent hematological malignancy that is characterized by the clonal proliferation of mature B lymphocytes, which represents the most common form of leukemia in adults (16). CLL primarily occurs in middle-aged and elderly individuals and is typically identified through peripheral blood lymphocytosis and generalized painless lymphadenopathy. Bone marrow biopsy and immunophenotyping are critical for achieving a definitive diagnosis (17,18). The typical immunophenotypic profile of CLL includes positivity for CD5, CD19 and CD23 (19,20). Overall, PTC is confined to the thyroid gland, progresses relatively slowly and carries a favorable prognosis. By contrast, CLL has a protracted clinical course, with long-term remission possible but a cure remaining elusive.

The simultaneous occurrence of PTC and CLL in the same patient is exceedingly rare, with only sporadic case reports documented in the literature (7,8). Such 'dual primary' malignancies have been described almost exclusively in isolated cases and small case series, with an estimated incidence of ~0.04%. In a large cohort study of 17,196 patients with PTC, only 0.04% were found to have a concomitant

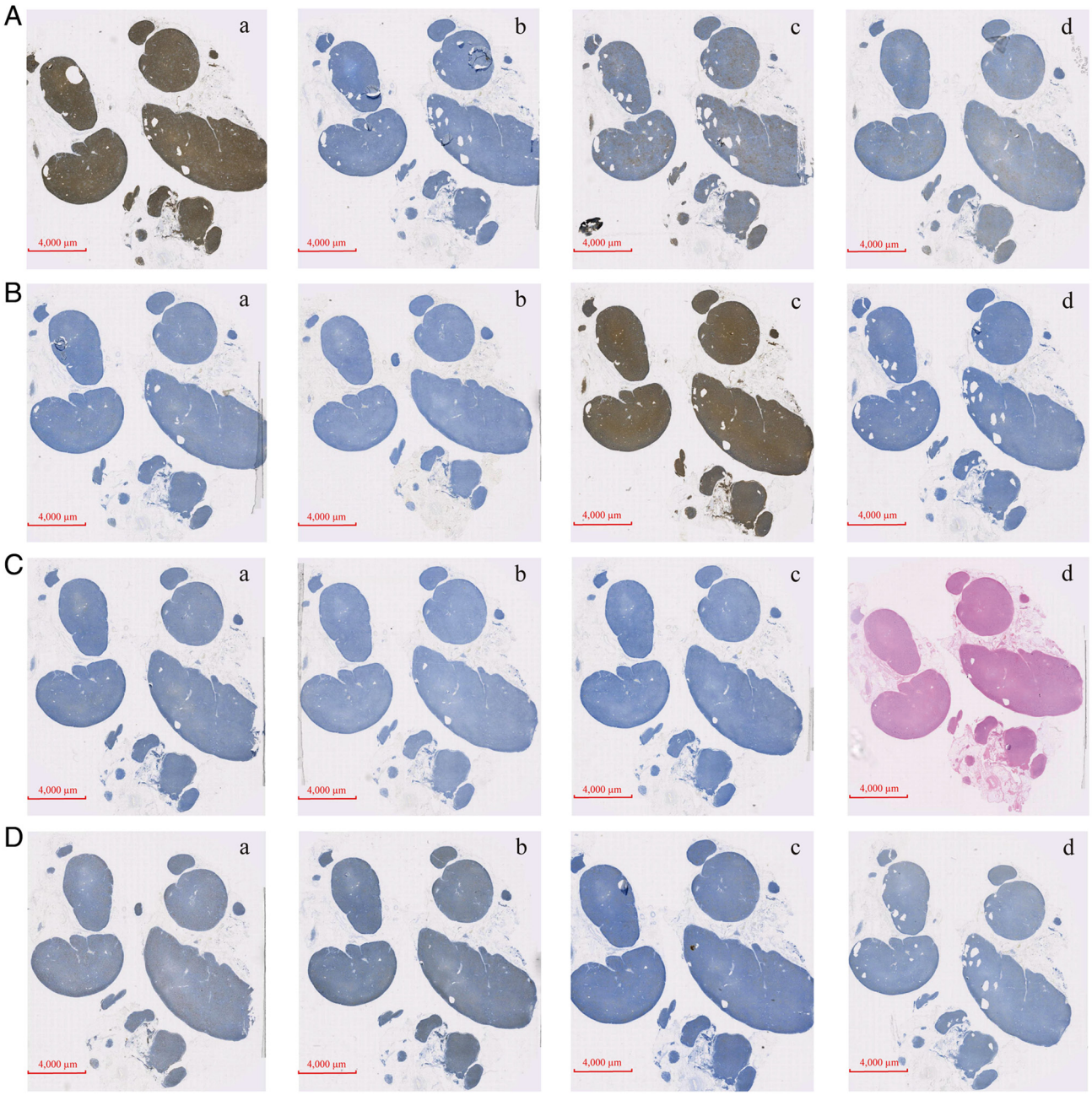

Figure 5. Fine-needle aspiration biopsy of the right supraclavicular lymph node suggesting an indolent lymphoma of small B-cell origin. Immunohistochemical staining demonstrated the following results: (A-a) CD79a (positive), (A-b) BCL-6 (negative), (A-c) CD2 (negative) and (A-d) CD3 (negative). (B-a) CD5 (partial positive), (B-b) CD10 (negative), (B-c) CD20 (positive) and (B-d) CD21 (negative). (C-a) CD23 (weak positive), (C-b) CD30 (negative), (C-c) Cyclin D1 (negative) and (C-d) Epstein-Barr Virus-encoded small RNA (negative). (D-a) Ki-67 (~20% positive), (D-b) lymphoid enhancer-binding factor 1 (focal positive), (D-c) multiple myeloma oncogene-1 (focal positive) and (D-d) c-Myc (negative). All panels are whole-section scanned images; conventional microscopic magnification is not applicable. Scale bars, 4,000 μm.

indolent B-cell lymphoma, underscoring its rarity (21). The coexistence of PTC and CLL may not be entirely coincidental. CLL-associated immune dysregulation provides a biologically plausible, although unproven, explanation for the development of a second primary solid tumor. CLL is accompanied by abnormalities across both humoral and cellular immune compartments, where patients with CLL have an increased risk of 'secondary' primary malignancies compared with the general healthy population (22). The most frequently reported secondary cancers in this context include cutaneous malignancies, other lymphoid neoplasms and various solid tumors, such as lung and bronchus cancer, colorectal cancer, kidney cancer, thyroid cancer and soft-tissue sarcoma. Notably, the relative risk of thyroid cancer among patients with CLL has been reported to be nearly 3 times greater compared with that in the general population (23). In a previous cohort study of 2,028 untreated patients with CLL, 11.2% developed a subsequent malignancy during follow-up, with the overall risk of secondary cancer being 2.2 times higher compared with that observed in the general population (24). These epidemiological observations support the concept that CLL-related immune failure may create a permissive host environment for the

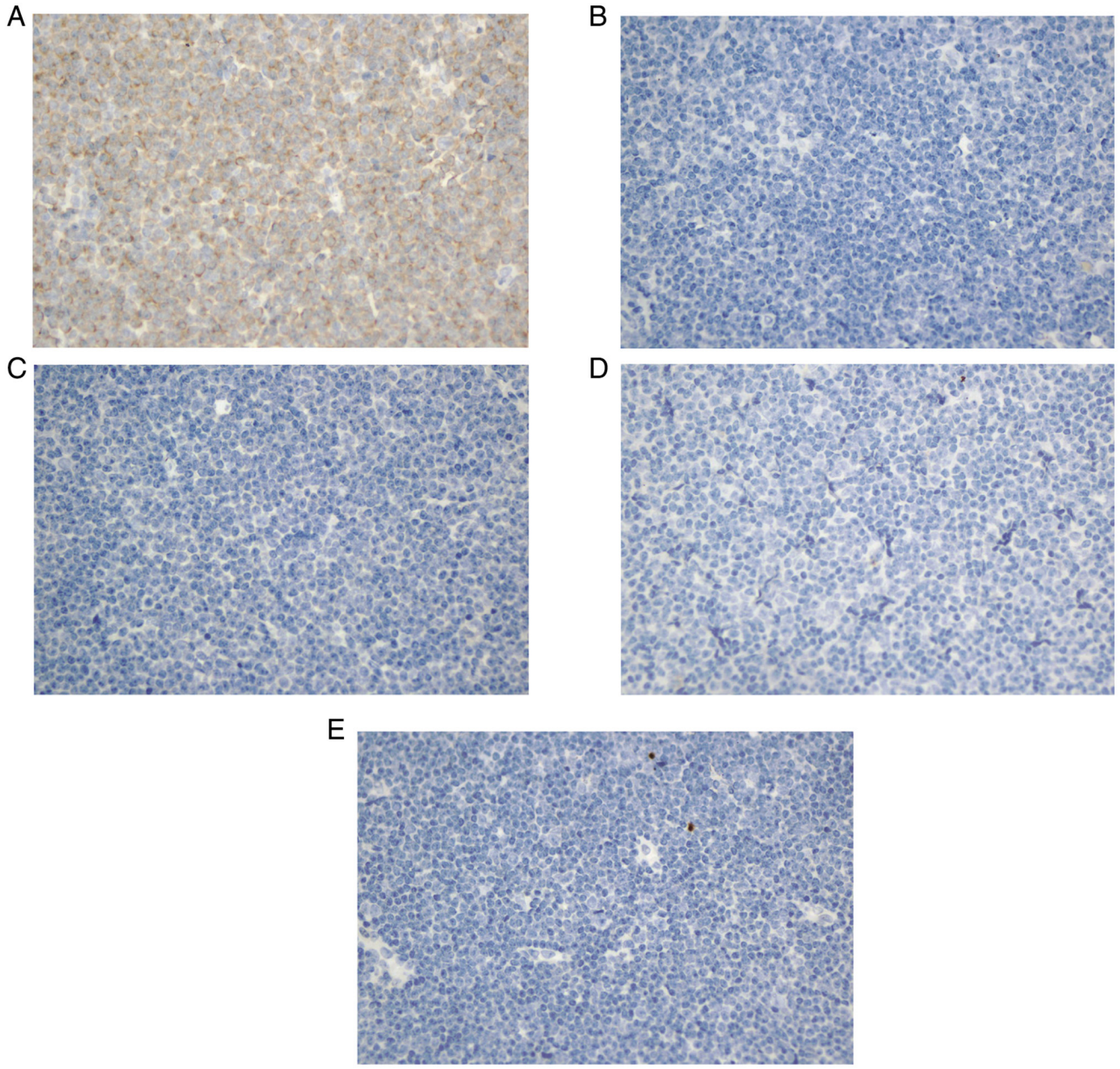

Figure 6. Additional immunohistochemical findings of the right supraclavicular lymph node. (A) BCL-2-positive staining. (B) SOX11-negative staining. (C) Anaplastic lymphoma kinase-negative staining. (D) Myeloperoxidase-negative staining. (E) Terminal deoxynucleotidyl transferase-negative staining. Original magnification, x400.

emergence such 'secondary' primary solid tumors, including PTC. Genetic predisposition may also serve a contributory role. Certain molecular alterations have been implicated in both diseases. The deleted in lymphocytic leukemia 1 gene, frequently deleted or downregulated in CLL, has been found to be upregulated in PTC, where it promotes thyroid cancer cell proliferation and invasion by sponging specific microRNAs (25). This raises the possibility that shared genetic or epigenetic alterations may contribute to the pathogenesis of coexisting PTC and CLL. Nevertheless, no definitive common pathogenic mutations have been established to date. Therefore, the concurrence of PTC and CLL is considered to be an opportunistic comorbidity arising from multiple contributing factors rather than a direct causal relationship (22,23).

In the present case, no recognized exogenous carcinogenic exposure was identified from the residential, occupational or lifestyle history of the patient, including ionizing radiation, radioactive materials, hazardous chemicals, smoking, alcohol consumption or known chronic infectious disease. Therefore, the coexistence of PTC and long-standing CLL is unlikely to be explained by a single environmental exposure. A more plausible interpretation is that the dual malignancies arose through a multifactorial process in which CLL-associated immune dysregulation may have lowered antitumor immune surveillance and facilitated the emergence of a second primary solid tumor. Beyond its identity as a clonal mature B-cell neoplasm, CLL is increasingly recognized as a systemic immune-disruptive disease, characterized by impaired humoral immunity, dysfunctional T-cell and natural killer-cell responses, altered antigen presentation, upregulated immune-checkpoint signaling and a tolerogenic tumor microenvironment (23,26). Recent reviews have further emphasized

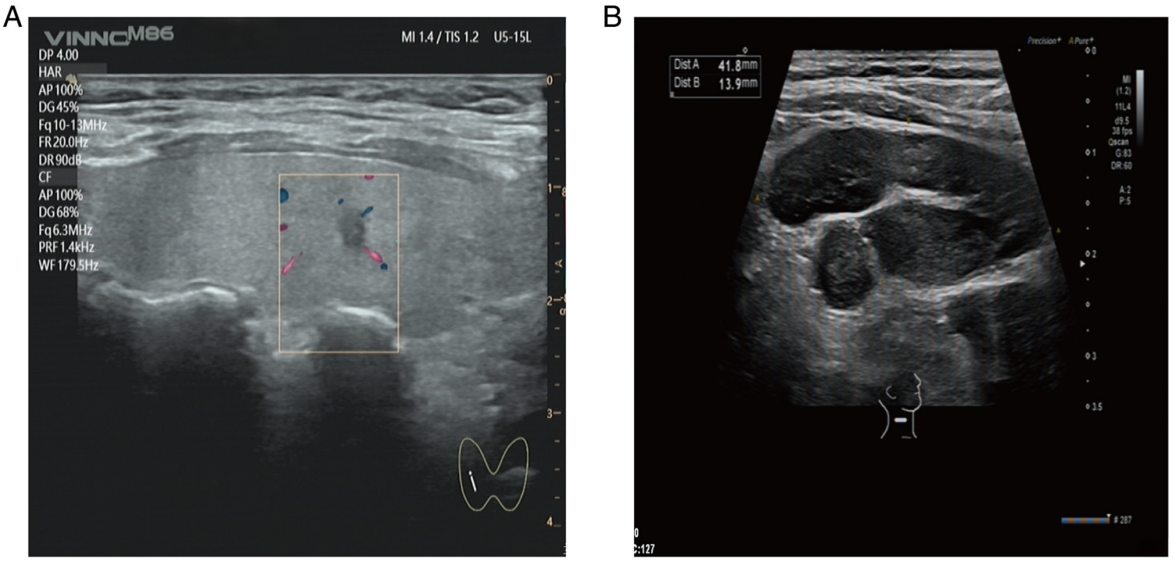

Figure 7. Neck ultrasonography. (A) Hypoechoic thyroid nodule in the right lobe (Thyroid Imaging Reporting and Data System 4a). (B) Enlarged cervical lymph node, with the largest node measuring ~3.1x1.0 cm on the right side and 1.5x1.0 cm on the left side.

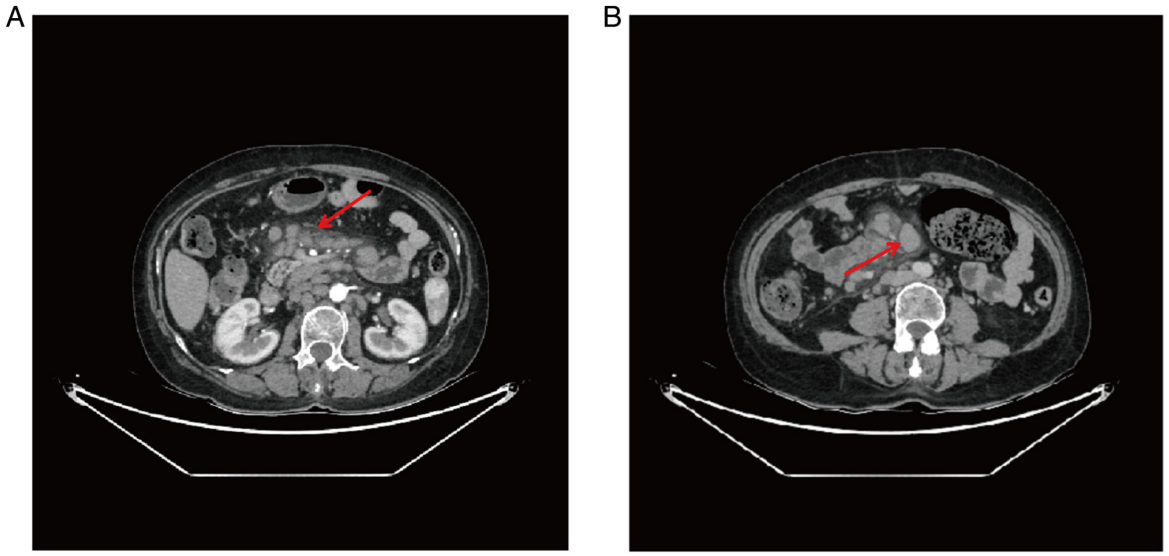

Figure 8. Contrast-enhanced abdominal computed tomography showing multiple enlarged lymph nodes in the abdominal and pelvic cavities (red arrows). (A) Enlarged lymph nodes in the upper abdominal region. (B) Enlarged lymph nodes in the pelvic cavity. The largest node measured ~4.7x2.4 cm and demonstrated mild enhancement.

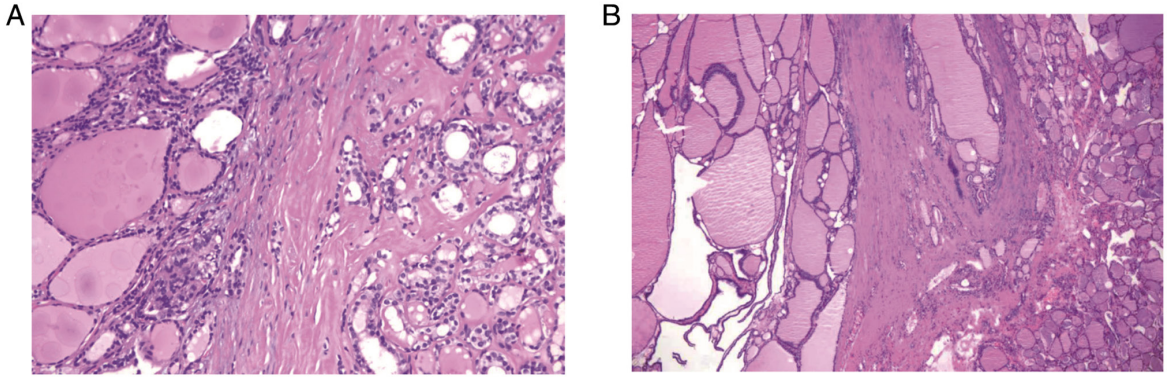

Figure 9. Postoperative histopathological findings of the thyroid gland. (A) Hematoxylin and eosin-stained section showing micropapillary carcinoma of the right lobe and isthmus, accompanied by nodular goiter (magnification, x200). (B) Hematoxylin and eosin-stained section showing nodular goiter with adenomatoid hyperplasia in the left lobe (x100 original magnification).

Table I. Timeline of patient clinical course.

Date/interval	Event/clinical findings	Diagnostic assessment	Intervention/ management	Outcome/ follow-up
~7 years prior to admission	History of CLL treated with traditional Chinese medicine	-	Symptomatic management	Stable disease
Several months prior to admission	Cervical lymphadenopathy, thyroid nodule detected	Physical exam, ultrasound	-	Suspicion of synchronous malignancy
Work-up phase	Enlarged cervical/axillary/ inguinal lymph nodes	Flow cytometry, immuno-histochemistry, radiology	-	Diagnosis of PTC + CLL
Surgery (index admission)	Thyroidectomy performed	Histopathology confirmed PTC (pT1aN0M0)	Surgery + initiation of levothyroxine (50 μg daily)	Successful recovery
2-year follow-up	Regular imaging and labs	Ultrasound, thyroglobulin tests	-	No recurrence, disease-free

PTC, papillary thyroid carcinoma; CLL, chronic lymphocytic leukemia.

that immune dysfunction in CLL is persistent and clinically relevant, affecting not only infection susceptibility but also immune surveillance, immune-cell cross-talk and the broader risk of secondary malignancies (26,27). Together, these immune defects may impair antitumor surveillance and reduce host capacity to eliminate transformed epithelial cells, thereby creating a permissive milieu for secondary malignancies, including solid tumors, such as PTC.

Nevertheless, a direct causal relationship between CLL and PTC cannot be proven from a single case. The development of dual primary malignancies in the present patient is best interpreted as the result of interacting factors, including age-related accumulation of oncogenic alterations, sex-related susceptibility to PTC, possible genetic or epigenetic predisposition and CLL-related impairment of immune surveillance. Therefore, rather than representing metastatic spread or a single unifying pathogenic pathway, the present case likely reflects the biologically plausible coexistence of two independent primary malignancies in the setting of long-standing immune dysregulation. This interpretation also underscores the need for the careful evaluation of new solid lesions in patients with CLL, even when the hematological disease appears clinically indolent. A recent 2026 case of synchronous PTC and CLL presenting with cervical lymphadenopathy similarly emphasized that lymph node enlargement in patients with thyroid nodules may reflect hematological disease rather than metastatic thyroid carcinoma, whereby definitive histopathological and immunohistochemical assessment is essential for appropriate management (10).

The coexistence of thyroid carcinoma and hematological malignancy presents substantial diagnostic challenges. In the present case, the thyroid nodule was accompanied by widespread lymphadenopathy, a presentation that could easily suggest thyroid carcinoma with regional lymph node metastasis. However, further investigations revealed that the enlarged lymph nodes were not metastatic PTC but rather the result of CLL involvement. Lymphocytic infiltration is frequently observed in PTC tissue, particularly in association with Hashimoto's thyroiditis (28,29). By contrast, infiltration of the thyroid gland by CLL may closely mimic autoimmune lymphocytic infiltration under microscopy, making histological differentiation difficult (30). Therefore, in cases of thyroid carcinoma with dense monomorphic lymphocytic infiltration, clinicians should maintain a high index of suspicion for concomitant lymphoproliferative disorders, such as CLL. Immunohistochemistry and flow cytometry are indispensable adjuncts for establishing the correct lineage and avoiding diagnostic misclassification. Detection of monoclonal B-cell populations (such as clones co-expressing CD5, CD19 and CD23) by flow cytometry strongly supports the diagnosis of CLL (7,16). Histopathologically, immunohistochemistry enables separation of the two tumor components. In particular, PTC cells express epithelial and thyroid-related markers, whereas infiltrating lymphocytes express B-cell and CLL-associated markers (such as CD20, CD5 and CD23) but lack T-cell and germinal center markers. A recent report described the case of a patient with preexisting indolent SLL who developed suspicious cervical lymphadenopathy after thyroidectomy for PTC. FNA yielded only CLL-like lymphocytes, yet the aspirate demonstrated markedly elevated thyroglobulin levels, raising suspicion for occult PTC metastasis. Subsequent lymph node dissection confirmed the presence of metastatic PTC deposits within CLL-involved lymph nodes (9). This case, reported by Rejeb *et al* (9), highlights the diagnostic complexity of PTC coexisting with CLL, underscoring the need for the integration of tumor markers and when necessary, a repeat biopsy, to avoid misdiagnosis.

In the present case, the combined immunohistochemical and flow-cytometric findings established the thyroid lesion as PTC and the nodal disease as CLL. The distinct histomorphological and immunophenotypic profiles of the two lesions prevented misclassification of CLL-related lymphadenopathy as metastatic PTC and ensured appropriate staging and management. Although active surveillance is recognized in

several international guidelines as a reasonable option for carefully selected patients with low-risk papillary thyroid microcarcinoma, management in the present case was individualized and was not dictated by tumor size alone (31-33). Recent reviews continue to support active surveillance as a safe and increasingly accepted option for carefully selected low-risk PTC, but also emphasize that eligibility depends on reliable imaging, the absence of suspicious nodal disease, patient preference and the feasibility of structured follow-up (34-36). According to Recommendation 42 of the Chinese Guidelines for the Diagnosis and Treatment of Thyroid Nodules and Differentiated Thyroid Cancer (Second Edition, 2023), thyroid lobectomy with isthmusectomy is strongly recommended, with moderate-quality evidence, for differentiated thyroid cancer lesions measuring <1 cm in the absence of high-risk features. Therefore, surgery represented a guideline-concordant management option rather than a departure from accepted care (37).

Crucially, the present case was not a straightforward case of an isolated, incidentally detected PTC. The patient had a 7-year history of CLL and presented with persistent, generalized lymphadenopathy involving the cervical, axillary, mediastinal, abdominal, pelvic and inguinal regions. In such a setting, preoperative risk stratification was particularly challenging, as enlarged lymph nodes could represent CLL involvement, occult PTC metastasis or coexistence of both processes within the same nodal basin. Although preoperative cytology and flow cytometry favored CLL-related nodal involvement, they could not fully exclude occult metastatic PTC, particularly in the setting of extensive cervical lymphadenopathy. Surgical resection with a central compartment lymph node dissection therefore provided definitive histopathological staging, excluded occult nodal metastasis in the dissected nodal basin and informed subsequent surveillance intensity.

In addition, patient preference was an important ethical and clinical consideration. The diagnosis of concurrent malignancies imposed a substantial psychological burden and the patient consistently expressed a strong preference for definitive surgical treatment rather than prolonged observation. After shared decision-making and multidisciplinary discussion involving the thyroid surgery and hematology teams, this patient-centered approach also enabled definitive pathological staging and remained consistent with the patient's informed values and psychological needs.

The prognosis of patients with concomitant PTC and CLL depends on the stage and biological behavior of each malignancy, in addition to the effectiveness of treatment (4). Overall, early-stage PTC, with papillary microcarcinoma as a representative subtype, is associated with a highly favorable prognosis. Papillary thyroid microcarcinoma (≤1 cm) has an exceptionally low mortality rate and >90% 10-year survival rate (38). CLL is an indolent lymphoma that can also have a prolonged natural history. Low-risk patients may survive for years with observation alone already sufficient (16). In the present case, the 64-year-old patient had a 0.3-cm papillary carcinoma with no lymph node metastases (stage pT1aN0M0) and was considered clinically cured following surgery. This specific CLL, which was diagnosed 7 years earlier, remained in a stable early stage, where no disease progression was observed during the 2-year follow-up. The patient has since maintained a good quality of life without additional therapy for CLL. However, the prognosis in similar cases may vary depending on tumor burden and pathological subtype of PTC. Sezer *et al* (8) reported the case of a patient with PTC who had local invasion and distant metastases alongside CLL and succumbed within 1 year postoperatively. In addition, in CLL, late-stage complications, such as Richter's transformation, which refers to the progression of CLL into aggressive diffuse large B-cell lymphoma, can markedly shorten survival time (39). These considerations highlight the necessity of comprehensive surveillance.

As a result of the present case, a multidisciplinary, long-term follow-up strategy is recommended. For the monitoring of thyroid carcinoma recurrence and metastasis, postoperative surveillance should include the periodic measurement of serum Tg and anti-Tg antibodies, in addition to high-resolution neck ultrasonography at least every 6-12 months. In patients who have undergone a total thyroidectomy, any unexplained rise in Tg or suspicious imaging findings should prompt further imaging (such as whole-body positron emission tomography-CT or iodine scans) to localize potential recurrent or metastatic disease (3,40). For the monitoring of hematological disease progression, in stable CLL, hematological evaluation with blood counts and relevant chemistries is recommended every 3 months. Key parameters include lymphocyte doubling time, cytopenias and constitutional symptoms, such as night sweats or weight loss. Early-stage asymptomatic disease is generally managed with observation, whilst rapid lymphocyte escalation, progressive lymphadenopathy or splenomegaly, or bone marrow failure warrant treatment initiation.

In summary, patients with concomitant PTC and CLL require sustained, multidisciplinary follow-up. Surveillance must focus not only on detecting the recurrence of thyroid carcinoma but also on monitoring the evolution of leukemia. With individualized follow-up plans and proactive management strategies, the majority of patients with this rare dual malignancy can achieve a good quality of life and prolonged survival time.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

JM contributed to image acquisition and drafting of the manuscript. TG analyzed patient data and contributed to the revision of the manuscript. SX performed histopathological image acquisition and assisted in manuscript drafting. HT

contributed to data interpretation and critical revision of the manuscript. AS contributed to the conception and design of the study, interpretation of the clinical data, and critical revision of the manuscript. LZ contributed to the conception and design of the study, interpretation of the clinical and pathological data, and critical revision of the manuscript. JM, TG and SX confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was reviewed and approved by the Institutional Medical Ethics Committee of the Second Hospital of Lanzhou University (approval no. 2025A-951). All procedures were performed in accordance with the Declaration of Helsinki and relevant guidelines and regulations.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the present study and associated images.

Competing interests

The authors declare that they have no competing interests.

References

1. Han Y, Hou L, Zhao B, Gao L and Li S: Risk factors for neck nodal metastasis in papillary thyroid cancer with BRAF V600E mutation. Front Endocrinol (Lausanne) 13: 884428, 2022.
2. Kitahara CM and Schneider AB: Epidemiology of thyroid cancer. Cancer Epidemiol Biomarkers Prev 31: 1284-1297, 2022.
3. Limaiem F, Rehman A and Mazzoni T: Papillary Thyroid Carcinoma. In: StatPearls (Internet). StatPearls Publishing, Treasure Island, FL, 2025.
4. Boucai L, Zafereo M and Cabanillas ME: Thyroid cancer: A review. JAMA 331: 425-435, 2024.
5. Yu K, Wu X, Dai L, Le Q, Xie Y, Wang Y and Zhang W: Risk factors associated with lymph node metastasis in papillary thyroid cancer: A retrospective analysis based on 2,428 cases. Front Oncol 14: 1473858, 2024.
6. Reid-Nicholson M, Moreira A and Ramalingam P: Cytologic features of mixed papillary carcinoma and chronic lymphocytic leukemia/small lymphocytic lymphoma of the thyroid gland. Diagn Cytopathol 36: 813-817, 2008.
7. Ahmed OI and Salih ZT: Dual malignancy in a thyroid; papillary thyroid carcinoma and small lymphocytic lymphoma; a report of a case with a cyto-histologic correlation. Diagn Cytopathol 45: 851-856, 2017.
8. Sezer H, Yazici D, Tezelman S, Demirkol MO, Ünal OF, Dilege S, Taşkın OC, Peker O, Kapran Y, Çolakoğlu B, *et al*: Concomittant occurence of well-differentiated thyroid carcinoma metastasis and chronic lymphocytic leukemia in the same lymph node along with internal jugular vein thrombus: A case report. Indian J Pathol Microbiol 64: 149-151, 2021.
9. Rejeb S, Sakly S, Hachicha A, Dridi K and Turki S: Synchronous cervical lymph node involvement with a papillary thyroid carcinoma and small lymphocytic lymphoma: A case report. J Surg Case Rep 2025: rjaf038, 2025.
10. Farnin R, Altindag H, Lienenluke R, Hammer A, Gebrehiwot L, Engler J, Mittermeier J and Vorländer C: Synchronous papillary thyroid microcarcinoma and chronic lymphocytic leukemia: A rare interdisciplinary case. Cureus 18: e107194, 2026.
11. Zhou J, Yin L, Wei X, Zhang S, Song Y, Luo B, Li J, Qian L, Cui LG, Chen W, *et al*: 2020 Chinese guidelines for ultrasound malignancy risk stratification of thyroid nodules: The C-TIRADS. Endocrine 70: 256-279, 2020.
12. Tuttle RM, Haugen B and Perrier ND: Updated American joint committee on cancer/tumor-node-metastasis staging system for differentiated and anaplastic thyroid cancer (Eighth Edition): What changed and why? Thyroid 27: 751-756, 2017.
13. Hao Z, Cui H, Li Y, Wu W, Wang Y, Dan H, Lou L, Wang H and Zhao P: Simultaneous occurrence of papillary thyroid carcinoma, medullary thyroid carcinoma, and lymphoma: A case report. Medicine (Baltimore) 103: e39363, 2024.
14. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, *et al*: 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 26: 1-133, 2016.
15. Laishram H, Jagadale K, Shelke P and Bharadwaj R: Cross-sectional study to determine the diagnostic accuracy of cytokeratin-19 immunomarker in the diagnosis of thyroid malignancy with histopathology as gold standard. Niger Postgrad Med J 32: 61-67, 2025.
16. Mukkamalla SKR, Taneja A, Malipeddi D and Master SR: Chronic lymphocytic leukemia. In: StatPearls (Internet). StatPearls Publishing, Treasure Island, FL, 2025.
17. Rawstron AC, Fazi C, Agathangelidis A, Villamor N, Letestu R, Nomdedeu J, Palacio C, Stehlikova O, Kreuzer KA, Liptrot S, *et al*: A complementary role of multiparameter flow cytometry and high-throughput sequencing for minimal residual disease detection in chronic lymphocytic leukemia: an European Research Initiative on CLL study. Leukemia 30: 929-936, 2016.
18. Rawstron AC, Kreuzer KA, Soosapilla A, Spacek M, Stehlikova O, Gambell P, McIver-Brown N, Villamor N, Psarra K, Arroz M, *et al*: Reproducible diagnosis of chronic lymphocytic leukemia by flow cytometry: An European research initiative on CLL (ERIC) & European society for clinical cell analysis (ESCCA) Harmonisation project. Cytometry B Clin Cytom 94: 121-128, 2018.
19. Hallek M, Shanafelt TD and Eichhorst B: Chronic lymphocytic leukaemia. Lancet 391: 1524-1537, 2018.
20. Rasul KH, Wsoo MA, Hassan DH, HamadaminSK and Qadr ZJ: Immunophenotypic properties association of CLL and ALL patient cells by flow cytometry analysis. J Taibah Univ Med Sci 19: 981-989, 2024.
21. Zhang Y, Song Y, Cheng R and Zhai Q: Concurrent papillary thyroid carcinoma and incidental cervical lymph node indolent B cell non-Hodgkin lymphoma: Clinicopathological features, outcomes, and potential relationships. World J Surg Oncol 23: 145, 2025.
22. van der Straten L, Levin MD, Dinnessen MAW, Visser O, Posthuma EFM, Doorduijn JK, Langerak AW, Kater AP and Dinmohamed AG: Risk of second primary malignancies in patients with chronic lymphocytic leukemia: A population-based study in the Netherlands, 1989-2019. Blood Cancer J 13: 15, 2023.
23. Sayin S, Kiliacslan E, Yildirim M, Ozturk HBA, Yilmaz ES, Albayrak M, Kaptan MK and Ayli M: Evaluation of second primary cancer risk among chronic lymphocytic leukemia patients: Multicenter study. Asian Pac J Cancer Prev 24: 1971-1977, 2023.
24. Xiong YY, Liu ZJ, Chen L, Yuan FF, Yin QS, Mi RH, Zhang B, Du JW, Zhang QL, Lin QD, *et al*: Synchronous lymphoma and carcinoma-clinical analyses of 17 patients. Zhonghua Xue Ye Xue Za Zhi 39: 277-280, 2018 (In Chinese).
25. Li R, Wan T, Qu J, Yu Y and Zheng R: Long non-coding RNA DLEUI promotes papillary thyroid carcinoma progression by sponging miR-421 and increasing ROCK1 expression. Aging 12: 20127-20138, 2020.
26. Narkhede M and Ujjani CS: Immune dysfunction and consequences in chronic lymphocytic leukemia. J Natl Compr Canc Netw 23: e247090, 2025.
27. Juarez-Salcedo LM and Loscertales J: Clinical implications of immune dysfunction in chronic lymphocytic leukemia. Cancers (Basel) 18: 1323, 2026.
28. Yao S and Zhang H: Papillary thyroid carcinoma with Hashimoto's thyroiditis: Impact and correlation. Front Endocrinol (Lausanne) 16: 1512417, 2025.
29. Monabbati S, Fu P, Asa SL, Pathak T, Willis JE, Shi Q and Madabhushi A: Machine vision-detected peritumoral lymphocytic aggregates are associated with disease-free survival in patients with papillary thyroid carcinoma. Lab Invest 104: 102168, 2024.
30. Vurgun NA, Yalcin N, Turk NS, Fenkci SM and Çağlıyan GA: Thyroid infiltration by chronic lymphocytic leukemia: A rare case report with cytological and flow cytometry findings. Diagn Cytopathol 53: E133-E137, 2025.

31. Sawka AM, Ghai S, Rotstein L, Irish JC, Pasternak J, Monteiro E, Chung J, Su J, Xu W, Esemezie AO, *et al*: Long-term durability of active surveillance of small, low-risk papillary thyroid cancer. JAMA Surg 160: 1117-1124, 2025.
32. Kim MJ, Moon JH, Lee EK, Song YS, Jung KY, Ji Ye Lee JY, Kim JH, Kim K, Park SK and Park YJ: Active surveillance for low-risk thyroid cancers: A review of current practice guidelines. Endocrinol Metab (Seoul) 39: 47-60, 2024.
33. Lee EK, Kim MJ, Kang SH, Koo BS, Kim K, Kim M, Kim BH, Kim JH, Moon S, Back K, *et al*: 2025 Korean thyroid association clinical management guideline on active surveillance for low-risk papillary thyroid carcinoma. Endocrinol Metab (Seoul) 40: 307-341, 2025.
34. Wu Z, Zhang K, Zhou H, Wan L, Zhong J, Li C, Gong L and Peng Y: Active surveillance for low-risk papillary thyroid carcinoma: Integrating guidelines, emerging evidence, and directions. iScience 29: 115832, 2026.
35. Lee JY, Lee MK, Lim HK, Lee CY, Sung JY, Yoon JH, Hahn SY, Shin JH, Kim JH, Jung SL, *et al*: Standardized ultrasound evaluation for active surveillance of low-risk thyroid microcarcinoma in adults: 2024 Korean society of thyroid radiology consensus statement. Korean J Radiol 25: 942-958, 2024.
36. Nguyen VC, Song CM, Ji YB, Moon S, Park JH, Kim DS and Tae K: Outcomes and effectiveness of active surveillance for low-risk papillary thyroid carcinoma: A systematic review and meta-analysis. Eur Arch Otorhinolaryngol 282: 2239-2252, 2025.
37. Chinese Medical Association Endocrinology Society, Subspecialty Group of Thyroid and Metabolic Surgery of Chinese Medical Association Surgery Society, Head and Neck Cancer Specialized Committee of China Anti-Cancer Association. Guidelines for the Diagnosis and Treatment of Thyroid Nodules and Differentiated Thyroid Cancer (Second Edition). Chin J Endocrinol Metab 39: 181-226, 2023 (In Chinese).
38. Lan Y, Luo Y, Zhang M, Jin Z, Xiao J, Yan L and Zhu Y : Quality of life in papillary thyroid microcarcinoma patients undergoing radiofrequency ablation or surgery: A comparative study. Front Endocrinol (Lausanne) 11: 249, 2020.
39. Shen Y, Coyle L, Kerridge I, Stevenson W, Arthur C, McKinlay N, Fay K, Ward C, Greenwood M, Best O, *et al*: Second primary malignancies in chronic lymphocytic leukaemia: Skin, solid organ, haematological and Richter's syndrome. EJHaem 3: 129-138, 2022.
40. Filetti S, Durante C, Hartl D, Leboulleux S, Locati LD, Newbold K, Papotti MG and Berruti A; ESMO Guidelines Committee: Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann Oncol 30: 1856-1883, 2019.