

Small Lymphocytic Lymphoma of the Thyroid Mimicking Plasmacytoma

Meenu Gill^a Ashima Batra^a Ashok Sangwaiya^a Samta Shakya^b
Sumiti Gupta^a Rajeev Sen^a

^aDepartment of Pathology, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak, and

^bGeneral Hospital, Sirsa, India

What Is Known about This Topic

- Primary thyroid gland lymphomas (PTLs) are uncommon tumors.
- Small lymphocytic lymphoma (SLL) is the least common type of thyroid lymphomas.
- SLL type of PTL revealing plasmacytic differentiation has never been described.

What Does This Case Report Add

- The differential diagnosis of predominant plasmacytoid cells on thyroid fine-needle aspirates should also include PTL with extensive plasmacytic differentiation, besides plasmacytoma.
- SLL should also be considered in case of PTLs with extreme plasma cell differentiation.
- Further studies are required to assess plasmacytic differentiation in various thyroid lymphomas so as to differentiate them from plasmacytomas, the two entities having a different line of management.

Key Words

Primary thyroid lymphoma · Small lymphocytic lymphoma · Plasmacytoma · Fine-needle aspiration cytology

Abstract

Primary thyroid gland lymphomas (PTLs) typically occur in middle- to older-aged individuals in the setting of lymphocytic thyroiditis with a predilection for females. Diffuse large B-cell lymphoma is the most frequent histologic subtype of thyroid lymphomas. Small lymphocytic lymphoma (SLL) be-

longs to the least common subtypes of thyroid lymphoma. It is often associated with the involvement of lymph nodes, bone marrow, spleen, liver and, extremely rarely, other organs. PTLs with plasmacytic differentiation or extensive infiltration by plasma cells have been observed in marginal zone B-cell lymphomas in the thyroid but have never been described in a setting of SLL. Here, we present a case of primary SLL of the thyroid mimicking extramedullary plasmacytoma on fine-needle aspiration cytology.

© 2014 European Thyroid Association
Published by S. Karger AG, Basel

Introduction

Primary thyroid gland lymphomas (PTLs) are uncommon tumors that have been estimated to represent approximately 5% of all thyroid neoplasms and 2.5–7% of all extranodal lymphomas. Studies have shown that PTLs typically occur in middle- to older-aged women and arise in the setting of autoimmune thyroiditis (lymphocytic thyroiditis, Hashimoto's disease) [1].

The term 'primary' designates patients with lymphomatous involvement of the thyroid at diagnosis, the disease being localized or disseminated to nodal or extranodal sites [2]. Patients present with a mass in the thyroid, usually noticeably enlarging, and commonly have symptoms related to compression of neck structures by the tumor. With radioisotopic ^{131}I scanning, a cold nodule or areas of decreased uptake are common [1].

Lymphoma involving the thyroid gland is rare. Diffuse large B-cell lymphoma (DLBCL) and mucosa-associated lymphoid tissue lymphoma (MALT) are the two most common histologic subtypes of PTL [3]. Small lymphocytic B-cell lymphoma (SLL) is an extremely rare type of thyroid lymphoma (about 4% of cases) [4]. Cervical lymph nodes are the most frequently involved site, followed by a variety of other nodal and extranodal sites, including mediastinal lymph nodes, gastrointestinal tract, bone marrow, lung, bladder, liver, and spleen [1]. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) presenting initially as a thyroid abnormality is extremely rare, with very few reported cases in the literature [3].

Case Report

A 60-year-old postmenopausal female presented with swelling involving the midline of the neck measuring 6 cm in largest dimension for the past 1 month. She also had an enlarged lymph node of 1.5 cm diameter in the left cervical region. She was otherwise asymptomatic and her medical and family histories were unremarkable. There was no history suggestive/documentated evidence of lymphocytic thyroiditis. Routine laboratory tests were normal and hormonal evaluation showed subclinical hypothyroidism (serum thyroid-stimulating hormone (TSH), 12.8 IU/ml (normal range 0.25–5.25 IU/ml); free T_3 and free T_4 were within normal range). Antithyroid antibodies were negative. Thyroid ultrasonography revealed that bilateral thyroid lobes and isthmus were bulky. Normal parenchyma was replaced by heteroechoic areas and vascularity was increased. Retrosternal extension of the mass was also evident.

Cytological examination of thyroid and left cervical lymph node obtained during fine-needle aspiration revealed a similar appearance with a predominant cell population of small- to medium-sized cells revealing paracentral to eccentric nuclei with clock-face chromatin and abundant sky-blue cytoplasm along with few Hurthle cells (fig. 1, 2). There was no evidence of lymphocytic thyroiditis in the smears. A provisional diagnosis of lymphoma/plasmacytoma was made and patient was advised immunoelectrophoretic studies and skeletal imaging for confirmation, however all turned out to be normal.

Subsequently, a biopsy was performed from cervical lymph node. Histopathological and immunohistochemistry findings in the specimen led to the diagnosis of small lymphocytic B-cell lymphoma (SLL CD20+, CD19+, CD5+, CD23+, κ +, λ -) (fig. 3). To confirm thyroid involvement, flow cytometry of the biopsy material sampled from the thyroid was performed showing B-cell immunophenotype with plasma cell differentiation: CD19+/CD20+, CD23+/CD5+, sCD79b+, CD38+, CD10-, κ + and λ -/weak reaction.

Staging procedures including peripheral blood and bone marrow examination, CT scan of thorax, abdomen and pelvis did not

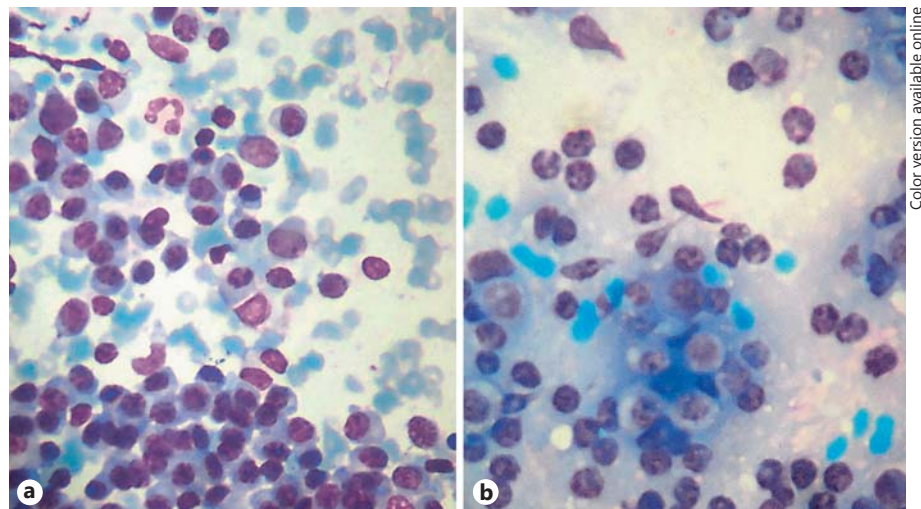


Fig. 1. Fine-needle aspirate of the thyroid (a) and lymph node (b) revealed the presence of cells with plasmacytoid differentiation. Giemsa stain. $\times 400$.

reveal any other involvement. Serum lactate dehydrogenase and β_2 -microglobulin levels were within normal range. The patient was started on chemotherapy according to a COP (cyclophosphamide, vincristine and prednisolone) regimen with good response and is still under follow-up.

Discussion

PTL, with an estimated annual incidence of 2 cases per million, is a rare thyroid malignancy. Almost all cases are of B-cell origin. Thyroid is a rare site of primary extranodal non-Hodgkin's lymphoma. PTL affects middle- to older-aged individuals, predominantly women. The most

common clinical presentation is a rapidly growing neck mass, which is reported in 70% of patients, whereas compression symptoms and signs are present in 30% and B symptoms are reported in 10% of patients. Most patients are diagnosed with stage I disease [5]. Cervical/perithyroidal lymph nodes were the most common nodal sites involved, usually identified at, or shortly after initial surgery, followed by mediastinal and abdominal lymph nodes [1].

The most common histologic subtype is DLBCL. MALT is the second most common subtype, and SLL is one of the rarest [5]. A vast majority of cases of PTL arise in the setting of Hashimoto's thyroiditis. It is estimated that the relative risk of developing a thyroid lymphoma is increased 67- to 80-fold in patients with Hashimoto's thyroiditis [5]. The few cases (<7%) that did not have documented lymphocytic thyroiditis may have been either inadequately sampled or the lymphoma may have completely obliterated any residual thyroid tissue [1].

The initial diagnostic method for thyroid lymphoma should consist of a fine-needle aspiration biopsy with the use of ancillary techniques such as flow cytometry and immunohistochemistry for improved diagnostic accuracy. CLL/SLL is one of the rarest subtypes of lymphoma that can involve the thyroid gland. Diagnosis of this entity is difficult, particularly before the recognition of systemic involvement, requiring the expertise of a multidisciplinary team for early detection and optimal management [3].

Plasma cells and plasmacytic differentiation are common in PTL. The cases previously reported in various studies as extramedullary plasmacytomas of the thyroid

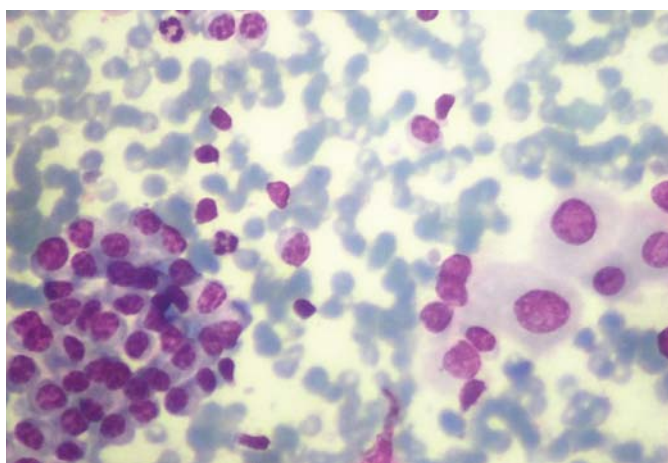


Fig. 2. Fine-needle aspirate of the thyroid revealed the presence of few Hurthle cells along with cells having plasmacytoid differentiation. Giemsa stain. $\times 400$.

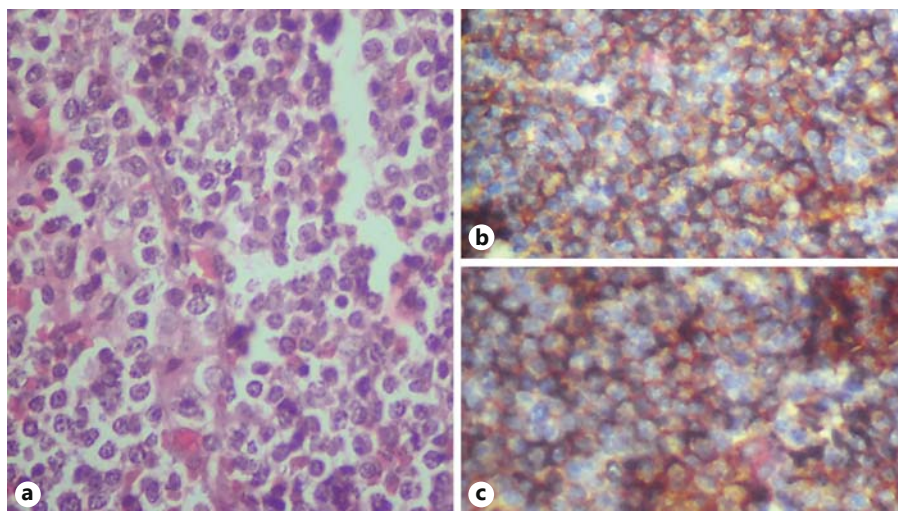


Fig. 3. Photomicrograph showing effacement of the lymph nodes by a monotonous population of small round lymphocytes with clumped chromatin, inconspicuous nucleoli and barely visible cytoplasm (**a**; HE, $\times 400$). These cells stained positive for CD5 (**b**; IHC, $\times 400$) and CD23 (**c**; IHC, $\times 400$).

represented marginal zone B-cell lymphoma (MZBL) with extreme plasma cell differentiation [6–8]. No case of SLL thyroid has so far been described as having plasmacytic differentiation.

Overall, PTLs have a favorable outcome with appropriate therapy, but prognosis depends on both clinical stage and histology. MZBL and stage IE tumors have an excellent prognosis, whereas tumors with a large cell component or DLBCL or stage greater than IE have the greatest potential for a poor outcome [1]. The treatment of primary lymphomas of the thyroid gland, as well as infiltration changes associated with CLL/SLL, remains controversial. The recommended strategy includes chemotherapy, radiotherapy, and in particular cases also surgery and immunochemotherapy with monoclonal antibodies [4].

Conclusion

It should be emphasized that the diagnosis of PTL based on fine-needle aspiration biopsy is not always possible with extensive plasmacytic differentiation posing a major diagnostic problem. SLL should also be considered in case of PTLs with extreme plasma cell differentiation. We report a case of SLL thyroid presenting with extensive plasmacytic differentiation. Further studies are required to assess plasmacytic differentiation in various thyroid lymphomas so as to differentiate them from plasmacytoma – the two entities having a different line of management and prognosis.

Disclosure Statement

The authors declare that no financial or other conflicts of interest exist in relation to the content of the article.

References

- 1 Derringer GA, Thompson LD, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL: Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. *Am J Surg Pathol* 2000;24:623–639.
- 2 Thieblemont C, Mayer A, Dumontet C, Barbier Y, Callet-Bauchu E, Felman P, et al: Primary Thyroid lymphoma is a heterogeneous disease. *J Clin Endocrinol Metab* 2002;87:105–111.
- 3 Shin J, Chute D, Milas M, Mitchell J, Siperstein A, Berber E: A rare case of chronic lymphocytic leukemia/small lymphocytic lymphoma presenting in the thyroid gland. *Thyroid* 2010;20:1019–1023.
- 4 Andrysiak-Mamos E, Becht R, Sowińska-Przepiera E, Pobłocki J, Syrenicz J, Zdziarska B, et al: Case report: rare case of infiltration of small lymphocytic B-cell lymphoma in the thyroid gland of female patient with B-cell chronic lymphocytic leukemia (CLL-B/SLL-B). *Thyroid Res* 2013;6:1.
- 5 Vassilatou E, Economopoulos T, Tzanela M, Rontogianni D, Karakitsos P, Magou C, et al: Coexistence of differentiated thyroid carcinoma with primary thyroid lymphoma in a background of Hashimoto's thyroiditis. *J Clin Oncol* 2011;29:e709–e712.
- 6 Anscombe AM, Wright DH: Primary malignant lymphoma of the thyroid – a tumour of mucosa-associated lymphoid tissue: review of 76 cases. *Histopathology* 1985;9:81–97.
- 7 Hussong JW, Perkins SL, Schnitzer B, Hargreaves H, Frizzera G: Extramedullary plasmacytoma. A form of marginal zone cell lymphoma? *Am J Clin Pathol* 1999;111:111–116.
- 8 Isaacson PG: Lymphoma of the thyroid gland. *Curr Top Pathol* 1997;91:1–14.
- 9 Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M: Report of the Committee on Hodgkin's Disease Staging Classification. *Cancer Res* 1971;31:1860–1861.