Journal of the American Society of Cytopathology (2016) 5, 170–176

Available online at www.sciencedirect.com

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journal homepage: www.jascyto.org/

ORIGINAL ARTICLE

Multi-institutional study of fine-needle aspiration for thyroid lymphoma

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Received 4 August 2015; received in revised form 2 November 2015; accepted 3 November 2015

KEYWORDS
Thyroid lymphoma;
Diffuse large B-cell lymphoma;
Lymphocytic thyroiditis;
Flow cytometry;
MALT lymphoma

Introduction Primary thyroid lymphoma is a rare neoplasm accounting for 1% to 5% of thyroid malignancies. We study the efficacy of fine-needle aspiration (FNA) in diagnosing thyroid lymphoma.
Methods Pathology databases from our three institutions were searched for thyroid FNA biopsies having a diagnosis of lymphoma or atypical lymphoproliferative cells, or a corresponding tissue diagnosis of thyroid lymphoma having a prior FNA biopsy.
Results Sixty-eight cases were retrieved from 64 patients; 67 cases with histologic confirmation. Forty-six specimens were from women (68%), ages 21 to 87 years (mean = 60). Forty-seven aspirates were diagnosed as lymphoma (n = 29) or suspicious (n = 18) for lymphoma (sensitivity = 73%), 11 atypical, 7 benign, 2 unsatisfactory, and 1 suspicious for carcinoma. Follow-up surgical diagnoses included diffuse large B-cell lymphoma (n = 43), classical Hodgkin lymphoma (5), chronic lymphocytic leukemia (5), and other cases (11). Only 12 of 64 patients (13 specimens) had a known diagnosis of lymphoma prior to FNA. Light chain restriction was detected in 34 specimens (by flow cytometry [FCM] in 32 cases or polymerase chain reaction, in 2 cases). FCM was polyclonal (n = 7) or inconclusive (2) with 25 cases not having FCM performed or not having enough viable cells for evaluation. Four cases showed lymphocytic thyroiditis on surgical follow-up with 2 of these cases having a small monoclonal lymphoid population detected by FCM.
Conclusions Diffuse large B-cell lymphoma was the most common lymphoma in this series (63%). The sensitivity of FNA with the optional use of FCM was 71% with a specificity of 99%.

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2213-2945/$36
http://dx.doi.org/10.1016/j.jasc.2015.11.002

Introduction

Primary thyroid gland lymphoma (PTL) is a rare neoplasm that accounts for approximately 5% of all thyroid tumors and 2.5% to 7% of all extranodal lymphomas.[1] Diffuse large B-cell lymphoma (DLBL) account for 50% to 68% of PTL cases, closely followed by mucosa-associated lymphoid tissue (MALT) lymphoma in 105 to 23% of cases; the remaining cases are a variety of lymphomas including follicular lymphoma (FL), small lymphocytic lymphoma (SLL) and mantle cell lymphoma (MCL).[2-7] Most patients present with low stage (stage IE and IIE) and have a good clinical outcome.[8,9]

Materials and methods

Specimens were retrieved from the anatomic pathology database at Washington University School of Medicine (WUSM), The Ohio State University Wexner Medical Center (WMC), and Cleveland Clinic Foundation (CCF) using the following CoPath computer search codes: *lymphoma* or *atypical lymphoid population* or *monomorphic lymphocytes* within the final diagnosis under a part type of *thyroid, neck mass, or FNA* between January 2000 and October 2013. All patients 18 years and older at the time of diagnosis were included. The search yielded a list that included both surgical thyroidectomy and cytology FNA specimens. If any patient had both a FNA and a follow-up surgical biopsy/thyroidectomy and a diagnosis of *lymphoma* or *atypical lymphoid population* or *monomorphic lymphocytes* on either specimen, the specimen was included. Thirty-five specimens (33 patients) were recovered from the WUSM database, 24 (22 unique patients) specimens were recovered from the WMC database, and 9 unique patients/specimens were recovered from the CCF database, for a total of 68 specimens (64 unique patients).

The clinical data collected for each patient included age, sex, final FNA diagnosis, clinical presentation (airway stenosis/deviation, extent of thyroid involvement at FNA), autoimmune status, surgical specimen type, surgical specimen diagnosis, and ancillary testing (flow cytometry results, immunohistochemical stains, cytogenetics, and molecular testing).

Preparation of specimens for morphologic evaluation varied greatly within each institution, let alone between institutions. Aspirate smears were either combined with or without a liquid monolayer preparation (Sure Path or ThinPrep), a liquid concentration technique (cytospin or MEGA Funnel technique), or cell block. Aspirate smears were stained with any combination of Romanowsky or Papanicolaou methods. The medium by which a majority of the specimens were sent for flow cytometry (FCM) evaluation was RPMI (Roswell Park Memorial Institute) medium with a minority of specimens submitted in saline. Only 2 specimens had polymerase chain reaction (PCR) analysis performed from cell block material.

All statistical analysis was performed using SAS 9.3 software (SAS Institute Inc., Cary, N.C.). To demonstrate the relationship between ordered and nominal data, Kendall's Tau-b value and asymptotic standard error (ASE) were generated to calculate the Z score and *P* value.

Results

Sixty-eight cases from 64 patients were retrieved. Only 13 specimens had a prior diagnosis of lymphoma before FNA. Sixty-seven specimens had histologic confirmation by thyroid biopsy/lobectomy (n = 44), bone marrow biopsy (n = 8), cervical lymph node biopsy (n = 11), stomach biopsy (n = 2), or a tissue diagnosis performed at an outside institution (n = 2). None of the tissue specimens were collected on the same day as the FNA. One patient with DLBL received treatment without histologic confirmation (Table 1). Thirteen patients had a clinical diagnosis of lymphocytic thyroiditis (data not shown). Eleven were proven to have DLBL, one FL and one MALT lymphoma. A majority of specimens had a final diagnosis of DLBL (n = 43), followed by classical Hodgkin lymphoma (5), chronic lymphocytic leukemia (CLL) (5), high grade

Table 1 Demographics classified by final diagnosis.

Final diagnosis	Total	Age range in years (mean)	Female sex (%)	Initial diagnosis (n)	Surgical confirmation (n)
DLBL	43	29-85 (63.2)	29 (67.4)	38	BM (1) LN (5) Stomach(2) Thyroid (33) OSH(1) No tissue (1)
CHL	5	28-59 (36.2)	3 (60)	3	LN (3) Thyroid (2)
CLL/SLL	5	47-71 (61.6)	4 (80)	1	BM (4) LN (1)
NHL-HG	3	54-85 (72)	2 (66.7)	3	BM (2) Thyroid (1)
FL	2	48-71 (59.5)	1 (50)	2	Thyroid (2)
D-H	1	63	1	0	BM
Burkitt	1	21	1	1	LN
MALT	1	53	0	1	Thyroid
MCL	1	87	1	0	OSH
PCN	1	54	1	1	Thyroid
LG-NHL	1	70	0	1	LN
LT	4	32-61 (48.5)	3 (75)	NA	Thyroid (4)
Total	68	21-87 (60)	46 (68)	51	

Abbreviations: LT, lymphocytic thyroiditis; DLBL, diffuse large B-cell lymphoma; CHL, classical Hodgkin lymphoma; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; NHL, non-Hodgkin lymphoma; HG, high grade; LG, low grade; FL, follicular lymphoma; D-H, double hit lymphoma; MALT, marginal zone lymphoma; MCL, mantle cell lymphoma; PCN, plasma cell neoplasm; BM, bone marrow; LN, lymph node; OSH, outside hospital tissue confirmation; NA, not applicable.