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A Rare Presentation of Lymphoma: Pancreatic and Thyroid Involvement

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Abstract Primary thyroid lymphoma is a rare form of thyroid malignancies. It is usually seen in middle aged and elderly females. Its diagnosis is not always easy because it is rare and has not specific signs and symptoms. The risk of development of thyroid lymphoma is higher after Hashimoto's thyroiditis. The most common form of thyroid lymphoma is diffuse large B cell lymphoma. Patients may present with obstructive symptoms due to progressive growth of mass. In the present report, we aimed to present a 59-year-old female patient admitted with rapidly growing neck mass, severe dyspnea, stridor and dysphagia.

Keywords: *thyroid lymphoma, diffuse large B-cell lymphoma, neck mass, dyspnea, stridor*

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1. Introduction

Lymphomas are malignancies originating from lymphoid tissue, which are classified as Hodgkin and non-Hodgkin lymphomas. Most of time, primary lymphomas involve lymph nodes, although they may also be seen in some extranodal soft tissues and organs such as thyroid tissue, nasopharynx, tonsillar tissue, spleen and gastrointestinal system [1]. Primary thyroid lymphoma (PTL) involves thyroid tissue and/or regional lymph nodes. PTL usually originates from B cells of lymphoid tissue. It is a rare malignancy; it constitutes 5% of all thyroid malignancies and 3% of extranodal non-Hodgkin lymphomas [2,3,4,5]. It is usually seen between the ages of 50-70 years and in females. It was suggested that lymphocytic thyroiditis (Hashimoto's thyroiditis) is the underlying pathology in most of the patients [6,7,8]. The most common presentation is rapidly growing neck mass. This rapidly growing mass may cause some obstructive symptoms such as dysphagia, hoarseness, dyspnea and stridor [9]. Fine needle aspiration biopsy (FNAB) is usually not sufficient to make the diagnosis. Most of the patients are diagnosed after thyroid surgery made with the suspicion of carcinoma. In this report, we presented a thyroid lymphoma case presented with rapidly growing mass, severe dyspnea and stridor to emphasize its difficulty in diagnosis and need for urgent intervention.

2. Case Report

A 59-year-old female patient presented with a 3 months history of severe dyspnea, stridor, progressive hoarseness, dysphagia and a neck mass. She was admitted to another clinic with hoarseness and neck mass 3 months ago and examined. On these examinations, thyroid function tests showed euthyroidism, anti-TPO and anti-TG were positive. Ultrasonography of neck showed enlarged, heterogeneous, hypoechoic and pseudonodular goiter. On thyroid I-131 scintigraphy, iodine uptake was very low. After these examinations, she was diagnosed with thyroiditis and prescribed NSAID. Her symptoms did not develop and she was admitted again with the same symptoms 2 weeks later. For further evaluation of neck mass, neck MRI was performed and strong contrast enhancing infraglottic mass lesion which was 25 mm in diameter, invading left thyroid lamina and left half of the cricoid cartilage and obliterated thyroid gland borders was seen. There were multiple lymphadenopathies (> 10 mm on short axis) at the inferior part of the mass, thoracic inlet and paratracheal region. Fine needle aspiration biopsy and core biopsy were performed to exclude thyroid cancer. These specimens were not diagnostic. Since dyspnea and dysphagia were also added to her symptoms, patient was admitted to our clinic for further examination and treatment. On physical examination, BP was 120/80 mm/Hg, pulse rate was 105/min, respiratory rate was 19/min, and body temperature was 36.6 °C. No cyanosis was observed. The patient was dyspneic and had stridor. A hard, painless and immobile mass lesion which was 3 cm in diameter was palpated on the left thyroid lobe at the anterior part of the neck. Breath sounds were normal on auscultation. Physical examinations of other organ systems were all normal. There was a mass lesion arising from left thyroid region, reaching paraglottic area and causing external compression in larynx on laryngoscopic examination. The

mucosal surface was intact and left vocal cord was paralytic. Laboratory results were shown in Table 1. On the neck ultrasonography (USG), thyroid gland was enlarged and trachea was narrowed. Thyroid parenchyma had heterogenic and pseudonodular appearance (Figure 1). Doppler USG of thyroid gland showed decreased parenchymal vascularity. The mass lesion diameter was 35 mm on control neck MRI (Figure 2). Since her previous biopsy specimens were not diagnostic, 18F-fluorodeoxyglucose positron emission tomography/ computed tomography (PET/CT) was performed for differential diagnosis of benign and malignant mass. PET/CT images showed that there was globally increased FDG uptake (SUVmax=7,5) at the thyroid region and it could not make a differentiation between inflammatory pathology and malignancy. There was also increased FDG uptake (SUVmax=3,3) at upper paratracheal lymph node. Soft tissue lesion on pancreatic tail, which was 39x43 mm in size was reported as malignant process (SUVmax=6,6). Increased FDG uptake of a peripancreatic lymph node (SUVmax=5,0), which was 14x13 mm in size was accepted as probable metastatic lymph node (Figure 3). On abdominal MRI, pancreatic tail was minimally expanded, heterogeneous and there was a hyperintense lesion 35x40 mm in size. Since a typical well-circumscribed mass lesion appearance was absent, no lesion was seen on pancreatic endoscopic ultrasonography (EUS). 1 mg/kg/day methylprednisolone infusion was commenced to relief obstructive symptoms. Thyroid isthmectomy was carried out for diagnosis. Histological examination of specimen revealed diffuse infiltration of crushed neoplastic cells accompanied by fibroblastic proliferation beginning from the thyroid tissue and extending through the surrounding soft tissues (Figure 4A), exhibiting lymphocytic thyroiditis (Figure 4B). Neoplastic cells had convoluted, large, vesicular nuclei including more than one nucleoli with clear or eosinophilic cytoplasm. Frequently, mitotic figures including atypical forms were noted. Apoptotic cells and histiocytes containing nuclear debris were also seen (Figure 4C-(Figure 4D). Immunohistochemically, tumor cells did not exhibit staining with pancytokeratin (Figure 5A) or thyroglobulin (Figure 5B). Presenting their nature of clonal B cell type, neoplastic cells reacted with antibodies such as CD20 (Figure 5C) and kappa (Figure 5D), while they were negative for lambda (Figure 5E). Ki-67 proliferation index was 80-85% (Figure 5F). Neoplastic cells were also negative for CD3, CD 30, MUM-1, TdT, CD68, ALK, Cyclin D1, CD23 and Bcl2. According to these features, tumor was diagnosed with “diffuse large B cell lymphoma, evolving in a background of extranodal marginal zone lymphoma” (Figure 5). After patient’s vital signs were clinically stabilized, R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, prednisolone) treatment was commenced. Remission was achieved after 3 courses of chemotherapy.

Table 1. Patient’s laboratory results.

	Reference range	Patient’s values
Fasting blood glucose	70-105 mg/dl	92
Urea	15-43 mg/dl	36
Creatinine	0,57-1,11 mg/dl	0,71
Uric acid	2,6-6 mg/dl	4
Total Protein	6-8,3 g/dl	7,1
Albumin	3,2-5,2 g/dl	4,5
ALT	0-55 U/l	13
AST	0-34 U/l	19
LDH	125-220 U/l	298
Sodium	136-145 mmol/l	144
Potassium	3,5-5,1 mmol/l	4,4
Sedimentation rate	0-20 mm/h	36
CRP	0-0,34 mg/dl	0,37
WBC	3980-10040 /ul	7,62
HBG	11,2-15,7 g/dl	13,2
PLT	150000-400000 /ul	234
FT3	2-4.2 pg/ml	3.01
FT4	0.8-1.8 ng/dl	0.83
TSH	0.55-4.78 mIU/ml	9.72
Anti-TPO	0-5 IU/ml	125
Anti-Tg	0-4 IU/ml	178

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; CRP: Cell reactive protein; WBC: White blood cell; HBG: Hemoglobin; PLT: Platelet; FT3: Free T3; FT4: Free T4; TSH: Thyroid stimulating hormone; Anti-TPO: Anti thyroid peroxidise; Anti-Tg: Anti thyroglobulin

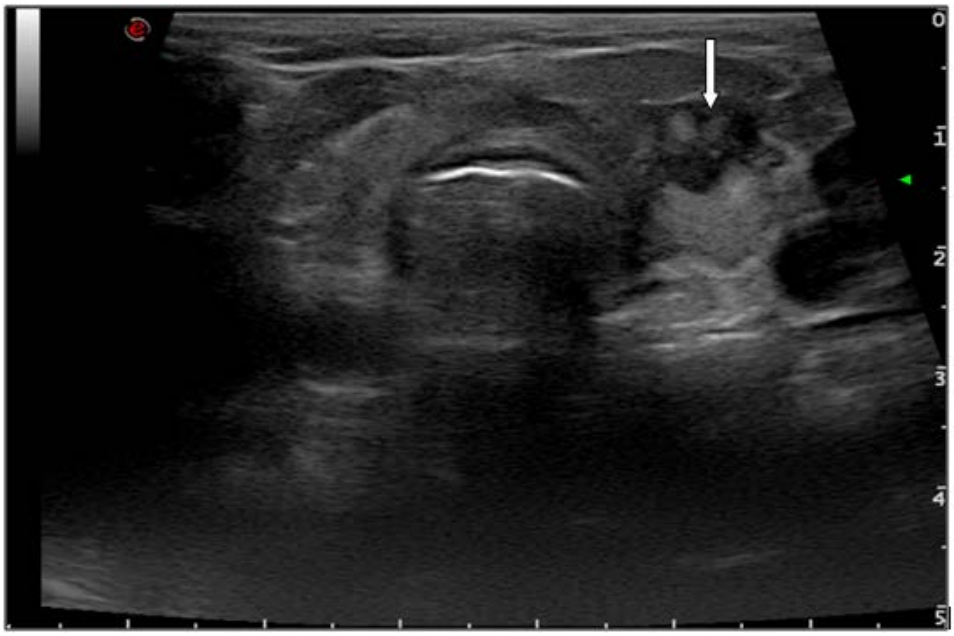

Figure 1. Thyroid ultrasonography

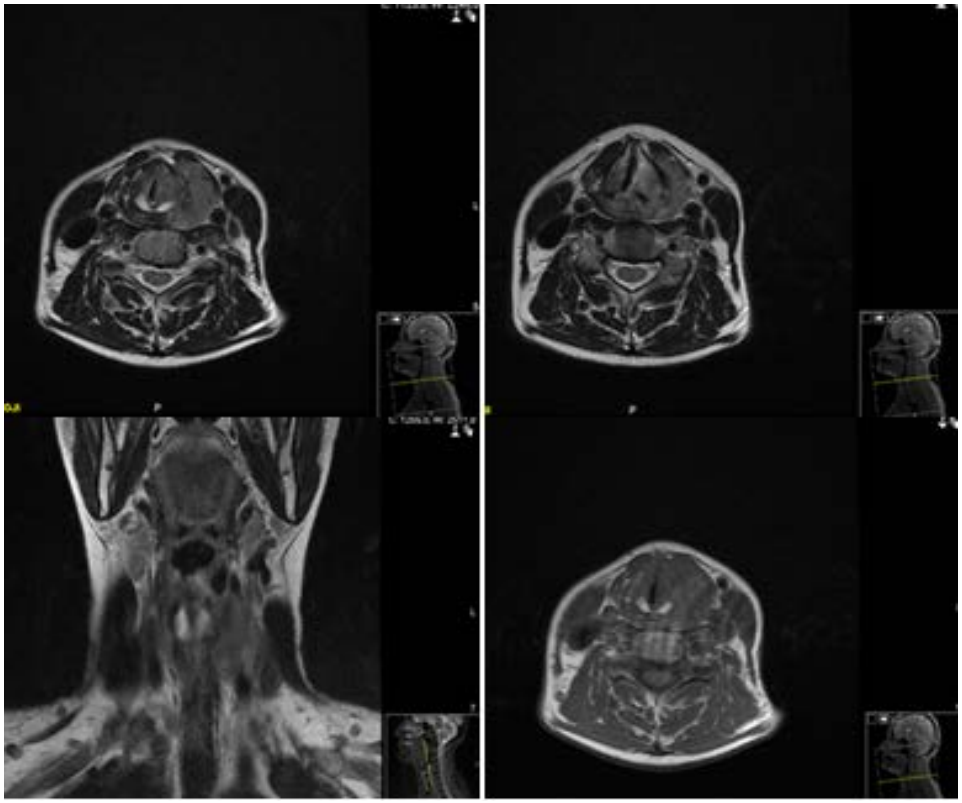

Figure 2. Neck MRI images with contrast. (Infraglottic, contrast enhancing mass lesion, invading left thyroid lamina and left half of cricoid cartilage, multiple lymphadenopathies, located at the inferior part of the mass, thoracic inlet and paratracheal region)

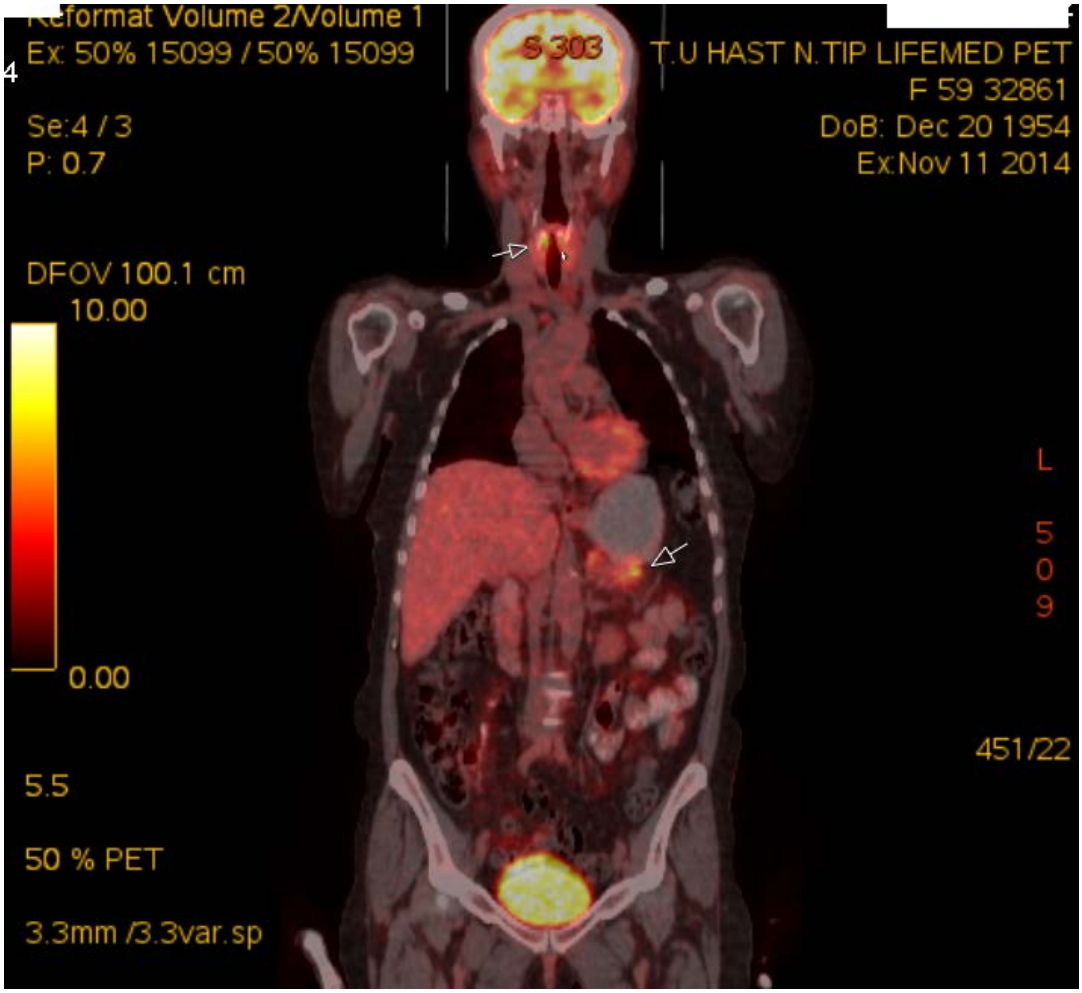

Figure 3. ^{18}F-FDG PET/CT images; globally increased FDG uptake at the thyroid region, increased FDG uptake at the upper tracheal lymph node, soft tissue lesion at pancreatic tail and peripancreatic lymph node

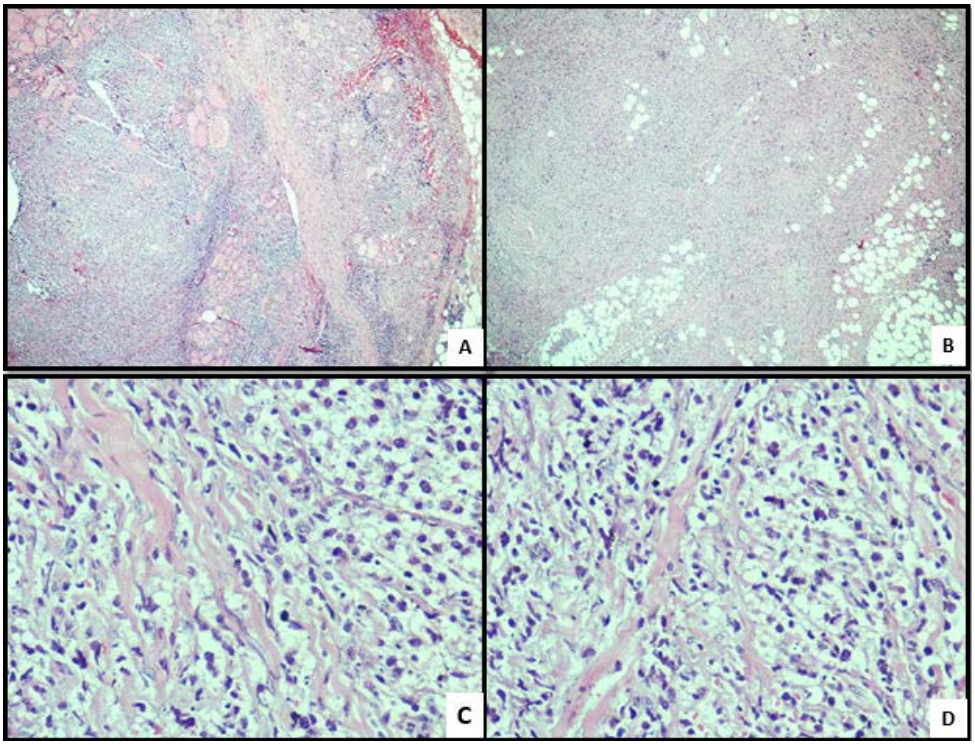

Figure 4. A-D. Diffuse infiltration of crushed neoplastic cells accompanied by fibroblastic proliferation beginning from the thyroid tissue exhibiting lymphocytic thyroiditis and extending through the surrounding soft tissues. Neoplastic cells had convoluted, large, vesicular nuclei including more than one nucleoli with clear or eosinophilic cytoplasm. Frequently, mitotic figures including atypical forms were noted. Apoptotic cells and histiocytes containing nuclear debris were also seen

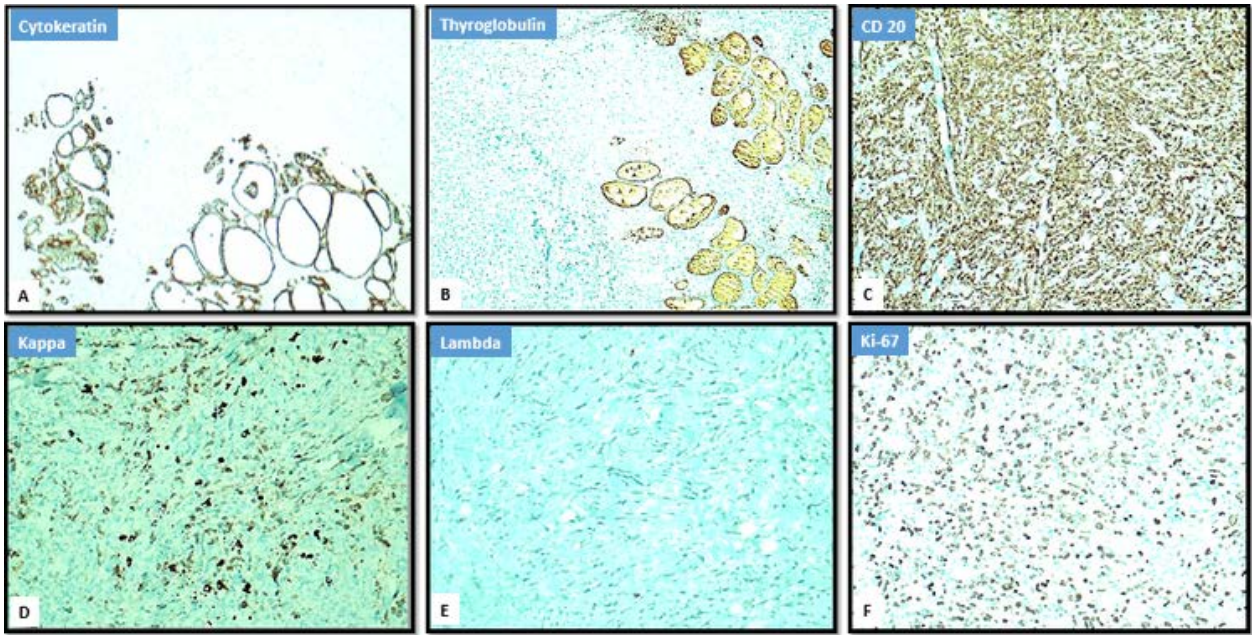

Figure 5. A-F. Tumor cells did not exhibit staining with pancytokeratin or thyroglobulin .Neoplastic cells reacted with antibodies such as CD20 and kappa , while they were negative for lambda . Ki-67 proliferation index was 80-85%

3. Discussion

The incidence of extranodal non-Hodgkin lymphoma is 10-35%. The most common histopathological type is diffuse B cell lymphoma [10]. Diffuse large B cell lymphoma (DLBCL) comprises nearly 70% of primary thyroid lymphomas, while 1/3 of primary thyroid lymphomas are mucosa associated lymphoid tissue (MALT) lymphomas [5]. Most of the patients have rapidly growing neck mass. Compression signs such as stridor, dysphagia and hoarseness are more rarely seen. Most of the patients are euthyroid and hypothyroidism may be detected in 10% of the patients [5,11,12]. Our patient also presented with rapidly growing neck mass and compression symptoms. She was euthyroid at presentation but subclinical hypothyroidism developed during follow up. Lymphoid tissue, which is normally not found in thyroid gland, may be histologically detected in case of autoimmune thyroid disease. Primary thyroid lymphoma is more common in patients with lymphocytic thyroiditis, especially in

Hashimoto thyroiditis (0.5%). The risk of developing lymphoma is 40-80 times higher in patients with Hashimoto thyroiditis when compared to general population [9,13]. In our case, thyroid lymphoma has also evolved in the background of Hashimoto's thyroiditis which was proven with clinical, laboratory and histopathological parameters. There is no specific laboratory test for the diagnosis of primary thyroid lymphoma. In some patients, high titers of anti-TPO and anti-Tg may be detected secondary to underlying thyroiditis, immunoglobulin A (IgA), IgM and IgG concentrations may be increased in 30% of the patients [2]. In our case, anti-TPO and anti-TG were positive and immunoglobulin levels were normal. Main diagnostic procedures include thyroid USG, needle biopsy and excisional biopsy. Pseudocystic and hypoechoic areas seen on thyroid USG may be misleading. In a series including 46 patients with thyroid lymphoma, 43 of the patients (93%) had asymmetrical pseudocystic areas on thyroid ultrasonography [12]. Our patient's thyroid USG revealed diffusely heterogeneous thyroid gland with bilateral pseudocystic nodular areas. Radiographic and radionuclide images can not differentiate carcinoma from Hashimoto's thyroiditis. Both lymphoma and Hashimoto's thyroiditis show diffuse increased uptake in thyroid tissue area on PET/CT imaging [14]. Our patient's PET-CT imaging showed diffusely increased uptake in both thyroid tissue and pancreas but there was no well-circumscribed pancreatic mass lesion on abdominal MRI. A meta-analysis of pancreatic carcinomas suggested that specificity of PET-CT was 80.1% and it was 93.2% for EUS [16]. EUS imaging of our case revealed no pancreatic lesion. Fine needle aspiration biopsy and core biopsy are sometimes non-diagnostic in primary thyroid lymphoma. Fibrosis, crushing artefacts and degeneration may lead to non-diagnostic results in fine needle biopsy, while small sample size and insufficient immunohistochemical evaluation make interpretation difficult. Open thyroid biopsy may be needed for histopathological examination and immunohistochemical analysis [12,16]. Since our patient's fine needle aspiration biopsy and core biopsy specimens were non-diagnostic, isthmectomy was performed. After histopathological and immunohistochemical examination, high grade B cell immune phenotype non-Hodgkin lymphoma diagnosis was established. Poor prognostic criteria for thyroid lymphomas are tumor grade >1E, tumor size >10 cm, presence of obstructive symptoms, mediastinal invasion and rapidly growing tumor size [10,17]. Our patient had severe dyspnea secondary to growing tumor size (tumor size increased 10 mm in 2 months), tracheal compression and vocal cord invasion. Patients may present with obstructive symptoms related to bleeding into thyroid tissue, undifferentiated thyroid carcinoma and acute enlargement of thyroid lymphoma. Our patient also had severe dyspnea and stridor and methylprednisolone infusion treatment was given to relieve these symptoms.

In conclusion, in patients presenting with severe dyspnea and rapidly growing neck mass, primary thyroid lymphoma should be considered. Early diagnosis could allow these patients to be treated without delay.

Competing Interest

The authors have no competing interests.

References

[1] Sirota, D.K., Segal, R.L., "Primary lymphomas of the thyroid gland", *JAMA*, 242(16), 1743-1746, Oct 1979.

[2] Pedersen, R.K., Pedersen, N.T., "Primary non-Hodgkin's lymphoma of the thyroid gland: a population based study", *Histopathology*, 28(1), 25-32, Jan 1996.

[3] Ansell, S.M., Grant, C.S., Habermann, T.M., "Primary thyroid lymphoma", *Semin Oncol*, 26(3), 316-323, Jun 1999.

[4] Ha, C.S., Shadle, K.M., Medeiros, L.J., Wilder, R.B., Hess, M.A., Cabanillas, F., Cox, J.D.," Localized non-Hodgkin lymphoma involving the thyroid gland", *Cancer*, 91(4), 629-635, Feb 2001.

[5] Derringer, G.A., Thompson, L.D., Frommelt, R.A., Bijwaard, K.E., Heffess, C.S., Abbondanzo, S.L., "Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases", *Am J Surgical Path*, 24(5), 623-639, May 2000.

[6] Au, W.Y., Fung, A., Ma, E.S., Shek, T.W., Hawkins, B.R., Liang, R., "HLA associations, microsatellite instability and epigenetic changes in thyroid lymphoma in Chinese", *Leuk Lymph*, 48(3), 531-534, Mar 2007.

[7] Al-Marzooq, Y.M., Chopra, R., Younis, M., Al-Mulhim, A.S., Al-Mommatten, M.I., Al-Omran, S.H., "Thyroid low-grade B-cell lymphoma (MALT type) with extreme plasmacytic differentiation: report of a case diagnosed by fine-needle aspiration and flow cytometric study", *Diagn Cytopath*, 31(1), 52-56, Jul 2004.

[8] Belal, A.A., Allam, A., Kandil, A., El Husseiny, G., Khafaga, Y., Al Rajhi, N., Ahmed, G., Gray, A., Ajarim, D., Schultz, H., "Ezzat A.Primary thyroid lymphoma: a retrospective analysis of prognostic factors and treatment outcome for localized intermediate and high grade lymphoma", *Am J Clin Oncology*, 24(3), 299-305, Jun 2001.

[9] Thieblemont, C., Mayer, A., Dumontet, C., Barbier, Y., Callet-Bauchu, E., Felman, P., Berger, F., Ducottet, X., Martin, C., Salles, G., Orgiazzi, J., Coiffier, B.," Primary thyroid lymphoma is a heterogeneous disease", *J Clin Endo Metab*, 87(1), 105-111, Jan 2002.

[10] Ansell, S.M., Habermann, T.M., Hoyer, J.D., Strickler, J.G., Chen, M.G., McDonald, T.J., "Primary laryngeal lymphoma", *Laryngoscope*, 107(11), 1502-1506, Nov 1997.

[11] Kossev, P., Livolsi, V., "Lymphoid lesions of the thyroid: review in light of the revised European-American lymphoma classification and upcoming World Health Organization classification", *Thyroid*, 9(12), 1273-1280, Dec 1999.

[12] Matsuzuka, F., Miyauchi, A., Katayama, S., Narabayashi, I., Ikeda, H., Kuma, K., Sugawara, M., "Clinical aspects of primary thyroid lymphoma : diagnosis and treatment based on our experience of 119 cases", *Thyroid* , 3(2), 93-99, Summer 1993.

[13] Onal, C., Li, Y.X., Miller, R.C., Poortmans, P., Constantinou, N., Weber, D.C., Atasoy, B.M., Igdem, S., Ozsahin, M., Ozyar, E., "Treatment results and prognostic factors in primary thyroid lymphoma patients: a Rare Cancer Network study", *Ann Oncology*, 22(1), 156-164, Jan 2011.

[14] Mikosch, P., Wurtz, F.G., Gallowitsch, H.J., Kresnik, E., Lind, P., "F-18-FDG-PET in a patient with Hashimoto's thyroiditis and MALT lymphoma recurrence of the thyroid", *Wien Med Wochenschr*, 153(3-4), 89-92, 2003.

[15] Tang, S., Huang, G., Liu, J., Liu, T., Treven, L., Song, S., Zhang, C., Pan, L., Zhang, T., "Usefulness of 18F-FDG PET, combined FDG-PET/CT and EUS in diagnosing primary pancreatic carcinoma: a meta-analysis", *Eur J Radiol* , 78(1), 142-150, Apr 2011.

[16] Austin, J.R., El-Naggar, A.K., Goepfert, H., "Thyroid cancers II: Medullary, anaplastic, lymphoma, sarcoma, squamous cell", *Otolaryngol Clin North Am*, 29(4), 611-627, Aug 1996.

[17] Green, L.D., Mack, L., Pasieka, J.L., "Anaplastic thyroid cancer and primary thyroid lymphoma: a review of these rare thyroid malignancies", *J Surg Oncol*, 94(8), 725-736, Dec 2006.