



Case Report

Coexistence of tuberculosis and extranodal marginal zone lymphoma of the thyroid gland: Case report and literature review

Sami Akbulut^{a,*}, Khaled Demyati^b, Ridvan Yavuz^c, Nilgun Sogutcu^d,
Emine Turkmen Samdanci^e, Yusuf Yagmur^c

^a Department of Surgery, Inonu University Faculty of Medicine, 44280, Malatya, Turkey

^b Department of Surgery, An-Najah National University Hospital, Faculty of Medicine and Health Sciences, An-Najah National University, 44839, Nablus, Palestine

^c Department of Surgery, Diyarbakir Education and Research Hospital, 21400, Diyarbakir, Turkey

^d Department of Pathology, Diyarbakir Education and Research Hospital, 21400, Diyarbakir, Turkey

^e Department of Pathology, Inonu University Faculty of Medicine, 44280, Malatya, Turkey

ARTICLE INFO

Keywords:

Thyroid
Multinodular goiter
Tuberculosis
Extranodal marginal zone lymphoma

ABSTRACT

Introduction: Primary thyroid tuberculosis (TB) is rare even in countries where TB disease is endemic, with the prevalence ranging from 0.1 to 1.15%. Primary thyroid lymphoma is uncommon, and the majority of lymphomas arising in the thyroid gland are non-Hodgkin's lymphomas of B-cell origin, of which about 25% is extranodal marginal zone B cell lymphoma (MALToma).

Case presentation: An 86-year-old Turkish female patient with thyroid nodules and cervical lymphadenopathies presented with large multinodular goiter and compressive symptoms. Total thyroidectomy and central lymph node dissection were performed. The revised histological and immunohistochemical revealed the coexistence of thyroid TB and MALToma. The patient received an anti-TB treatment for six months before a revised histopathological examination. About seven months after anti-TB treatment, the patient died due to an unknown cause.

Clinical discussion: Although six cases of thyroid TB and papillary thyroid cancer have been documented in the medical literature, no cases of TB and MALToma coexistence have been published so far, to our knowledge. Another essential feature of this study is that the initial pathological examination was reported as thyroid TB. A subsequent re-examination revealed that the patient had both TB and MALT lymphoma.

Conclusion: We discuss this rare association and the dilemma encountered in the diagnosis and management of this patient with a review of the literature.

1. Introduction

Tuberculosis (TB) has been described in many parts of the body, but the involvement of the thyroid gland is a scarce condition, with the prevalence ranging from 0.1 to 1.15% [1]. Tuberculosis initially affects the lungs in most cases, but it can involve other organs, whether as a primary disease or secondary to hematogenous or lymphatic dissemination. Primary thyroid TB with histopathological and microbiological evidence of TB within the thyroid gland with no evidence of extrathyroidal TB is an extremely rare condition, even in countries where tuberculosis is endemic. Secondary thyroid TB is associated with pulmonary or extrapulmonary tuberculosis, where disease dissemination

occurs through the hematogenous or lymphatic route or directly from the larynx or tubercular cervical lymphadenitis [1].

Thyroid cancer is the most common endocrine carcinoma, and papillary carcinoma is the most common type of thyroid cancer, accounting for 70%–80% of all thyroid carcinomas [2]. Primary thyroid lymphoma is distinctly uncommon, accounting for only 0.5%–5% of all thyroid malignancies and 2%–7% of all extranodal lymphomas [3–5]. The majority of lymphomas arising in the thyroid gland are non-Hodgkin's lymphomas of B-cell origin (Diffuse large B cell lymphoma [DLBCL: 50%], and Marginal zone B-cell lymphoma [MALToma: 25%]) [3,5].

Although the coexistence of malignant thyroid tumors and TB in the

* Corresponding author. Department of Surgery and Liver Transplant Institute, Inonu University Faculty of Medicine, Elazig Yolu 10. Km Malatya, 44280, Turkey.

E-mail addresses: akbulutsami@gmail.com (S. Akbulut), khaleddemyati@gmail.com (K. Demyati), drridvanyavuz@hotmail.com (R. Yavuz), nilgunsogutcu@gmail.com (N. Sogutcu), esamdanci@gmail.com (E.T. Samdanci), yusufyagmur@hotmail.com (Y. Yagmur).

<https://doi.org/10.1016/j.amsu.2022.103861>

Received 14 April 2022; Received in revised form 20 May 2022; Accepted 22 May 2022

Available online 2 June 2022

2049-0801/© 2022 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

same organ in a patient is extremely rare, this coexistence has been reported in various organs. Although only six cases of thyroid TB and papillary thyroid cancer have been reported in the literature, no cases of coexistence of TB and MALToma have been reported so far [6–11]. This study aimed to present a patient with extranodal marginal zone lymphoma (MALToma) and Thyroid TB and describe the dilemma encountered in the diagnosis and management of this patient.

2. Case report

An 86-year-old Turkish female patient was referred to our surgery outpatient clinic with multinodular goiter and dyspnea for further evaluation. Physical examination identified multiple thyroid nodules, with the most prominent nodule in the right thyroid lobe. The chest radiogram showed that the trachea had deviated to the left side. The thyroid ultrasonography revealed bilateral multiple solid hypoechoic nodules, with the largest being 47 × 35 mm, and there were numerous cervical lymphadenopathies on both sides. Preoperative biochemical analysis, including viral markers (Anti-HIV, HBsAg, Anti-HCV), were within normal limits. The patients underwent total thyroidectomy with central lymph node dissection. A 60 × 50 mm conglomerated lymph nodes adjacent to the right lobe were included in the surgical specimen. On the postoperative second day, the patient suffered severe dyspnea, and the fiber optic laryngoscopy showed bilateral vocal cord paralysis. Steroid therapy was initiated immediately; however, the dyspnea persisted, and a tracheostomy was performed. The patient stabilized and was discharged home with a tracheostomy. The histopathological analysis showed granulomas with central caseation necrosis surrounded by epithelioid histiocytes, Langhan's giant cells, and lymphocytes. The specimens to another center as consultation for differentiation of lymphoma and TB thyroiditis. The consultation results suggested that granulomatous diseases, including TB, should be included in the patient's differential diagnosis. The patient was evaluated and was considered to have primary thyroid TB because there were no other foci of tuberculosis in other organ systems. Therefore, the patient received an anti-TB treatment for six months. The patient's dyspnea gradually subsided during the therapy, and the tracheostomy was closed. The patient passed away for an unknown reason 14 months after thyroid surgery. The glass microscope slides of the patients were re-evaluated in another pathology department for academic research, and the thyroid gland was found to be infiltrated by atypical lymphocytes close to the granulomatous regions that had central caseation necrosis (Figs. 1–2). Immunohistochemical staining showed that the lymphocytes were CD-20 and Ki-67 positive (Figs. 3–4). These findings were evaluated as

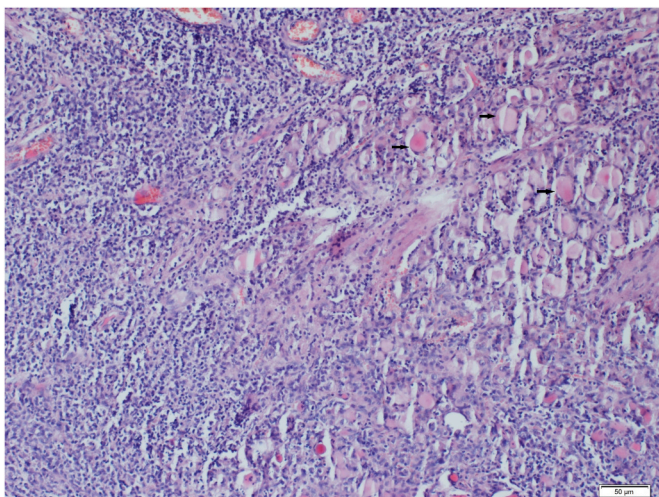


Fig. 1. Atypical lymphoid cells infiltrating the thyroid gland (arrows thyroid follicles) (HEx100).

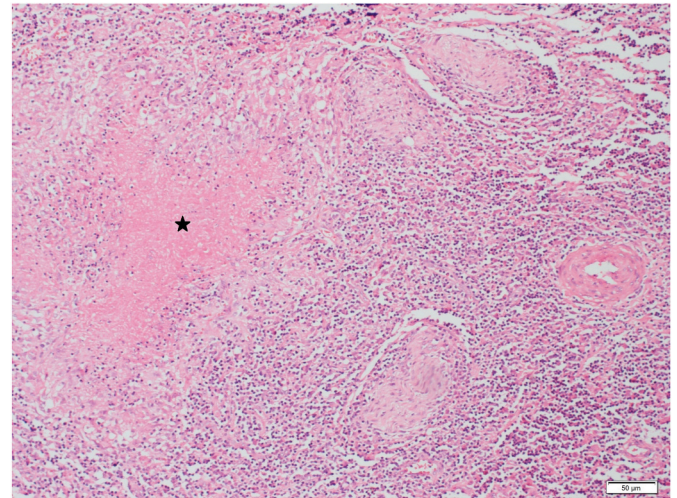


Fig. 2. Necrotizing granuloma adjacent to atypical lymphocytic infiltration (star granuloma) (HEx100).

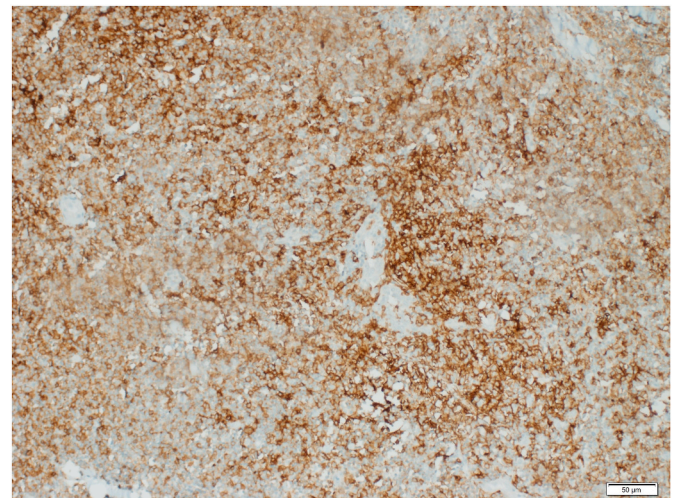


Fig. 3. Atypical lymphocytes were positively stained with CD 20 antibody (CD 20x100).

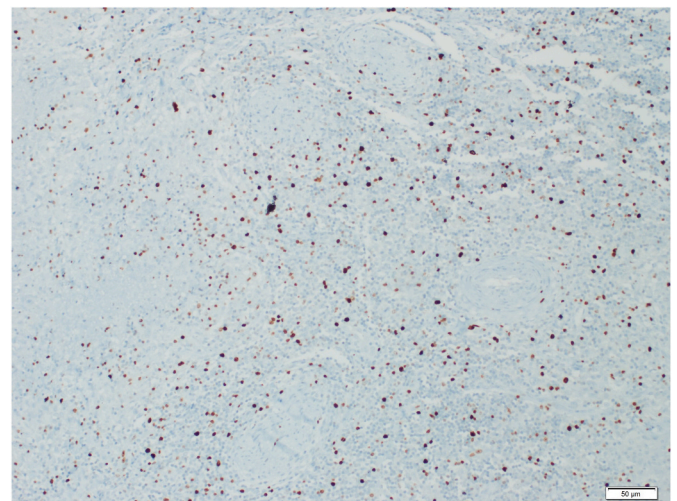


Fig. 4. Low proliferation index with Ki-67 antibody (Ki-67x100).

concomitant TB and extranodal marginal zone B cell lymphoma (MAL-Toma). This case report has been reported according to the SCARE Criteria [12].

3. Discussion

Several coexisting pathological conditions in the thyroid gland have been reported before, with the development of thyroid carcinoma in patients with Hashimoto's thyroiditis [13–15] and Graves' disease [16, 17] being most frequently reported. Coexisting thyroid TB and papillary thyroid cancer have been reported rarely in the literature [6–11]. However, based on our search of the literature, no cases of coexistence of primary thyroid TB and extranodal marginal zone B cell lymphoma have been reported so far. Our patient presented with sizeable multinodular goiter and compressive symptoms. The diagnosis of thyroid TB was only made on the histopathological examination. Coexisting primary thyroid extranodal marginal zone B cell lymphoma was only diagnosed when Immunohistochemical staining showed that the lymphocytes were CD-20 and Ki-67 positive (Figs. 3–4).

The involvement of the thyroid gland with TB is very rare, even in countries where tuberculosis is endemic [1]. While the more common secondary thyroid TB is the miliary spread of TB to the thyroid from hematogenous dissemination, thyroid involvement can be a primary manifestation of the disease. The most frequent clinical presentation is a solitary thyroid nodule that may present as a cystic nodule [18]. It may also present as diffuse multinodular swelling, rapid enlargement of a preexisting goiter, thyroid abscess with pain, fever, and other non-specific signs and symptoms [18–20]. Fine needle aspiration cytology finding of granulomatous inflammation suggests the diagnosis, and the sample is considered diagnostic when Ziehl-Neelsen stain and AFB culture are positive [21]. Imaging techniques are not very useful in forming a diagnosis [10]. In our patient, fine needle aspiration cytology (FNAC) was not performed before surgery because the patient has compressive symptoms, including respiratory distress. The diagnosis of Thyroid TB was made by the histological examination, which identified epithelioid cell granulomas with central caseous necrosis, peripheral lymphocytic infiltration, and Langerhan's giant cells.

Primary thyroid lymphoma (PTL) is a lymphoma that develops in the thyroid gland. It is a rare clinical entity usually manifested by a rapidly growing mass in the neck that can cause pressure symptoms [22]. The most common subtype of PTL is the diffuse large B cell lymphoma (DLBCL), followed by mucosa-associated lymphoid tissue (MALT) lymphoma or a mixed type [22,23]. PTL affects patients with Hashimoto's autoimmune lymphocytic thyroiditis at a rate of 0.5% [22]. Autoimmune thyroiditis is considered to carry an 80-fold risk compared to individuals without autoimmune thyroiditis [24]. Generally, the main complaint is neck swelling; some patients also show B symptoms such as night sweats, fever, and weight loss [2]. The mass can be nodular, diffused, or mixed in appearance. Ultrasound scans may suggest a diagnosis, but only the biopsy contributes to the definitive diagnosis. Fine needle aspiration biopsy can confirm the diagnosis of PTL in up to 70–80% of cases [22].

In conclusion, this study reported a rare case of coexisting PTL and thyroid TB, a diagnosis that is difficult to expect or made. Thyroid TB should be expected in countries where TB is common when suggestive symptoms present. While thyroid lymphoma should be expected in patients with autoimmune thyroiditis who present with a rapidly growing mass in the neck and pressure symptoms. The imaging findings are not diagnostic, and the diagnosis requires histological examination, which is usually made postoperatively.

Declaration of competing interest

The authors stated that they have no conflict of interest.

Funding

No financial support was received for this study.

Ethical approval

Ethics approval was not received due to its publication type as a case report.

Patient consent statement

Written and verbal informed consent was obtained from patients' relatives to publish this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Conceptualization, S.A., and N.S.; investigation, S.A., R.Y., K.D., Y. Y., and N.S.; writing—original draft preparation, S.A. and K.D.; writing—review and editing, S.A., Y.Y., E.T.S., and Y.Y.; project administration, S.A. and R.Y. All authors have read and agreed to the published version of the manuscript.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Registration of research studies

Trail registry number

1. Name of the registry:

Not applicable.

2. Unique Identifying number or registration ID:

Not applicable.

3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Not applicable.

Guarantor

The Guarantor for this work is Prof Sami Akbulut, who is the correspondent author and can be reached via email at akbulutsami@gmail.com

Acknowledgment

Not applicable

References

- [1] S. Akbulut, N. Sogutcu, Z. Arıkanoglu, S. Bakır, A. Ulku, Y. Yagmur, Thyroid tuberculosis in southeastern Turkey: is this the resurgence of a stubborn disease? *World J. Surg.* 35 (2011) 1847–1852, <https://doi.org/10.1007/s00268-011-1118-3>.
- [2] V. Cheng, J. Brainard, C. Nasr, Co-occurrence of papillary thyroid carcinoma and primary lymphoma of the thyroid in a patient with long-standing Hashimoto's thyroiditis, *Thyroid* 22 (2012) 647–650, <https://doi.org/10.1089/thy.2011.0228>.
- [3] C.M. Bacon, T.C. Diss, H. Ye, H. Liu, A. Goatly, R. Hamoudi, A. Wotherspoon, R. D. Gascoyne, A. Dogan, M.Q. Du, P.G. Isaacson, Follicular lymphoma of the thyroid gland, *Am. J. Surg. Pathol.* 33 (2009) 22–34, <https://doi.org/10.1097/PAS.0b013e31817d7470>.
- [4] Y.J. Nam, B.H. Kim, S.K. Lee, Y.K. Jeon, S.S. Kim, W.J. Jung, D.H. Kahng, I.J. Kim, Co-occurrence of papillary thyroid carcinoma and mucosa-associated lymphoid tissue lymphoma in a patient with long-standing Hashimoto thyroiditis, *Endocrinol Metab (Seoul)* 28 (2013) 341–345, <https://doi.org/10.3803/EnM.2013.28.4.341>.
- [5] L. Zhang, M. Castellana, C. Virili, A. Crescenzi, F. Giorgino, E. Zucca, L. Ceriani, F. Cavalli, L. Giovannella, P. Trimboli, Fine-needle aspiration to diagnose primary thyroid lymphomas: a systematic review and meta-analysis, *Eur. J. Endocrinol.* 180 (2019) 177–187, <https://doi.org/10.1530/eje-18-0672>.

- [6] M. Al Shareef, M. Khan, K. Al-Jabri, A. Eltayeb, Incidental caseating granuloma of thyroid gland presenting with concomitant Graves' disease and multifocal papillary microcarcinoma, *J Health Special* 1 (2013) 135–137, <https://doi.org/10.4103/1658-600X.120852>.
- [7] A. El Kohen, L. Essakalli, A. Amarti, L. Benchekroun, N. Jazouli, M. Kzadri, [Thyroid tuberculosis associated with papillary microcarcinoma of the thyroid gland: a case report], *Rev. Laryngol. Otol. Rhinol.* 122 (2001) 205–208.
- [8] N. Errami, A. Benjellounb, B. Hemmaouia, K. Nadoura, F. Benariba, Association of tuberculous thyroiditis and papillary carcinoma of the thyroid: a rare coincidence, *Pan Afr Med J* 19 (2014) 118, <https://doi.org/10.11604/pamj.2014.19.118.4805>.
- [9] K. Hizawa, K. Okamura, K. Sato, T. Kuroda, M. Yoshinari, H. Ikenoue, M. Fujishima, Tuberculous thyroiditis and miliary tuberculosis manifested postpartum in a patient with thyroid carcinoma, *Endocrinol. Jpn.* 37 (1990) 571–576, <https://doi.org/10.1507/endocrj1954.37.571>.
- [10] L. Meng, S. Hu, L. Huang, C. Xu, Papillary thyroid cancer coexisting with thyroid tuberculosis: a case report, *Oncol. Lett.* 7 (2014) 1563–1565, <https://doi.org/10.3892/ol.2014.1901>.
- [11] V.S. Suri, P. Sakhuja, V. Malhotra, R. Gondal, S. Singh, N. Sidhu, Co-existent tuberculosis and papillary carcinoma thyroid, *Trop. Doct.* 32 (2002) 118, <https://doi.org/10.1177/004947550203200228>.
- [12] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230, <https://doi.org/10.1016/j.ijss.2020.10.034>.
- [13] G. Graceffa, R. Patrone, S. Vieni, S. Campanella, S. Calamia, I. Laise, G. Conzo, M. Latteri, C. Cipolla, Association between Hashimoto's thyroiditis and papillary thyroid carcinoma: a retrospective analysis of 305 patients, *BMC Endocr. Disord.* 19 (2019) 26, <https://doi.org/10.1186/s12902-019-0351-x>.
- [14] C. Molnár, S. Molnár, J. Bedekovics, A. Mokánszki, F. Gyóry, E. Nagy, G. Méhes, Thyroid carcinoma coexisting with Hashimoto's thyroiditis: clinicopathological and molecular characteristics clue up pathogenesis, *Pathol. Oncol. Res.* 25 (2019) 1191–1197, <https://doi.org/10.1007/s12253-019-00580-w>.
- [15] S.I. Noureldine, R.P. Tufano, Association of Hashimoto's thyroiditis and thyroid cancer, *Curr. Opin. Oncol.* 27 (2015) 21–25, <https://doi.org/10.1097/cco.000000000000150>.
- [16] P. Premoli, M.L. Tanda, E. Piantanida, G. Veronesi, D. Gallo, E. Masiello E, S. Rosetti S, C. Cusini, F. Boi, J. Bulla, R. Rodia, S. Mariotti, V. Capelli, M. Rotondi M, F. Magri F, L. Chiovato, R. Rocchi, M.C. Campopiano, R. Elisei, P. Vitti, F. Barbato, T. Pilli, M.G. Castagna, F. Pacini, L. Bartalena, Features and outcome of differentiated thyroid carcinoma associated with Graves' disease: results of a large, retrospective, multicenter study, *J. Endocrinol. Invest.* 43 (2020) 109–116, <https://doi.org/10.1007/s40618-019-01088-5>.
- [17] J.U.L. Staniforth, S. Erdirmanne, G.D. Eslick, Thyroid carcinoma in Graves' disease: a meta-analysis, *Int. J. Surg.* 27 (2016) 118–125, <https://doi.org/10.1016/j.ijss.2015.11.027>.
- [18] L.K. Bansal, S. Gupta, A.K. Gupta, P. Chaudhary, Thyroid tuberculosis, *Indian J Tuberc.* 68 (2021) 272–278, <https://doi.org/10.1016/j.ijtb.2020.09.006>.
- [19] S. Chan Shin Jie, C.C. Tan, A rare case of primary tuberculosis in a solitary thyroid nodule, *Indian J. Tubercul.* 67 (2020) 360–362, <https://doi.org/10.1016/j.ijtb.2019.08.001>.
- [20] I. Oueslati, I. Sakka, O. Ismail, I. Akrouf, A. Marghli, M. Chihaoui, Tuberculosis of the thyroid gland presented as a rapid enlargement of a preexisting goiter, *Case Rep Endocrinol* (2018), 4369531, <https://doi.org/10.1155/2018/4369531>, 2018.
- [21] N. Gupta, K. Sharma, A. Barwad, M. Sharma, A. Rajwanshi, P. Dutta, A. Sharma, Thyroid tuberculosis - role of PCR in diagnosis of a rare entity, *Cytopathology* 22 (2011) 392–396, <https://doi.org/10.1111/j.1365-2303.2010.00830.x>.
- [22] E.T. Pavlidis, T.E. Pavlidis, A review of primary thyroid lymphoma: molecular factors, diagnosis and management, *J. Invest. Surg.* 32 (2019) 137–142, <https://doi.org/10.1080/08941939.2017.1383536>.
- [23] J. Yi, P. Yi, W. Wang, H. Wang, X. Wang, H. Luo, P. Fan, A multicenter retrospective study of 58 patients with primary thyroid diffuse large B cell lymphoma, *Front. Endocrinol.* 11 (2020) 542, <https://doi.org/10.3389/fendo.2020.00542>.
- [24] Y.J. Chai, J.H. Hong, H. Koo do, H.W. Yu, J.H. Lee, H. Kwon, S.J. Kim, J.Y. Choi, K. E. Lee, Clinicopathological characteristics and treatment outcomes of 38 cases of primary thyroid lymphoma: a multicenter study, *Ann Surg Treat Res* 89 (2015) 295–299, <https://doi.org/10.4174/ast.2015.89.6.295>.