*American Journal of Multidisciplinary Research & Development (AJMRD)*
*Volume 05, Issue 09 (Sept - 2023), PP 45-49*
*ISSN: 2360-821X*
**www.ajmrd.com**

**Research Paper** **Open Access**

# Primary Malt Thyroid Lymphoma: a case report.

Kmira Zahra[1], Amira Guizani[1] , Rim Aidli[1] , Mouna Bellakhdhar[2], Monia Guermazi[1], SarraYacoub[3], Safaa Jemli[2], Dorra Chiba[3], MoniaZaier[1], Yosra Ben Youssef[1], Haifa Regaieg[1], Abderrahim Khelif[1].

1Department of Clinical Hematology, FarhatHached University Hospital, Sousse, Tunisia
2Departement of ENT, FarhatHached University Hospital, Sousse, Tunisia
3Departement of Pathology, FarhatHached University Hospital, Sousse, Tunisia
Corresponding author: Zahra Kmira

**Abstract:**
**Background.:** Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a mature B-cell neoplasm that accounts for 7–8 % of all B-cell lymphomas. This type of lymphoma tends to appear in patients with a history of autoimmune disease or chronic inflammatory disorders.
**Methods.** Here, we report the clinical presentation and the follow up of our primary MALT thyroid lymphoma.
**Results.** A 52-year-old female patient presents with cervical lymphadenopathy that has been progressing for four months. Upon the discovery of a thyroid goiter, a cervical ultrasound revealed two thyroid nodules classified as EUTIRADS 5, with normal thyroid function tests. Following a total thyroidectomy, histological and immunohistochemical examination of the operative specimen confirmed the diagnosis of thyroid MALT lymphoma. The staging assessment indicated a localized lymphoma in the thyroid. The decision was not to give immunochemotherapy and to monitor the patient closely with no evidence of disease recurrence after follow-up for 8 months.
**Conclusion**. This case is notable for the unexpected presentation of MALT lymphoma within a nodular thyroid. Given its rarity, there is no consensus for the diagnostic and therapeutic approach of affected patients.

**Keywords:** Malt Lymphoma; prognosis; treatment.

## I. Introduction:

Mucosa-associated lymphoid tissue (MALT) lymphomas were recognized as extranodal marginal zone B-cell lymphomas since the Revised European- American Lymphoma (REAL) classification of 1994 and the World Health Organization (WHO) classification of 1999[1,2].MALT lymphomas are Non Hodgkin B cell lymphomas that primarily occur in the stomach and also in non-

gastrointestinal sites, such as the salivary glands, thyroid gland, skin, ocular adnexa, prostate and conjunctiva[3]. MALT lymphomas are indolent lymphomas, although dissemination to other mucosal sites, bone marrow, or lymph nodes may occur in approximately 30% of cases at diagnosis [3].In this article, we report the clinical presentation, the treatment, and the outcome of a primary MALT thyroid lymphoma discovered after thyroidectomy.

**Case report**: A 52-year-old female was referred to the hematology department in October 2022 for additional management of a thyroid MALT lymphoma diagnosed after pathologic exam of total thyroidectomy specimen. She had a history of Breast cancer in 2011, treated with lumpectomy and radio chemotherapy and Adenocarcinoma of the colon in 2020, treated with surgery and chemotherapy. The patient reported four-months 'symptoms of increasing cervical lymphadenopathy. Physical examination showed a thyroid goiter with bilateral centimetricjugulo-carotid lymphadenopathies leading to perform a cervical ultrasound demonstratingtwo thyroid nodules classified as EUTIRADS 5.Her thyroid function tests were normal. Subsequently, the patient underwent a total thyroidectomy. Histological examination showed an extensive and diffuse lymphomatous infiltrate made of numerous and non-atypicalplasma cellsadmixed with large sheets of monotonous small lymphocytesinfiltrating thyroid follicle inducing lymphoepithelial lesions (figure 1). Residual thyroid parenchyma showedhistologic signs of thyroiditis with increased fibrosis, lymphocytic infiltrate and germinal center formation.Immunohistochemical study confirmed malignancy highlighting extensivemonotypic plasmatic cells expressingCD138 and only kappa light chains. Lymphocytes surrounding theplasmacyticcells, expressed CD20, BCL2 and were negative for CD5, CD10, CD23, Cycline D1.

Complete blood cells showed white blood cell count 6900/$mm^3$, 70% granulocytes, 74.9% lymphocytes, 18.6% monocytes, hemoglobin 8g/dl with MCV at 57$\mu^3$ and platelets 378 000/mm3. The ferritin level was 10ng/ml confirming her iron-deficiency.The level of lactate dehydrogenase was normal at 262UI/l (reference range ≤ 270 U/L).The examination of the ENT was normal. Tomography Emission scans or TEP-scan revealed only intense and diffuse hypermetabolism in the ascending colon. In consequence of this finding, colonoscopy with biopsy was performed showing no malignancies. The decision was not to give immunochemotherapy and to monitor the patient closely with no evidence of disease recurrence after follow-up for 8 months.

## II. Discussion:

MALT lymphomas is a rare entity, however it makes up 23–30% of primary thyroid lymphomas (PTL)[4] , which is accounting for only 5% of thyroid malignancies and 2% of extranodal lymphomas[1]. They are considered as indolent lymphomas, although in nearly 30% of cases, at the diagnosis, dissemination to other mucosal sites, bone marrow, or lymph nodes can be found[3]. It usually occurs in middle-aged to older individuals, whereas its incidence is low in individuals younger than 40 years of age and it affects mainly women [5]. This is similar to our case. Thyroid MALT lymphoma commonly presents with a rapid enlargement of a thyroid nodule in 80% of cases, typically occurring within the past one to three months. This growth may be accompanied by compressive symptoms, such as dyspnea, dysphagia, stridor, cough, hoarseness, and rarely, superior vena cava syndrome. Additionally, around one-third of cases may exhibit cervical lymphadenopathy[5][6]. Fever, weight loss and night sweats also known as B symptoms are less common[4]. Our case had neither compressive symptoms nor B symptoms.

Thyroid MALT lymphoma has an intricate pathogenesis that involves various factors, including chronic stimulation of the immune system. There are significant associations between

autoimmune diseases, chronic antigenic stimulation, and the occurrence of thyroid MALT lymphoma although the underlying mechanisms of its development remain unclear. The main risk factor for its occurrence is the presence of Hashimoto's thyroiditis (HT), an autoimmune condition affecting the thyroid gland. Patients with HT have a significantly higher risk of developing T MALT lymphoma, with a 40 to 80 times greater risk compared to individuals without HT[6]. Notably, it often manifests 20 to 30 years after the initial diagnosis of HT, further highlighting the association between chronic immune stimulation and the development of this lymphoma subtype.Diagnosis can be difficult and, although preparations from fine needle aspiration are improving in specificity and sensitivity, they are not yet reliable enough to replace core needle or surgical biopsy. This is due to the histopathological similarities between primary thyroid lymphoma and Hashimoto's thyroiditis. False-negative results mayoccur in 20% of cases [7].Thanks to advancements in core biopsy methods, open surgical biopsy is now necessary only when less invasive approaches have proven ineffective in precisely identifying the subtype of the lymphoma, particularly when the treatment strategies differ depending on the histological type [8]. Our patient underwent an open thyroidectomy. Current imaging techniques (ultrasound, computed tomography, scintigraphy, MRI, FDG-TEP) can prove the existence of a thyroid mass and help to stage the disease [5]. The use of ultrasound scans may suggest a diagnosis, but only the biopsy contributes to the definitive diagnosis. Also the ultrasound's sensitivity and specificity are highly limited, leading to a significant lack of accuracy in differentiating between diffuse large B cell lymphoma (DLBCL) and MALT lymphoma[7]. Computed tomography is required for staging and treatment planning once the diagnosis has been made. FDG-TEP can be used for the initial diagnosis and monitoring the therapeutic response [5]. The disease is staged according to the Ann Arbor classification modified by Mussoff.

Histologically, MALT lymphoma is characterized by lymphoepithelial lesions (LEL) follicular colonization generated from proliferating neoplastic marginal zone-related cells [3]. Plasmatic differentiation is a constant and striking feature in thyroid MALT lymphoma that may evoque an extra-medullary plasmocytoma. In our case, the BCL-2 expression, lymphoepithelial lesions and the diffuse nature of the infiltrate favored the diagnosis of an extensive plasmatic differentiation of MALT lymphoma rather than plasmocytoma [9]. These histopathological findings distinguish MALT lymphoma from benign lesions, but these lesions are not always clearly distinguishable. In such cases, analysis using molecular pathology is useful. In immunohistochemical staining, CD5, CD10, and CD23 are negative in MALT cases [5]. Several distinctive genetic abnormalities have been associated with MALT lymphoma. Among them, a specific genetic aberration t(3;14)(p14.1;q32)/FOXP1-IGH has been reported in thyroid MALT lymphoma cases[10]. However, the available studies on this specific aberration are limited in number.

Local treatments, using either surgery or radiotherapy alone, seem to be attractive treatment strategies because MALT lymphomas tend to remain localized for a long time[11], and achieving excellent overall survival rates[6,12]. Radiotherapy is currently primarily administrated as a standalone treatment. The effective radiation dose in radiation therapy is moderate (25 to 30 Gy) , highly effective and it can achieve local control without severe side effects with acceptable morbidity with MALT lymphoma [11]. Total thyroidectomy alone is an adequate treatment only for stage IE MALT lymphoma confined to the thyroid gland without lymph node involvement, otherwise, it is considered inadequate management associated with the likelihood of relapse. The five-year disease-free survival rate after radiotherapy alone ranges from 88% to 100%. Retrospective studies indicate that the addition of chemotherapy does not improve the outcome for patients with localized low-grade thyroid

lymphomas. It may be necessary to combine chemotherapy in cases where the disease extends beyond the thyroid or becomes widely disseminated. The most common chemotherapy regimen used is CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). Several recent retrospective series (level IV) have been suggesting a benefit of combinedchemo-radiation over loco-regional therapy (surgery/radiation) or chemotherapy alone[8]. Early diagnosis improves the prognosis for lymphoma of the thyroid. When the disease is confined only to the thyroid gland, the 5-year survival rate may reach 75% to 85%[13]. Recurrences can occur either within the same organ or in other extranodal sites. Finally, randomized studies are needed to explore the most effective treatment of this rare entity.

## III. Conclusion:

Thyroid MALT lymphomas are uncommon thyroid malignancies that typically arise in the presence of longstanding lymphocytic thyroiditis. They generally have an indolent course.Given the limited clinical evidence available, it is challenging to determine the most effective treatment and follow-up approach for patients with MALT lymphoma in the thyroid gland. However, a prudent strategy would involve a combination of minimally invasive surgical techniques and adjuvant therapy, especially for individuals with stage IE and IIE disease.Additionally, extended monitoring should be taken into account. Conducting randomized trials for this rare disease is difficult due to its low occurrence. Nevertheless, it would be beneficial to establish an international databank where various medical centers can contribute insights and accumulate knowledge to enhance our understanding of this condition.

**Acknowledgments:**

No acknowledgments

**Statement of Ethics**

This study was approved to be in accordance with standards for good scientific practice by the Committee for Research Ethics at FarhatHached University Hospital, Tunisia (Ref: CER: 60-2023).

**Disclosure Statement**

The authors have no conflicts of interest to declare.

**Funding Sources**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**Author Contributions**

Kmira Zahra[1], Amira Guizani[1] , Rim Aidli[1] , Safaa Jemli[2],Mouna Bellakhdhar[2]: Conception and writing of the manuscript

Monia Guermazi[1], SarraYacoub[3], Dorra Chiba[3]: preparing figure

MoniaZaier[1], Yosra Ben Youssef[1], Haifa Regaieg[1], Abderrahim Khelif[1]: revising the manuscript

## References:

[1] Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary ML, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the international lymphoma study group. Blood 1994; 84: 1361–1392.

[2] Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, VardimanJ,etal.World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid

tissues: report of the clinical advisory committee meeting, Airlie House, Virginia, November 1997. J ClinOncol 1999;17:3835–3849.

[3] Thieblemont C, Mayer A, Dumontet C, Barbier Y, Callet-Bauchu E, Felman P, et al. B. Primary thyroid lymphoma is a heterogeneous disease. J EndocrinolMetab 2002;87:104–113.

[4] S. Serefhanoglu, U. Tapan, I. Ertenli, U. Kalyoncu, and A. Uner. Primary thyroid marginal zone B-cell lymphoma MALT-type in a patient with rheumatoid arthritis .*Med Oncol 2010*, 27 (3): 826-832. doi: 10.1007/s12032-009-9293-x.

[5] ET. Pavlidis, and TE. Pavlidis. A Review of Primary Thyroid Lymphoma: Molecular Factors, Diagnosis and Management. Journal of Investigative Surgery 2017, 1–6. doi:10.1080/08941939.2017.1383536

[6] Walsh, Siun, Aoife J. Lowery, Denis Evoy, Enda W. McDermott, and Ruth S.Prichard. Thyroid Lymphoma: Recent Advances in Diagnosis and Optimal Management Strategies. *The Oncologist* 2013, 18 (9): 994-1003. https://doi.org/10.1634/theoncologist.2013-0036

[7] Karvounis, Evangelos, IoannisKappas, Anna Angelousi, Georgios-MariosMakris, and Eva Kassi. Mucosa-Associated Lymphoid Tissue Lymphoma of the Thyroid Gland: A Systematic Review of the Literature. European Thyroid Journal 2020, 9(1): 11-18. https://doi.org/10.1159/000502204.

[8] L. A. Mack and J. L. Pasieka. An Evidence-Based Approach to the Treatment of Thyroid Lymphoma.*World J Surg2007*, 31(5): 978-986. doi: 10.1007/s00268-005-0768-z.

[9] E. Campo , N. L. Harris , E. S. Jaffe , S. A. Pileri , H. Stein , J. Thiele , et al.WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues Revised 4th Edition.

[10] Sasaki, Yosuke, EisukeShiozawa, Natsuko Watanabe, Mayumi Homma, Jaeduk Yoshimura Noh, Koichi Ito, et al. T (3;14) (P14.1;Q32)/FOXP1-IGH Translocation in Thyroid Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT Lymphoma) . LeukemiaResearch2020,95:106399.https://doi.org/10.1016/j.leukres.2020.106399

[11] T. Kahara, N Iwaki, H Kaya, T Kurokawa, T Yoshida, K Ishikura, et al. Transition of thyroid autoantibodies by rituximab treatment for thyroid MALT lymphoma .Endocr J 2011, 58 (1): 7-12. doi: 10.1507/endocrj.K10E-166.

[12] Beasley, M.J. Lymphoma of the Thyroid and Head and Neck. *Clinical Oncology* 2012, 5: 345-51. https://doi.org/10.1016/j.clon.2012.02.010.

[13] J. I. Hamburger. Lymphoma of the Thyroid .*Ann Intern Med 1983*, 99 (5): 685. doi: 10.7326/0003-4819-99-5-685.