MALT LYMPHOMA PRESENTING IN THE THYROID GLAND: A REPORT OF THREE CASES AT VIETNAM NATIONAL CANCER HOSPITAL

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Abtract:

Primary lymphoma presenting in the thyroid gland is rare, accounting for 2-8% of thyroid malignancies and 1-2% of extranodal malignancies. Mucosal lymphoid tissue-associated lymphoma (MALT) is one of the rare variants, first described by Isaacson and Wright in 1984. Primary MALT lymphoma of the thyroid gland accounts for 6-28% of tumors, closely related to chronic inflammatory or local autoimmune processes because thyroid tissue has no lymphatic organs. The coexistence between local inflammation and tumor formation causes many difficulties in disease diagnosis. Clinically, most patients are diagnosed at the age of over 60, with about 30% of patients having symptoms of local compression related to the tumor such as difficulty swallowing, shortness of breath, hoarseness. The standard treatment in MALT lymphoma is radiotherapy combined with chemotherapy; Surgery is valuable in diagnosis and symptom resolution. For asymptomatic patients regardless of stage who can be closely monitored, no treatment is required. In general, MALT lymphoma has a good prognosis, different from other histopathological types such as diffuse large B-cell lymphoma. Currently, there are not many reports on this clinical form, so we report 3 clinical cases, thereby drawing experience in the diagnosis and treatment of MALT lymphoma in the thyroid gland.

Key words: Primary thyroid lymphoma; MALT.

1. INTRODUCTION

Primary thyroid lymphoma (PTL) is a rare malignant disease, accounting for approximately 2–8% of all thyroid malignancies and less than 1–2% of all extranodal lymphomas. PTL primarily belongs to the group of non-Hodgkin B-cell lymphomas. Among these, diffuse large B-cell lymphoma (DLBCL) is the most common subtype, comprising 60–80% of cases, followed by mucosa-associated lymphoid tissue (MALT) lymphoma also known as extranodal marginal zone B-cell lymphoma accounting for 6–28% of cases. Several studies have demonstrated a strong association between thyroid MALT lymphoma and chronic lymphocytic thyroiditis (Hashimoto's thyroiditis). This correlation presents diagnostic challenges in both cytological and histopathological evaluations, as MALT lymphoma must be differentiated from other primary thyroid neoplasms with similar presentations. Treatment options for thyroid MALT lymphoma include surgery, radiotherapy and chemotherapy, with a generally more favorable prognosis compared to other histological subtypes of thyroid lymphomas. However, due to the rarity of this disease, there are limited reports in the medical literature. Therefore, we present three clinical cases of thyroid MALT lymphoma to review its pathological characteristics and treatment outcomes.

1.1. Clinical case descriptions

Three cases of thyroid MALT lymphoma treated at Vietnam National Cancer Hospital between March 2016 and May 2019 were included in this study. The clinical presentation, diagnostic workup, and treatment details are summarized in Table 1.

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	Patient 1	Patient 2	Patient 3
Age	56	69	42
Sex	Female	Female	Female
Medical history	Healthy	Healthy	Healthy
Thyroid tumor size	4 cm	8 cm	4 cm
Tumor location	Bilateral lobes	Bilateral lobes	One lobe
Cervical lymphadenopathy	Bilateral, max 17 mm	Bilateral, max 17 mm	None
Other lymphadenopathy	Bone marrow, abdominal lymph nodes	None	None
B symptoms	Absent	Absent	Absent
TSH	Normal	Normal	Normal
FT4	Normal	Normal	Normal
Diagnosis	After total thyroidectomy	After total thyroidectomy	After hemithyroidectomy
Histopathology	MALT lymphoma	MALT lymphoma	MALT lymphoma
Ann Arbor Stage	IVAE (thyroid, cervical and abdominal lymph nodes, bone marrow)	IIE (thyroid, cervical lymph nodes)	IE (thyroid only)
Treatment	Observation	Surgery + R-CVP	Surgery + R-CVP
Survival status	Alive	Alive	Alive
Follow-up duration	24 months	49 months	81 months

The mean age of the three patients was 54 years (range: 42–69 years), and all were female. All patients presented with a palpable neck mass, and one reported dysphagia due to compressive effects of a large thyroid tumor. Other clinical signs were stable.

On physical examination, all three patients had large thyroid masses with bilateral cervical lymphadenopathy. The mean tumor size was 5.3 cm (range: 4–8 cm). None of the patients exhibited B symptoms.

Neck ultrasound was the initial imaging modality employed, revealing multifocal lesions involving both thyroid lobes. The lesions appeared as heterogeneous hypoechoic or hyperechoic masses. All three patients underwent fine-needle aspiration cytology (FNAC), which failed to suggest a diagnosis of non-Hodgkin lymphoma in any case. Consequently, thyroidectomy (total or lobectomy) was performed for diagnostic purposes. Intraoperative frozen section analysis was suggestive of lymphoma, which was subsequently confirmed by routine histopathological examination. Immunohistochemistry supported the diagnosis of MALT lymphoma, with tumor cells positive for CD20, CD22, and CD79a, and negative for CD5 and CD10.

Regarding disease staging, two patients were classified as stage IIAE according to the Lugano classification and received chemotherapy with the R-CVP regimen. The number of cycles ranged from 3 to 9, with complete response observed in both cases. The remaining patient was staged as IVAE; however, due to the absence of clinical symptoms and not meeting GELF criteria for treatment initiation, the patient was managed with active surveillance. During a mean follow-up period of 17 months (range: 5–24 months), all patients remained alive with no evidence of disease progression.

2. DISCUSSION

Primary MALT lymphoma of the thyroid is an indolent subtype with a typically slow progression and minimal clinical symptoms. While B symptoms are commonly seen in 40–50% of non-Hodgkin lymphomas (NHL), they are rare in MALT lymphoma, making early clinical diagnosis challenging for physicians. Although the exact pathogenesis of thyroid MALT lymphoma remains unclear, Kuper-Hommel et al. suggested that the disease arises as a result of chronic autoimmune stimulation, particularly associated with Hashimoto's thyroiditis. This mechanism is similar to that observed in gastric MALT lymphoma, which is commonly linked to Helicobacter pylori infection. In 2009, Munemasa and colleagues studied B-cell reactivity to thyroglobulin, demonstrating that immunohistochemical analysis of MALT lesions revealed thyroglobulin presence in follicular dendritic cells within the germinal centers.

Fine-needle aspiration (FNA) is often the first-line diagnostic tool for thyroid nodules. However, in the case of thyroid lymphomas, especially MALT subtype, cytological features can closely resemble reactive lymphoid infiltrates seen in Hashimoto's thyroiditis, thereby reducing diagnostic accuracy. Sangalli et al. analyzed 17 cases of thyroid lymphoma and found that only 4 out of 10 MALT lymphoma cases were correctly diagnosed via cytology. In our three reported cases, cytological evaluation failed to indicate lymphoma. Histopathology and immunohistochemistry remain essential for definitive diagnosis, with MALT lymphoma showing positivity for CD20, CD22, and CD79a, and negativity for CD5 and CD10.

MALT lymphoma is a low-grade malignancy with slow progression; however, complete cure is rare, and relapse may occur, particularly in advanced stages. Treatment strategies are not standardized due to the rarity of the disease and vary depending on stage and histological subtype. Chemotherapy and radiotherapy are the mainstays of treatment. Radiotherapy is considered the treatment of choice for localized disease and can potentially result in cure. Surgery plays a limited therapeutic role and is primarily used for diagnosis via biopsy or in symptomatic cases to relieve airway obstruction. It may be considered in selected cases with localized, resectable lesions such as those in the breast, lung, colon, or thyroid. In a study by Nam YJ, Kim BH, and Lee SK et al., patients with localized disease who underwent thyroidectomy showed a 100% 5-year survival rate. Similarly, Saito et al. demonstrated that for stage IE MALT lymphoma, surgical management was associated with fewer treatment-related complications such as xerostomia from radiotherapy and reduced local recurrence. For patients with longstanding, asymptomatic lesions, active surveillance can be considered across all stages, and treatment may be deferred unless clinical criteria for intervention such as those defined by the Groupe d'Etude des Lymphomes Folliculaires (GELF) are met. Chemotherapy remains an important option for advanced-stage disease. Common regimens include R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone).

In our report, all three patients underwent thyroidectomy (total or lobectomy) primarily for diagnostic confirmation and to alleviate

compressive symptoms. In the first case, although the disease was staged as IV, the patient remained asymptomatic and did not meet GELF treatment criteria; therefore, active surveillance was adopted. After a 3-year follow-up, the disease showed signs of progression but did not yet warrant treatment. The other two patients received R-CVP chemotherapy according to GELF criteria and achieved good treatment responses. They remained disease-free at follow-ups of 49 and 81 months, respectively.

Prognosis is largely dependent on disease stage. In general, MALT lymphoma has a favorable prognosis, with median overall survival exceeding 10 years. The MALT-IPI prognostic index (age >70 years, stage III/IV disease, elevated LDH) can help stratify patients by risk. Five-year overall survival (OS) rates in low, intermediate and high-risk groups are approximately 99%, 93% and 64%, respectively. In our study, the median follow-up duration was 51 months (range: 24–81 months). All patients were alive at the time of last follow-up, with no evidence of relapse or disease progression.

These findings underscore that although complete cure is uncommon, MALT lymphoma particularly when presenting in the thyroid has an indolent course with favorable prognosis. Patients may remain asymptomatic and live for many years with the disease without requiring immediate treatment.

3. CONCLUSION

Primary MALT lymphoma of the thyroid is a rare entity, and its diagnosis often poses significant challenges. Chemotherapy and radiotherapy remain the mainstays of treatment, while surgery is typically reserved for diagnostic purposes or to alleviate compressive symptoms. Active surveillance is an appropriate management strategy in asymptomatic cases. The prognosis is generally favorable, with a median overall survival exceeding 10 years.

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