REVIEW

Primary thyroid lymphoma: Case report and review of the literature

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Abstract Primary thyroid lymphoma (PTL) is defined as a lymphoma involving only the thyroid gland or both thyroid gland and neck lymph nodes, without contiguous spread or distant metastases from other areas of involvement at diagnosis. Despite its rarity, PTL should be promptly recognized because its management is quite different from the treatment of other neoplasms of the thyroid gland.

In the present study, we report a case of PTL treated by surgery and adjuvant chemotherapy. Otherwise, literature review allowed us to define main characteristics of this located lymphoma.

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1. Case report

A 67-year-old woman presented with a rapidly growing (2 weeks) painless thyroid enlargement with a left supraclavicular neck mass, without compressive symptoms. The CT scan showed a multi nodular goiter with a suspicious left nodule measuring 3 cm. It also showed lymph nodes of left II, III, IV groups, two of which were necrotic, without other abnormalities (Fig. 1).

Fine Needle Aspiration of both thyroid nodule and supraclavicular lymphadenopathy found suspicious cells suggestive of malignancy.

She had, then, undergone total thyroidectomy with radical left neck dissection taking away the jugular vein and sternocleido-mastoid muscle. Frozen section exam revealed metastatic lymphadenopathy and unspecified thyroid malignant neoplasm. Postoperative course was marked by acute dyspnea,
related to left vocal cord paralysis, which needed a tracheotomy.

Definitive histology (Fig. 2) concluded to diffuse large B-cell Lymphoma of thyroid with metastatic regional lymph nodes.

Assigned Ann Arbor classification was IIE. Treatment was, hence, completed by chemotherapy. She had six RCHOP chemotherapy cycles (Rituximab–Cyclophosphamide–doxorubicine–vincristine–prednisone). After 12 months follow-up, our patient is disease free.

2. Discussion

Primary thyroid lymphoma is an uncommon pathological entity and constitutes 5% of all thyroid malignancies. It occurs in less than 3% of all non-Hodgkin’s extra-nodal lymphomas. It is an uncommon condition which, to be categorized as such, must only affect the thyroid gland and, eventually, the loco-regional lymph nodes. Primary disease in other location should be ruled out. Diagnosis of PTL is complex, and surgery is often required to make a definitive diagnosis. Therapeutic management has greatly changed over time, and chemotherapy, with or without radiotherapy is the current treatment of choice.

PTL is more commonly observed in females than in males (F/M = 4/1). Most patients present in the 7th decade of life (average age 67 years), with a rapidly enlarging neck mass. Preexisting chronic autoimmune (Hashimoto’s) thyroiditis is a well-recognized risk factor predisposing to the development of PTL. It has been reported that the risk of PTL among patients with autoimmune (Hashimoto’s) thyroiditis is 40 times greater compared to that of the general population. It takes a long time (20–30 years) to develop PTL after the onset of lymphocytic thyroiditis.

Normally, the thyroid gland does not contain native lymphoid tissue. Intra-thyroid lymphoid tissue develops under pathological conditions, and mainly in patients with autoimmune (Hashimoto’s) thyroiditis, probably as a result of chronic antigenic stimulation. This acquired lymphoid tissue resembles mucosa-associated lymphoid tissue and can evolve to non-Hodgkin lymphoma of B-cell origin, which is the most common type of PTL. Diffuse large B-cell lymphoma (DLBCL) and extra-nodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) lymphoma are its common subtypes (representing 70% and 15–30% of all primary non-Hodgkin PTLs, respectively).

A rapidly growing (usually within 1–3 months), painless thyroid enlargement, either in the form of goiter or discrete nodule, is the most common clinical presentation in PTL. Pressure symptoms (dysphagia, dyspnea, stridor, cough, hoarseness, superior vena cava syndrome) are often present. This clinical presentation can be confused with anaplastic thyroid carcinoma like in our case. Because of the frequent coexistence of Hashimoto’s thyroiditis, many patients are hypothyroid or under thyroid hormone replacement therapy. Classic B-type symptoms of fever, night sweats and weight loss are less common. Clinical examination can detect diffuse or nodular thyroid enlargement.

Because of the frequent coexistence of Hashimoto’s thyroiditis, circulating antibodies to thyroid peroxidase are positive in a large percentage of patients (60%).

Imaging studies (ultrasonography, computed tomography) reveal a diffusely enlarged thyroid gland (resembling goiter) or a nodular thyroid gland (solitary or multiple thyroid nodules, commonly cold), mimicking thyroiditis or a primary thyroid follicular lesion.

Nowadays, fine-needle aspiration (FNA) is an essential tool in the management of thyroid diseases. However, FNA has yielded inconsistent results in the diagnosis of PTL. Rates of achieving a positive diagnosis range widely, in the literature, from 25% up to 90%. PTL should be strongly considered when the aspirated specimen predominantly consists of lymphocytes.

PTL should be differentiated from lymphomas at other sites. This is especially important given the rarity of PTL. In this case, lymphoma of the thyroid gland could be the result...
of secondary involvement of the gland by the tumor. Moreover, PTL should be differentiated from Hashimoto’s thyroiditis and from poorly differentiated, undifferentiated or anaplastic thyroid carcinomas. Adjunctive techniques (immuno-histo-chemistry, flow cytometry, etc.) are of particular importance in differentiating PTL from anaplastic thyroid carcinoma; this is an important consideration given that management and prognosis of these two diseases is totally different.

The role of surgery in the management of PTL remains highly controversial. There are reports in the literature supporting the role of surgery in the management of selected patients with PTL. Surgery alone has been proposed for the management of localized (stage IE, ANN ARBOR Classification) intra-thyroidal lymphoma.9-12 When there is any question of incomplete surgical resection, adjuvant external beam radiation therapy should be considered postoperatively.

Like surgery, external beam radiation therapy alone has been proposed for the management of localized (stage IE) lymphoma. There is evidence that radiation therapy can achieve local control of the disease. The radiation field includes the neck plus the upper mediastinum and the treatment dose is moderate (30–50 Gy).11-13

Chemotherapy can control distant dissemination of the disease, while radiation therapy can achieve local control of the lymphoma. The conventional chemotherapeutic regimen for PTL includes cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP). Typically, patients with PTL respond rapidly to this regimen. Systemic chemotherapy is usually associated with the typical radiation therapy (chemo-radiation therapy). Most commonly, radiation therapy is used after 3–6 courses of chemotherapy.10,12 Combined chemo-radiation therapy is associated with a significantly lower risk of distant failure. Rituximab has recently been effectively used (with cyclophosphamide, mitoxantrone, vincristine, and prednisolone) in elderly patients with diffuse large B-cell lymphoma of thyroid.14

The prognosis of patients depends on the histological grade of the tumor and the stage of the disease. MALT lymphomas tend to have a more indolent course and a better prognosis compared with patients with diffuse large B-cell lymphoma (DLBCL) or mixed histological subtypes, which have a more aggressive clinical course. Patients with MALT lymphoma had significantly higher complete response rates than those with DLBCL both for early as well as for advanced disease. Overall, 5-year survival ranges between 50 and 60%.15,16

References