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ORIGINAL ARTICLE

The incidence of primary thyroid lymphoma in thyroid malignancies

Tiroit neoplazileri içinde primer tiroit lenfoma sıklığı

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Objectives: We investigated the incidence of primary thyroid lymphoma in thyroid malignancies.

Patients and Methods: A total of 304 patients whose diagnoses were made as thyroid malignancies between January 1990 and December 2000 were retrospectively evaluated. Of these, primary thyroid lymphoma was documented in four female patients (1.3%; mean age 56.2 years; range 40 to 65 years). Findings from history, physical examination, blood biochemistry, thyroid hormone levels (T_3, T_4, TSH, thyroglobulin), thyroid scintigraphy, fine-needle aspiration biopsy, and cervical computed tomography (CT) were evaluated. Histopathologic results were evaluated according to the Revised European-American Lymphoma (REAL) classification.

Results: The most common complaints on admission were a rapidly growing cervical mass, hoarseness, and dyspnea. In all the cases, thyroid hormone levels were normal, but thyroglobulin levels were 5 to 10 times as high as normal. Preoperative fine-needle aspiration was not helpful in two cases, whereas cervical CT was diagnostic. Pathologic diagnosis was diffuse large B cell lymphoma in all the cases. Postoperatively, three cases underwent chemotherapy and one case chemotherapy combined with radiotherapy. All the patients were operated on before 1997; one patient died, the remaining three patients have been under follow-up with no recurrences.

Conclusion: In our cases, treatment of localized thyroid lymphoma by surgery combined with chemotherapy or/and radiotherapy was effective.

Key Words: Lymphoma/pathology/surgery; thyroid neoplasms/pathology/surgery; thyroidectomy.

Amaç: Tirot malignitesi tanısı konan olgular içinde primer tiroit lenfoma sıklığı araştırıldı.

Hastalar ve Yöntemler: Ocak 1990 ile Aralık 2000 tarihleri arasında tirot malignitesi saptanan 304 olgunun geriye dönük incelemesinde dört olguda (%1.3) primer tiroit lenfoması saptandı. Tümü kadın olan dört hastanın yaş ortalaması 56.2 (dağılım 40-65) idi. Tüm hastalar fizik muayene, tam biyokimya incelemesi, tiroit hormon düzeyleri (T_3, T_4, TSH, tiroglobulin), tiroit sintigrafisi, tiroit ince iğne aspirasyon biyopsisi ve boyun bilgisayarlı tomografisi (BT) ile değerlendirildi. Histopatolojik sonuçlar REAL (Revised European-American Lymphoma) sınıflandırmasına göre değerlendirildi.

Bulgular: Hastalarda en yaygın şikayet boyunda büyüyen kitle, nefes darlığı ve horlamaydı. Tüm hastaların tiroit hormon seviyeleri normal, tiroglobulin düzeyleri ise normalden 5-10 kat yüksek bulundu. Ameliyat öncesi değerlendirmede iki hastada ince iğne aspirasyon biyopsisi sonuç vermezken boyun BT'si tanıda yardımcı oldu. Tüm hastalarda histopatolojik tanı B hücreli lenfoma idi. Ameliyat sonrasında üç hastaya kemoterapi, bir hastaya radyoterapi ve kemoterapi uygulandı. Hastaların tümü 1997 yılından önce ameliyat edildi; bir hasta kaybedildi, üç hasta nüks olmaksızın izlenmektedir.

Sonuç: Lokalize tiroit lenfomalı olgularımız dikkate alındığında, cerrahi tedavi ile birlikte kemoterapi ve/veya radyoterapinin etkili olduğunu söyleyebiliriz.

Anahtar Sözcükler: Lenfoma/patoloji/cerrahi; tiroit neoplazisi/patoloji/cerrahi; tiroidektomi.

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Although primary thyroid lymphomas are rarely encountered, there has been a gradual increase in its incidence in recent years. Of all extranodular non-Hodgkin's lymphomas, 2-3% arise in the thyroid gland. Early diagnosis is important because primary thyroid carcinomas account for 5% or less of all thyroid cancers.[1,2,3] The most characteristic presentation is a rapidly enlarging neck mass often associated with dysphagia.[4] The choice of treatment is still controversial. Despite the fact that non-Hodgkin's thyroid lymphomas respond to both chemotherapy and radiotherapy, there are still proponents of radical surgical resection. However, the role of surgery seems to be limited to obtaining tissue for diagnosis and to limited resection when the airway is compromised.[2,4-7] As reported in different series, the five-year survival of primary thyroid lymphomas ranges from 42% to 74%.[8]

PATIENTS AND METHODS

Between January 1990 and December 2000, 304 thyroid malignancies were detected and treated in the Department of General Surgery of Istanbul Medical Faculty. Four of these (1.3%) were primary thyroid lymphomas. All the patients were females with a mean age of 56.2 years (range 40 to 65 years).

Findings from history, physical examination, blood biochemistry, thyroid hormone levels (T_3, T_4, TSH, thyroglobulin), thyroid scintigraphy, fine-needle aspiration, and cervical computed tomography (CT) scans were evaluated. In three cases signs of laryngeal obstruction were evident, for which indirect laryngeal examinations were also performed. Histopathologic evaluations were made according to the Revised European-American Lymphoma (REAL) classification. In order to define the primary focus, postoperative abdominal and thoracic CT scans were routinely obtained.

RESULTS

The most common complaints were a rapidly growing cervical mass, hoarseness, and dyspnea. The duration of complaints ranged from five months to two years. Preoperatively, all the patients had normal thyroid hormone levels (euthyroid), whereas thyroglobulin levels were 5 to 10-fold high. Thyroid scintigraphy revealed a hypoactive solitary nodule in three cases, and multinodular goitre in one case. Fine-needle aspiration yielded insufficient material in two cases, while in the remaining two cases malignant lymphoid cells were obtained.

In all the cases, cervical CT scans were obtained preoperatively. In one case a cervical mass was observed, extending from the level of thyroid to the T_1 vertebral body, and deviating the larynx to the left with invasion to the right vocal cord.

Indirect laryngoscopic examination showed a fixed paralytic vocal cord at the paramedian line. In all the cases, postoperative abdominal and thoracic CT scans were obtained. There were no systemic findings except for one case in which cranial CT scan disclosed cranial metastasis.

All the cases underwent bilateral total thyroidectomy. Histopathologic findings were as follows: the lymphomas ranged in size from 2.5 cm to 9 cm on cross section. The tumors were firm to soft solid masses. The cut surface was tan or white-gray in color, homogeneous to mottled appearance. Microscopically, all cases had a background of Hashimoto's thyroiditis with reactive follicles and Hurthle cell transformation of the thyrocytes. Neoplastic cells demonstrated centroblastic, immunoblastic, monocytoid B cell and plasmacytoid differentiation (Fig. 1, 2). A lymphoepithelial lesion could be identified in one case and immunohistochemically neoplastic lymphoid cells showed positive immunoreactivity to CD20 antibody.

In one case tracheotomy was indicated. All the patients were discharged on the third postoperative day and referred to the oncology department.

The patient with cranial metastasis received combination chemotherapy CHOP (doxorubicin 50 mg/m^2, cyclophosphamide 750 mg/m^2, vincristine 1.4 mg/m^2, prednisone mg/m^2) and radiotherapy (a total of 40 Gy given as a fractionated course over 4 weeks). She died from respiratory depression in the third postoperative month.

The remaining three patients received chemotherapy alone. They have been under follow-up without any recurrences.

DISCUSSION

The rate of lymphomas in all thyroid malignancies is 5 percent, though there has been an increase in the number of new cases in recent years. This neo-

plasm occurs most frequently in the sixth decade. In contrast to lymphomas of other organs, thyroid lymphomas are 2 to 6 times more common in women.[2,5] The chance of a lymphoma to arise from the thyroid tissue is very low. In different series, the incidence of thyroid lymphomas was reported to be approximately 2.5%.[9] Hashimoto's disease, chronic lymphocytic thyroiditis, frequently accompanies thyroid lymphomas. Rasbach et al.[10] showed on histopathological examinations that 78% of lymphomas were associated with chronic lymphocytic thyroiditis. Sirota and Segal[11] reported that the rate of thyroid lymphomas was 1.4 percent in patients with Hashimoto's disease. Holm et al.[12] evaluated 829 patients with chronic lymphocytic thyroiditis and reported that the risk of lymphoma development was as high as 67 times.

It was suggested that lymphomas could arise from active lymphocytes on the background of chronic lymphocytic thyroiditis. Therefore, a thyroid mass and positive antithyroid antibodies may not only suggest Hashimoto's disease, but also a primary thyroid lymphoma.[13]

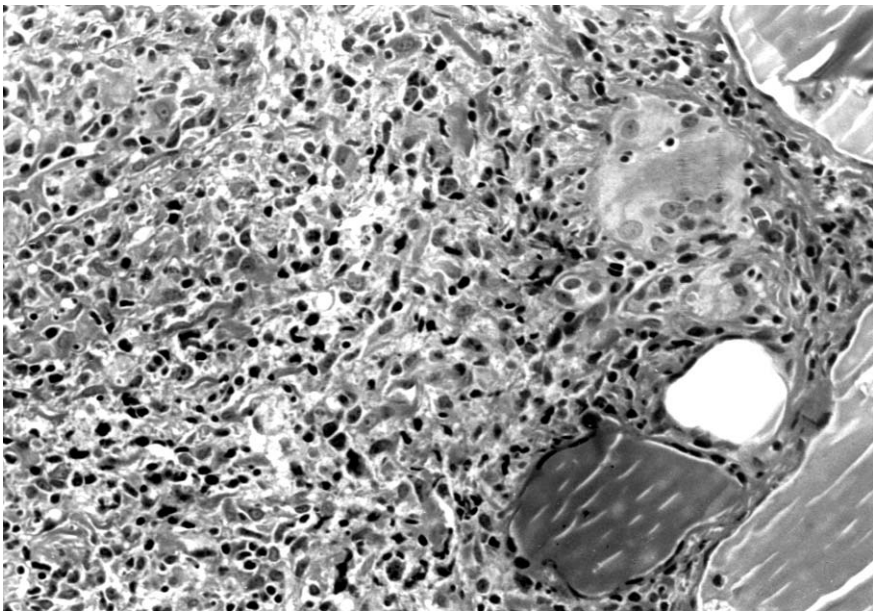

Fig. 1 - *Neoplastic cells with a diffuse growth pattern surrounding thyroid follicles (H-E x 300).*

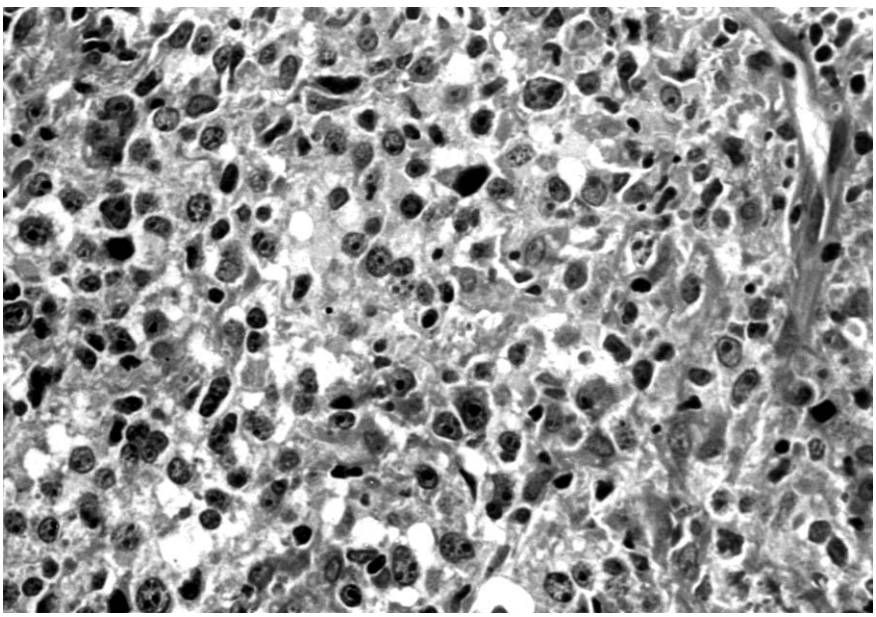

Fig. 2 - *Neoplastic lymphoid cells showing centroblastic, immunoblastic differentiation (H-E x 500).*

Apart from Hashimoto's disease, this neoplasm may also be associated with autoimmune disorders, such as Sjögren's syndrome, and immunosuppressive conditions. It has been suggested that Epstein-Barr virus can play an important role in the development of chronic lymphocytic thyroiditis and thyroid lymphoma.[14]

In general, thyroid lymphomas are seen as small or large solitary nodules, but they may sometimes present as a diffuse or multinodular goitre. In our patients, three hypoactive solitary nodules and one multinodular goitre were observed. Thyroid lymphomas are different from other thyroid malignancies, in that an important number of cases are clinically hypothyroid or thyroid hormone levels are low.[15] Clinical and pathological indicators of prognosis are controversial. Several authors found no correlation between histologic type and prognosis,[4] whereas, some stated that nodular lymphomas had a better prognosis than that of diffuse tumors.[4,16,17]

Fine-needle aspiration is the keystone in diagnosis. However, false negative results may be seen. Discrimination between a lymphoma and lymphocytic thyroiditis may be difficult. In our patients, fine-needle aspiration was ineffective in two cases. Ogawa et al.[18] underlined the value of ultrasound-guided fine-needle aspiration cytology for thyroid nodules.

The most common type of thyroid lymphoma is large cell non-Hodgkin's lymphoma.[19] In our patients, all cases were large cell immunoblastic tumors.

The preferred treatment for thyroid tissue lymphomas is bilateral total thyroidectomy. Many patients present with tracheal obstruction at diagnosis. Hence, if radiation therapy is the choice of treatment, the patients need a tracheotomy before all else. After surgery, irradiation of cervical lymph nodes and systemic chemotherapy is effective.[15,19,20]

Early diagnosis influences the survival. The prognosis of tumors localized in the thyroid is good. The five-year survival rate is approximately 80 percent for tumors localized in the neck; however, tissue invasion may result in a decrease of 35 to 40 percent. The mean five-year survival rate of thyroid lymphomas has been reported as 42 to 74 percent.[8]

In conclusion, thyroid lymphomas are relatively rare. However, in case of an enlarging mass in the neck they should be kept in mind. Ultrasound-guided fine-needle aspiration cytology is an appropriate initial step when there is a high index of suspicion for a non-Hodgkin's lymphoma. Finally, in primary thyroid lymphomas localized in the thyroid, surgery associated with chemotherapy and/or radiotherapy may give favorable results.

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