***Original Article / Çalışma - Araştırma***

# Diagnosis and treatment of malignant lymphomas of parotid gland

## Parotis bezi malign lenfomalarında tanı ve tedavi

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***ABSTRACT***

**Objectives:** This study aims to report surgical outcomes of primary parotid lymphomas and to discuss the histopathological subtypes, incidence rates, and clinical course.

**Patients and Methods:** Between January 2002 and December 2014, eight patients (2 males, 6 females; man age 46.6 years; range 25 to 60 years) who were diagnosed with primary parotid lymphoma and underwent parotidectomy were retrospectively analyzed. Demographic characteristics of the patients, histopathological subtypes, disease stage, and survival rates were recorded.

**Results:** The ratio of the patients diagnosed with lymphoma was 2.82% among all patients, while 18.1% of the malignancies were lymphomas. Fine needle aspiration biopsy was non-diagnostic. CD20-positive low-grade B-cell lymphoma was the most common histopathological subtype in 37.5% of the patients.

**Conclusion:** Based on our study results, the fine needle aspiration biopsy is not helpful in the diagnosis of the lymphomas of the parotid gland. Although rarely seen, lymphomas of the parotid gland should be considered in the differential diagnosis.

***Keywords:*** Parotid gland; primary parotid lymphoma; salivary gland neoplasm.

***ÖZ***

**Amaç:** Bu çalışmada primer parotis lenfomaların cerrahi sonuçları bildirildi ve histopatolojik alt tipleri, insidans oranları ve klinik seyri tartışıldı.

**Hastalar ve Yöntemler:** Ocak 2002 - Aralık 2014 tarihleri arasında primer parotis lenfoma tanısı konulan ve parotidektomi yapılan sekiz hasta (2 erkek, 6 kadın; ort. yaş 46.6 yıl; dağılım 25-60 yıl) retrospektif olarak incelendi. Hastaların demografik özellikleri, histopatolojik alttipleri, hastalık evresi ve sağkalım oranları kaydedildi.

**Bulgular:** Lenfoma tanısı konulan hastaların tüm hastalar içerisindeki oranı %2.82 olup malign olguların %18.1'ini lenfomalar oluşturdu. İnce iğne aspirasyon biyopsisi tanısal değildi. CD20 pozitif düşük grade B hücreli lenfoma, hastaların %37.5'inde en sık görülen histopatolojik alt tip idi.

**Sonuç:** Çalışma sonuçlarımıza göre, ince iğne aspirasyon biyopsisi parotis bezi lenfomalarının tanısında yardımcı değildir. Nadir görülmesine rağmen, parotis bezi lenfomaları ayırıcı tanıda göz önünde bulundurulmalıdır.

***Anahtar Sözcükler:*** Parotis bezi; primer parotis lenfoma; tükürük bezi neoplazisi.

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Non-Hodgkin and Hodgkin lymphoma are the most frequently observed head and neck tumors after squamous cell carcinoma and thyroid carcinomas.[1] In the head and neck region, 23% of non-Hodgkin lymphomas and 4% of Hodgkin lymphomas are located extranodally.[2] They are most frequently observed in Waldeyer's ring, the nasal cavity-paranasal sinuses, oral cavity and salivary glands.

Primary lymphomas of the salivary gland are rarely observed. Primary malignant lymphomas constitute 1.7-3.1% of all salivary gland neoplasms and 0.6-5% of tumors and tumor-like lesions of the parotid gland.[3]

The aim of this study is the retrospective investigation of patients who presented with parotid masses and underwent surgery with the diagnosis of primary parotid lymphoma, and to evaluate the histopathological subtypes, incidence rates and clinical course in the light of the related literature.

## PATIENTS AND METHODS

For the purposes of the study, 278 patients (148 males, 130 females; mean age 54.4 years; range 8 to 85 years) who were operated on due to parotid masses at Akdeniz University School of Medicine, Department of Otorhinolaryngology, between January 2002 and December 2014 were retrospectively evaluated. The patients' age, sex, type of surgery, and histopathology results were assessed. The files of those who were diagnosed with parotid lymphoma were evaluated in detail. The age, sex, histopathological subtype and cell type, disease grade, applied therapies, histopathology results and the survival of these patients were recorded. Metastatic parotid gland lymphomas were excluded from the study.

## RESULTS

According to histopathology results, 234 (84.1%) of the patients had benign lesions, while 44 (15.9%) had malignant lesions.

Of the 278 patients, eight (2 males, 6 females; mean age 46.6 years; range 25 to 60 years) were diagnosed with lymphomas. Lymphomas constituted 2.82% of all the patients enrolled in the study and 18.1% of the malignant cases. Based on histopathological subtype of these cases, three patients had CD20-positive low grade B-cell lymphoma (37.5%), two patients had extranodal marginal zone lymphoma (25%), two patients had Hodgkin's lymphoma (25%), and one patient had CD20-positive high grade B-cell lymphoma (12.5%) (Figure 1).

The lesions were located in the superficial lobe in all eight patients. The fine needle aspiration biopsy (FNAB) performed in all these patients before surgery did not point to any malignancies. All the patients had undergone superficial parotidectomies and their treatment was planned in consultation with the hematology clinic after diagnosis. The clinical data, disease grades and the therapies they received are presented in Table 1.

## DISCUSSION

Extranodal lymphomas of the head and neck are rarely observed.[4] Those that are located in the parotid gland are extremely rare (0.2-0.8%).[5] They originate from the mucosa-associated lymphoid tissue (MALT) or intraglandular lymph nodes in the parenchyma. While a mass lesion in the parotid gland may be the initial finding of the disease, it may also be a secondary focal point. In all eight patients included in our study, the first point of diagnosis of the disease was the parotid. In the study by Barnes et al.[6] including 41 patients with parotid lymphoma, 33 patients (80.4%) had primary lesions, while eight patients (19.6%) had secondary lesions. The great majority of the lymphomas in the salivary glands were non-Hodgkin and B-cell lymphomas (84-94%), whereas Hodgkin's lymphoma was observed in 3-16%.[7-9] T-cell lymphomas were rather rare.[10]

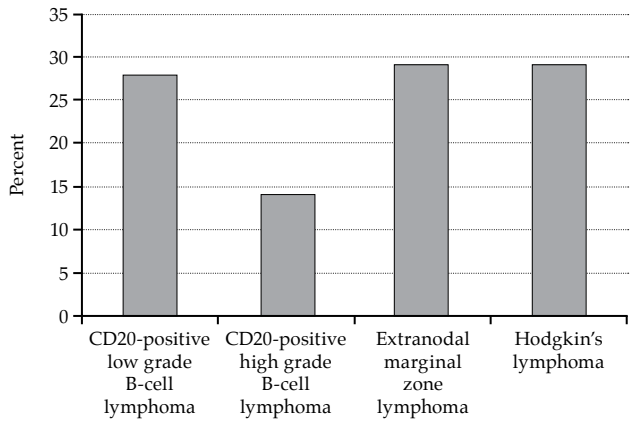


***Figure 1.*** *Distribution of the patients according to the histopathological subgroups.*

**Table 1.** The general characteristics, disease grade, survival and applied therapy

| Patient | Age/Gender | Histopathological subgroup | Disease (grade) | Location | Survival (months) | Therapy |
|---|---|---|---|---|---|---|
| 1 | 60/F | CD20-positive low grade B-cell lymphoma | 3 | Right superficial lobe | 108 | 6 sessions of CHOP |
| 2 | 52/F | CD20-positive high grade B-cell lymphoma | 3 | Right superficial lobe | 36 | 8 sessions of RCHOP |
| 3 | 35/F | Extranodular marginal zone lymphoma | 3 | Right superficial lobe | 84 | 6 sessions of CHOP+RT |
| 4 | 56/F | Hodgkin's lymphoma | 2A | Left superficial lobe | 24 | 8 sessions of ABVD |
| 5 | 48/M | CD20-positive low grade B-cell lymphoma | 1A | Left superficial lobe | 18 | 8 sessions of RCHOP |
| 6 | 25/F | Extranodular marginal zone lymphoma | 1A | Right superficial lobe | 36 | 8 sessions of CHOP |
| 7 | 53/F | CD20-positive low grade B-cell lymphoma | 1A | Left superficial lobe | 20 | Therapy data could not be obtained since the patient was transferred to another center |
| 8 | 44/M | Hodgkin's lymphoma | 1A | Left superficial lobe | 7 | 4 sessions of ABVD |

CHOP: Cyclophosphamide, doxorubicin, vincristine and prednisone; R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; RT: Radyoterapi; ABVD: Adriamycin, bleomycin, vinblastine and dacarbazine.

As we mentioned before, parotid lymphomas may originate from the intraglandular lymph nodes or the parenchyma (MALT). This point is clinically relevant and the lymphomas originating from the parenchyma may be of lower grade and more curable than the intraglandular lymphomas.[6,10]

The condition is mostly observed between 50-80 years of age.[11,12] The incidence of disease between females and males in the literature vary. Tiplady et al.[13] and Feinstein et al.[14] reported the F/M ratio as 1.3/1, while Barnes et al.[6] reported it as 1.1/1. In our study, this ratio was 3/1. We are of the opinion that this different result from the literature is associated with the lower number of patients in our study.

These lymphomas are usually observed as unilateral, painless, and rapidly growing masses and may be accompanied by cervical lymphadenopathies. They may rarely be located in both parotid glands and involve both parotids and the submandibular gland.[15,16] Primary parotid lymphomas may be concurrent with autoimmune diseases. The most commonly observed concurrent autoimmune disease is Sjögren's syndrome. In patients with primary Sjögren's syndrome, the risk of lymphomas has been reported as 4.3-6% and 80% of these are MALT lymphomas.[17,18] None of our patients had a history of concurrent autoimmune disease.

Different classification systems may be used in malignant lymphomas. The World Health Organization classification (1998), Working Formulation for Clinical Usage (1982) classification, and the Revised European-American Lymphoma classification (REAL-1994) are among the leading ones. The Working Formulation is a system based on histopathology and cytopathology. However, it does not consider the immunobiological features of the tumor.[19] The REAL classification includes all the immunological, molecular, genetic, cytogenetic, clinical and prognostic data.[20] In cases with Hodgkin's lymphoma, the Rye classification is usually used. Our patients were also classified according to these classifications. The great majority of primary parotid lymphomas originate from the B-cells. They may be large cell, small cell or mixed type lymphomas. The small cell type is usually accompanied by Mikulicz's disease and an underlying condition.[21] The MALT/Marginal zone types are slow growing tumors with a good

prognosis. However, the large cell lesions show rapid progression.

In conclusion, primary parotid lymphomas are rare occurrences and their incidence is higher after the age of 50. They usually appear as unilateral and painless masses. They are most frequently diagnosed as B-cell non-Hodgkin lymphomas. Although rarely observed in the parotid gland, lymphoma should also be considered in the differential diagnosis.

**Declaration of conflicting interests**

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