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Olgu Sunumu / Case Report

# Non-Sebaceous Lymphadenoma: A Rare Salivary Gland Tumor

## Non-Sebasöz Lenfadenoma: Nadir Görülen Bir Tükrük Bezi Tümörü

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**Abstract:** Lymphadenomas comprise a very rare group of salivary gland tumors, the two types of which are defined as sebaceous and non-sebaceous lymphadenomas. In the case presented here, a patient presented with swelling in the right parotid gland, and the mass seen by ultrasonography was suggestive of pleomorphic adenoma. According to fine needle aspiration biopsy, the presence of lymphoid and epithelial cells first suggested a diagnosis of Warthin tumor. However, the presence of cystic degenerated ductal structures and the solid, benign nature of the epithelial islands intertwined with mature lymphoid cells in the biopsied specimen showed no sebaceous differentiation, and thus, the case was reported as "non-sebaceous lymphadenoma." We aimed to present the relevant literature and our case of non-sebaceous lymphadenoma, whose clinicopathological features and etiopathogenesis are not clearly understood, since it is considered to be underreported due to its sonographic and histomorphological similarities to pleomorphic adenoma and Warthin tumor.
**Keywords:** Maxilla; Salivary gland, Lymphadenoma, Lymphoepithelial lesion

**Özet:** Lenfadenomalar tükrük bezi tümörleri içinde oldukça nadir görülen bir gruptur. Parotis bezinde ileri yaşlarda sıklığı artmaktadır. Sebasöz ve non-sebasöz lenfadenomalar olmak üzere iki grupta incelenmektedir. Lenfadenomalar klinik, ultrasonografik ve morfolojik olarak birçok tükrük bezi tümörü ile benzer özellikler göstermektedir. Bizim olgumuzda sağ parotis lojunda şişlik şikayeti ile başvuran hastanın ultrasonografisinde görülen lezyon pleomorfik adenomu düşündürmüştür. İnce iğne aspirasyon biyopsisinde görülen lenfoid stroma ve epitelyal özellikler ilk olarak Warthin tümörünü akla getirmiştir. Ancak eksizyon materyalinde uniform özellikte lenfoid hücrelerin içinde sakin görünümde yer yer kistik yer yer solid epitel adalarının görülmesi, epitelde atipi, mitoz saptanmaması üzerine vaka da lenfadenoma düşünülmüştür. İncelenen kesitlerde sebasöz diferansiyasyon izlenmemesi ile de olgumuz 'Non-sebasöz lenfadenoma' olarak raporlandı. Literatürde lenfadenoma vakası oldukça az görülmektedir. Bunun sebebi belki de sonografik ve histomorfolojik benzerliğinden dolayı plemorfik adenom veya Warthin tümörü olarak yanlış tanı alan vakalardır. Patogenezinin net olarak aydınlatılabilmesi ve ayırıcı tanısında belli kriterlerin kullanılabilmesi için daha geniş çalışmalara ihtiyaç duyulmaktadır. Biz de non sebasöz lenfadenoma olarak raporladığımız bir vakayı sunarak literatüre katkı sağlamayı amaçladık.
**Anahtar Kelimeler:** tükrük bezi, lenfadenoma, lenfoepitelyal lezyon

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## 1. Introduction

Lymphadenoma is a tumor seen in adults over the age of 30 and is believed to account for 0.1% of all salivary gland tumors (1,2). This tumor type was first described by McGavran et al. in 1960, and in the largest series, Seethala et al. reported 11 cases in 2007, and Lui et al. reported 10 cases in 2014, with few total case reports to date (3,4,5).

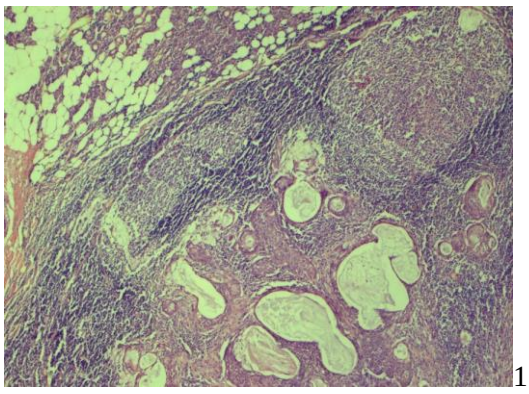
In lymphadenoma, epithelial cells with a prominent lymphoid component are observed. This tumor type is divided into two subtypes according to whether these histological features are accompanied by sebaceous differentiation: non-sebaceous and sebaceous lymphadenoma. The sebaceous type accounts for approximately two-thirds of all lymphadenoma cases, and the parotid gland is the most common site of lymphadenomas with a rate of 80%.

Preoperative errors are common in lymphadenomas. These lesions present as well-limited, mostly encapsulated masses that mimic common benign neoplasms of the salivary gland even on cytopathological examination.

***Case Report***

A 58-year-old female patient presented to the KırıkkaleUniversity, Faculty of Medicine Otorhinolaryngology outpatient clinic due to continuous swelling of the right parotid area over 6–7 months. In the ultrasound imaging review, fine needle aspiration biopsy was performed, which resulted in a preliminary diagnosis of pleomorphic adenoma of the right parotid gland, and a 1.3 × 0.9-cm uniformly limited lesion was observed.

A Warthin tumor was considered primarily based on the presence of lymphoid and epithelial cell populations in the cytology preparations, as well as the presence of bulging epitheloid cells such as oncocytes. This patient underwent surgical resection of the mass, and according to the macroscopic examination of the specimen, a lesion 1.5 × 1 × 1 cm in size that was dirty white-gray in color and had a solid, myxoid appearance was observed on the sectional surface of the tissue. In the microscopic examination of the lesion, cystic duct structures and solid squamous and basaloid cell islands were observed in the mature lymphoid tissue, which was surrounded by an incomplete fibrous capsule (Figure 1,2). Focal oncocytic changes were also present, but no nuclear atypia, mitosis, or tumor necrosis was found (Figure 3).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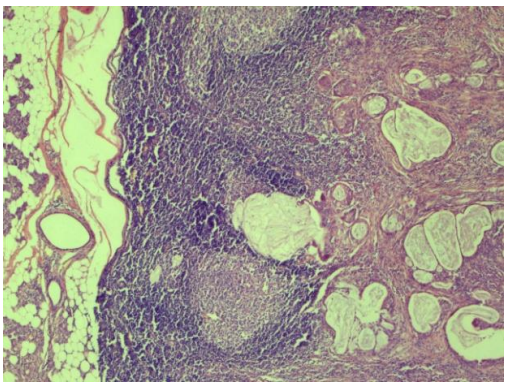
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**Figure 1,2.** Mature lymphoid stroma and cystic duct structures surrounded by incomplete capsules and solid squamous and basaloid cell islands in certain areas (4×; 10×; hematoxylin and eosin; H&E).

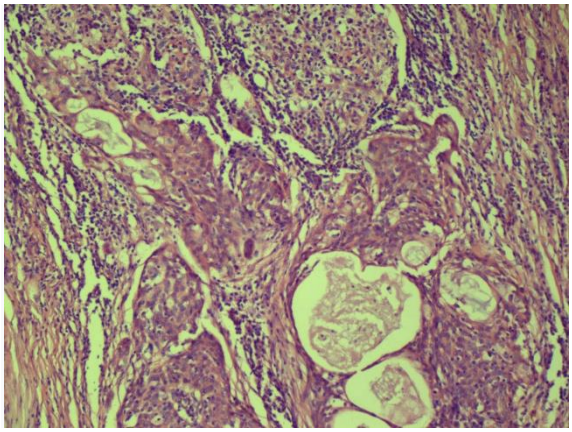

**Figure 3.** Cystic duct structures and squamous cell islands in which atypia, mitosis, and tumor necrosis were not observed (10×; hematoxylin and eosin; H&E)

In the immunohistochemical examination, the Ki-67 proliferation index was less than 5% in the epithelial cells described and pan-cytokeratin expression was also detected. (Figure 4). As for the morphology, a tumor covered by a two-layer epithelium, as seen in Warthin tumor, which formed papillae structures and was predominantly composed of oncocytic cells, was not observed. Tumor metastasis and malignant salivary gland tumors were ruled out due to the lack of atypia and anaplastic features.

This case was diagnosed as non-sebaceous lymphadenoma with no sebaceous component. No recurrence was observed throughout the 6-month follow-up.

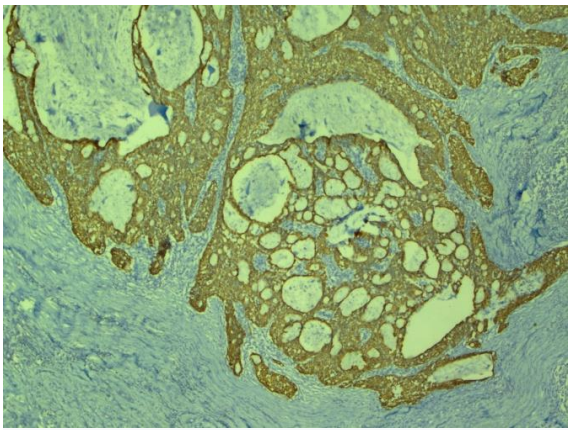

**Figure 4.** Positivity for pan-CK was detected in the epithelial component of the tumor (4×; pancytokeratin)

## 2. Discussion

It is not known whether the histogenetic forms of lymphadenomas are different variants of the same neoplastic process as that responsible for Warthin tumors or are a different entity than lymphadenomas. If Warthin tumors share a common pathogenic mechanism with lymphadenomas, it can be said that lymphadenomas originate from ductal epithelial inclusions trapped in an intraparotid lymph node or a node adjacent to the salivary gland. The continuity of these ducts with the salivary gland ducts or the presence of a subcapsular sinus observed in the periphery of the lesion sometimes supports this theory. It has been stated that oncocytic changes and hyperplasia of the epithelium in Warthin tumors are frequently triggered by smoking and that the incidence of Warthin tumors is 40 times higher in smokers (6,7). The most demonstrative feature that

distinguishes lymphadenomas from Warthin tumors is sebaceous or non-sebaceous squamous or basaloid epithelium. If we focus exclusively on epithelial features, we see that these patients are not exposed to a common mechanism of oxidative stress that can induce mitochondrial DNA damage that contributes to the formation of oncocytic epithelium. We can argue that the keratotic epithelium can be explained by the formation of microcysts that result from obstruction of the glandular lumina (8,9). On the contrary, we believe that the focal oncocytes we detected in our case may be related to the aging process. Some authors also investigated the potential viral etiology of these tumors, such as HPV, EBV, and HHV-8, but they did not report a significant relationship. The tendency of sebaceous lymphadenomas to occur in men and non-sebaceous lymphadenomas to occur in women is explained by the presence of relatively higher numbers of sebaceous glands in men (5). Normally, sebaceous cells are found in 10%–42% of parotid glands and 5%–6% of submandibular glands (11).

According to another theory of the formation of lymphadenomas, lymphoid stroma develops secondary to tumor tissue (11). Accordingly, the lesion is actually a basal cell adenoma or cystadenoma and develops with lymphoid proliferation as a result of mutual growth factors encountered in lymphocyte-epithelial interactions. However, unlike basal cell adenoma, palisading around the epithelial islands is not observed in lymphadenoma. The finding that these lesions are very well-limited suggests the accuracy of the theory of lymph node inclusions. Although we anticipated that lymphoid–epithelial interactions may result from tumor progression, we were unable to show the presence of a subcapsular sinusoid or a medullary hilar sinus in our case.

Regardless of what theory is conceivable in terms of the etiology of these tumors, lymphadenomas are important lesions because of their gross morphology and microscopic features and the differential diagnosis of malignant tumors such as mucoepidermoid carcinoma, metastatic adenocarcinoma, and lymphoepithelial carcinoma, as mentioned above. Lymphadenomas form scattered, irregular solid islands and consist of keratinized foci and ductus structures; they also share similar features to those of low-grade mucoepidermoid carcinoma. However, this lesion contains no mucin and contains only a few mucous cells. In addition, no significant keratinization is expected in mucoepidermoid carcinoma. Other malignancies can be eliminated by the absence of cytological atypia and increased mitosis as well as a lack of invasive features.

The malignant transformation of non-sebaceous lymphadenoma was first reported in 2019 by Kara et al. In that case, which was diagnosed as undifferentiated carcinoma in a background of non-sebaceous lymphadenoma, adjuvant radiotherapy was applied, and no recurrence was observed during the 10-month follow-up (12).

We found that presenting this case of benign neoplasia was worthwhile in terms of its rarity, histogenesis, and differential diagnosis. We also considered local excision to be curative.

## KAYNAKLAR


1. Hellquist H, Paiva-Correia A, Vander Poorten V et al. Analysis of the clinical relevance of histological classification of benign epithelial salivary gland tumours. *Adv Ther*. 2019;36:1950-74.
2. Kühn U, Köhler HH, Jecker P. Rare tumors of the parotid gland. Lymphadenoma of a sebaceous gland and extracranial metastasis from glioblastoma. *HNO*. 2003;51:417-20.
3. McGavran MH, Bauer WC, Ackerman LV. Sebaceous lymphadenoma of the parotid salivary gland. *Cancer*. 1960;13:1185-7.
4. Liu G, He J, Zhang C, Fu S, et al. Lymphadenoma of the salivary gland: *Report of 10 cases. Oncol Lett*. 2014;7:1097-101.
5. Seethala RR, Thompson LDR, Gnepp DR et al. Lymphadenoma of the salivary gland: Clinicopathological and immunohistochemical analysis of 33 tumors. *Mod Pathol*. 2012;25:26-35.
6. Kuzenko YV, Romanuk AM, Dyachenko OO, et al. Pathogenesis of Warthin's tumors. *Interv Med Appl Sci*. 2016;8:41-8.

7. Chung YF, Khoo ML, Heng MK, et al. Epidemiology of Warthin's tumour of the parotid gland in an Asian population. *Br J Surg.* 1999;86:661-4.
8. Sykara M, Ntovas P, Kalogirou EM, et al. Oral lymphoepithelial cyst: A clinicopathological study of 26 cases and review of the literature. *J Clin Exp Dent.* 2017;9:e1035-e43.
9. Lewis PD, Baxter P, Paul Griffiths A, et al. Detection of damage to the mitochondrial genome in the oncocytic cells of Warthin's tumour. *J Pathol.* 2000;191:274-81.
10. Gnepp DR. My journey into the world of salivary gland sebaceous neoplasms. *Head Neck Pathol.* 2012;6:101-10.
11. Auclair PL. Tumor-associated lymphoid proliferation in the parotid gland. A potential diagnostic pitfall. *In Oral Surg Oral Med Oral Pathol.* 1994;77:19-26.
12. Kara H, Sönmez S, Bağbudar S, Güllüoğlu M, Başaran B. Malignant Transformation of Parotid Gland Non-sebaceous Lymphadenoma: Case Report and Review of Literature [published online ahead of print, 2020 Jan 29]. Head Neck Pathol.