ACTA SCIENTIFIC CANCER BIOLOGY

Volume 3 Issue 1 January 2019

Case Report

# Primary Non-Hodgkins Lymphoma of the Parotid Gland: A Common Entity at an Uncommon Location

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**Received:** December 17,2018; **Published**: December 27, 2018

## Abstract

Primary lymphoma arising from the salivary gland is relatively rare and constitutes about 2 - 5% of extranodal lymphomas. The majority of them are non-Hodgkin lymphoma (NHL) and are of B cell in nature. Clinical presentation is not classical and the disease is often overlooked resulting in late diagnosis and delay in treatment. We hereby report a rare case of primary diffuse large B-cell lymphoma (DLBCL) of the parotid gland in an elderly female. The case was diagnosed on fine needle aspiration cytology (FNAC) of the left parotid gland as lymphoproliferative disorder suggestive of NHL large B cell and confirmed on histopathology as DLBCL. The cytology was correlated with the clinicoradiological findings and the case was diagnosed as primary parotid DLBCL. We are presenting this case for its rarity and highlighting the role of FNAC as a timely and useful diagnostic tool. On FNAC a high index of suspicion is warranted if predominant immature lymphoid population is observed. This will be helpful for quick and efficient diagnosis and early treatment.

**Keywords:** Extranodal; Non-Hodgkin Lymphoma; Primary Parotid Lymphoma; Salivary Gland Cytology

### Established facts and novel insights:

- Primary parotid gland lymphoma is an uncommon entity. The overall incidence is 0.3% of all tumors. 2% - 5% of salivary gland neoplasms and 5% of extranodal lymphomas are primary Non-Hodgkin lymphoma.
- It Mostly involve the parotid (70%) followed by the submandibular gland.
- The most common subtypes of NHL in the salivary glands are extranodal marginal zone B cell lymphoma of the mucosa associated lymphoid tissue (MALT) type, follicular B cell lymphoma and diffuse large B cell lymphoma (DLBCL).
- Clinical presentation is not classical and the disease is often overlooked resulting in late diagnosis and delay in treatment.
- It is difficult for surgeons to anticipate primary NHL in the salivary glands pre-operatively and pathologists too find it tedious to give a definitive and diagnostic report based on either frozen section or fine needle aspiration cytology (FNAC). This difficulty in pre and in making diagnosis often results in unnecessary radical operations of the patient with all its associated risks involved.
- The disease is often overlooked and diagnosis is delayed, causing further delay in the treatment. FNAC is a useful diagnostic tool. However, histological confirmation is mandatory for a definitive diagnosis. IHC is essential for categorization and further classification.
- A complete assessment and staging is mandatory before starting the appropriate therapy.

## Introduction

Lymphomas arise most commonly in lymph nodes and parenchymal organs, like liver and spleen, while other localizations are infrequent. Among tumors of lymphatic origin in the head and neck, Non-Hodgkins lymphomas (NHLs) contribute 2% - 4%. Primary parotid gland lymphoma is an uncommon entity. The overall incidence is 0.3% of all tumors, while it contributes 2% - 5% of salivary gland neoplasms and 5% of extranodal lymphomas [1]. The prevalence increases with age (peak incidence in fifth decade)

and the male/female ratio is 2:1. Parotid gland is most commonly involved (70%) followed by the submandibular gland. Predominantly parotid lymphomas are NHL and most of them are of B-cell origin with variable grade of differentiation and may involve lymph-nodes or structures having abundant lymphatic tissue. The most common subtypes of NHL in the salivary glands are extranodal marginal zone B cell lymphoma of the mucosa associated lymphoid tissue (MALT) type, follicular B cell lymphoma and diffuse large B cell lymphoma (DLBCL). However, to categorize them as a primary parotid lymphoma, the first clinical manifestation should arise in the parotid gland [2].

The pathophysiology of NHL is not known. They originate from intraparotid or periparotid lymph nodes, or lymphoid elements of other pathological states in the gland like sialadenitis, lymphoepithelial cysts and warthins tumor. The prevalence of this rare malignancy has risen in recent past and may be related to increased incidence of autoimmune disease and correlation of parotid lymphoma with Sjogren syndrome [3]. The Clinical presentation is not classical and the disease is often overlooked, resulting in late diagnosis and late treatment. The surgeons find it difficult to anticipate primary NHL in the salivary glands pre-operatively and pathologists also find it difficult to give a definitive and diagnostic report based on either frozen section or fine needle aspiration cytology (FNAC). This difficulty in diagnosis often results in unnecessary radical operations to the patient with all its associated risks involved. DLBCL is an infiltrative tumor which is associated with the destruction of the salivary gland. The treatment includes radiotherapy and chemotherapy. Surgical excision is required only for the diagnosis. In contrast to other extranodal locations of NHL, parotid gland involvement is more likely to be of low grade and the patients have a better prognosis than with other extranodal NHL [4]. We report a case of primary NHL of the parotid gland in a 70-years-old female that was diagnosed on FNAC with further histological confirmation.

## Case Report

A 70-years-old female, non-smoker, presented to surgery outpatient department with a swelling in the left parotid region for the last 2 years. The swelling was initially small in size and painless but has increased in size over the time. On examination, it was not tender, fixed to the underlying structures, hard in consistency and measured 6 cm × 5 cm. The skin overlying the swelling has no color changes (Figure 1). The facial nerve examination was found to be normal. The contrast-enhanced computed tomography (CECT) revealed a mass of 7.3 cm × 7 cm × 3 cm with heterogenous enhancement. It was seen arising from the deep lobe of the parotid and causing destruction of the fat planes. There was no evidence of bone destruction (Figure 2).

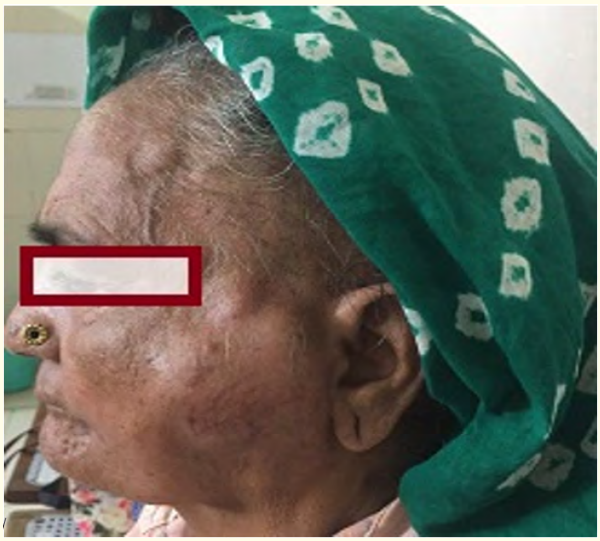

**Figure 1:** Photograph showing a hard, firm, fixed swelling in parotid region.

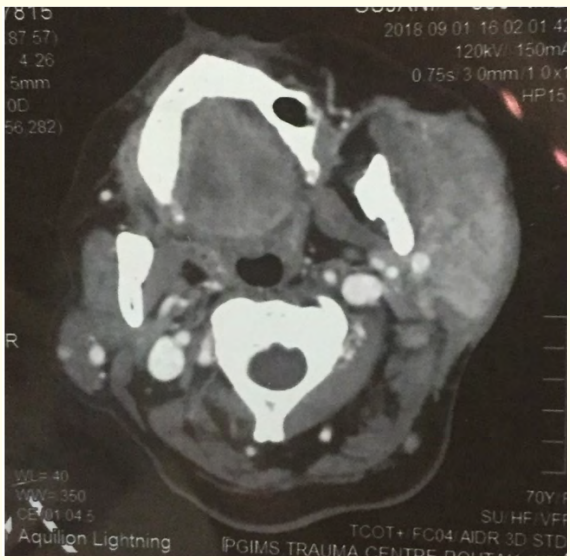


**Figure 2:** CECT showing a lobulated mass of 7.3 CM × 7 CM × 3 CM showing heterogenous enhancement. It was seen arising from the deep lobe of the parotid and causing destruction of the fat planes. THERE was no evidence of bone destruction.

Fine needle aspiration cytology (FNAC) was advised from the swelling. The aspirate was blood-mixed. Smears were highly cellular and comprised of heterogeneous population of atypical lymphoid cells consisting of large and intermediate sized lymphocytes with high N:C ratio, irregular nuclear contours, vesicular nuclear chromatin, prominent nucleoli and scanty agranular cytoplasm. Many atypical mitosis were also noted. The background showed lymphoglandular bodies along with normal salivary gland acini and ducts (Figure 3A and 3B). On FNAC it was diagnosed as lymphoproliferative disorder suggestive of NHL, possibly large B cell type. The core biopsy was performed. Histopathological examination revealed sheets of atypical lymphoid cells with vesicular nuclear chromatin and scanty cytoplasm. Mitotic count was 4/10 high power fields (hpf) with many atypical mitoses. The neoplastic cells were destroying glandular parenchyma and infiltrating periparotid fat (Figure 4). These neoplastic cells were positive for leukocyte common antigen (LCA), cluster of differentiation (CD) 20, CD 5 while negative for CD3, BCL-2 and Cytokeratin (Figure 5A and 5B). In view of the IHC findings, a diagnosis of high grade NHL favouring diffuse large B-Cell lymphoma (DLBCL) was rendered. However, her bone marrow examination was normal.

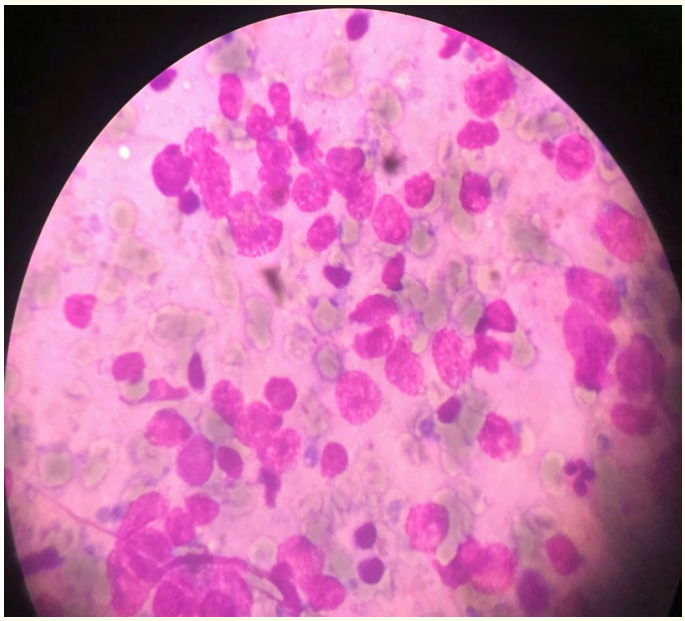

**Figure 3B:** Photomicrograph showing prominent nucleoli and irregular nuclear contours (Leishman, 400X).

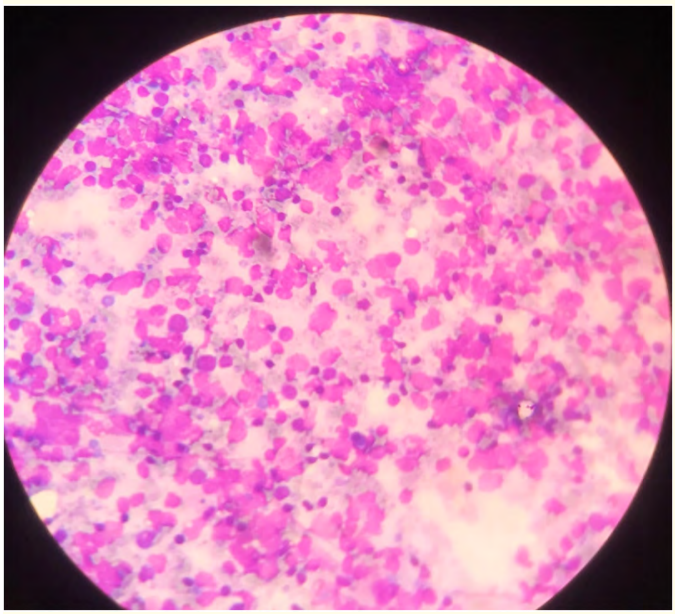

**Figure 3A:** Photomicrograph depicting atypical lymphoid cells with high N:C ratio (Leishman 200X).

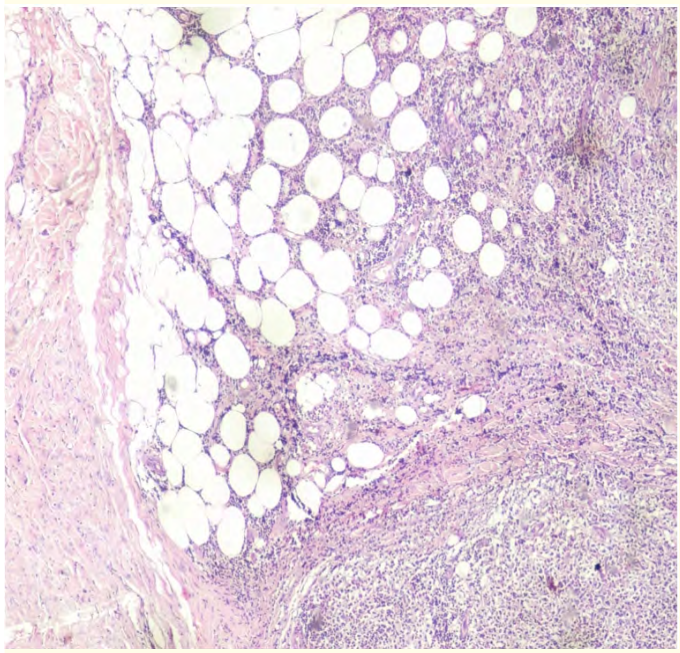

**Figure 4:** On HPE: atypical lymphoid cells causing destruction of parotis parenchyma and fat Planes (H&E40X).

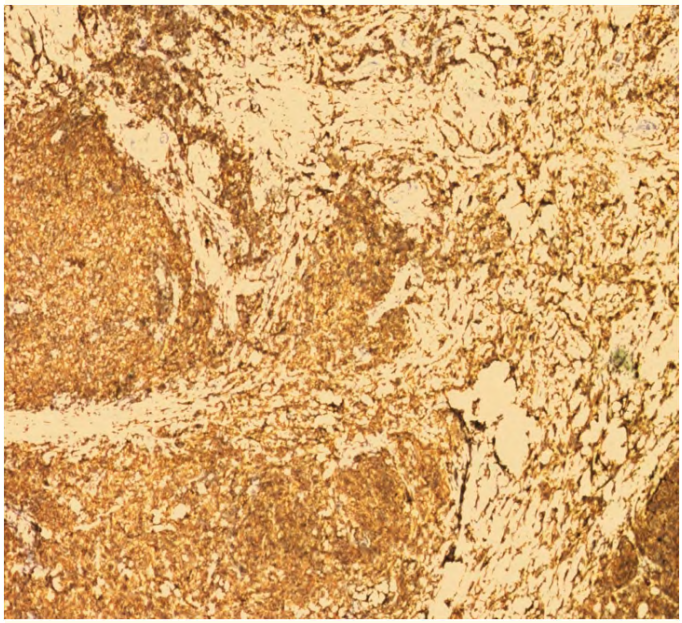

**Figure 5A:** On IHC tumor cells are strongly positive for CD 20 (100X).

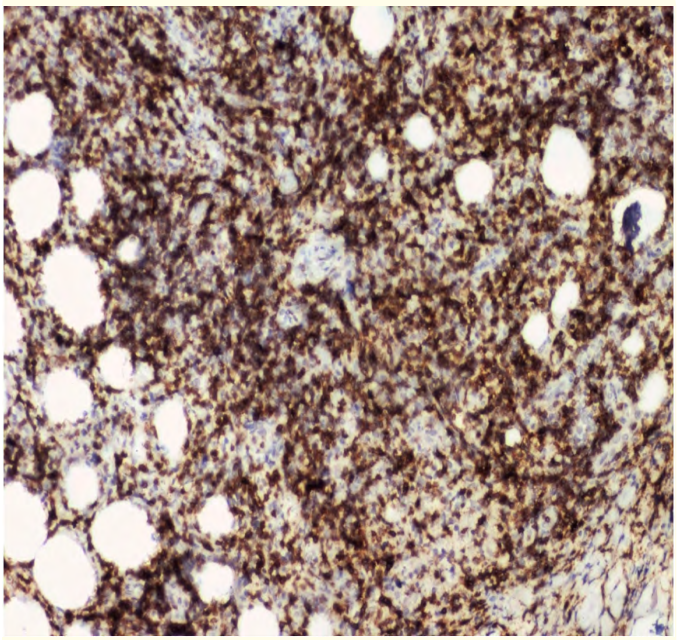

**Figure 5B:** On IHC tumor cells are strongly positive for CD 5 (100X).

Correlating with the clinical history and radiology, final diagnosis of a primary DLBCL of the left parotid gland was made. The patient was staged at Ann Arbor stage I. she was treated with local radiotherapy and six cycles of Rituximab-Cyclophosphamide Hydroxydaunorubicin-Oncovin-Prednisolone (R-CHOP) chemotherapy. Now she is on maintenance therapy with Rituximab and is doing well.

## Discussion

Among the lymphatic tumors of head and neck, Non-Hodgkins lymphomas (NHLs) contribute to 2% - 4%. The overall incidence of primary parotid lymphoma is just 0.3% of all tumors, 2% - 5% of salivary gland neoplasms and 5% of extranodal lymphomas [1]. The prevalence increases with age (peak incidence is in 5th decade) and the males are affected twice as common as females. It presents as a firm, unilateral, painless and progressive swelling in the parotid region. Facial nerve paresis and cervical lymphadenopathy may be an associated feature [5].

It most commonly involves the parotid (70%) followed by the submandibular gland. The lymphomas may arise from intra-parotid lymphoid tissue or parotid gland itself. There is a debate about the true origin of lymphomas within the parotid gland. According to Batsakis, the main reason for the propensity of parotid gland to be involved is related to the anatomy of the gland, rich lymphoid tissue [6]. NHL of the parotid gland may be extranodal if it arises from the mucosa associated lymphoid tissue (MALT) or nodal if the true origin is from lymph node within the gland. According to some authors, salivary glands do not normally contain MALT but they may acquire it as a result of an autoimmune inflammatory disorder like Sjogren's syndrome. Sjogren's syndrome is associated with 6.5 fold increase in the risk of NHL, 250 fold increase in the risk of parotid gland NHL and a dramatic 1000 fold increase in the risk of parotid gland MALT lymphoma. Most primary salivary gland lymphomas are B marginal zone lymphomas arising on a background of sialadenitis with autoimmune basis. Others include follicular lymphoma and diffuse large B cell lymphoma. However, primary T-cell lymphoma of the salivary gland is extremely rare [7].

The diagnosis of primary parotid lymphoma is difficult, when a new parotid gland mass is evaluated. The clinical presentation is indistinguishable from other benign parotid swellings, but there are few clinical and histological features that should alert the phy-

sician to consider lymphoma as possible aetiology of the swelling. Hyman and Wolff proposed criteria for the diagnosis of primary parotid lymphoma are: a) Involvement of the salivary gland as the first clinical manifestation of disease b) Histological proof that lymphoma involves the salivary gland parenchyma (rather than being confined to soft tissue and lymph node in the area) c) Architectural and cytological confirmation of the malignant nature of the infiltrate [3].

The diagnosis of parotid lymphoma is difficult on FNAC when prominent lymphoid population is seen. The differential diagnosis of salivary gland with lymphoid rich aspiration smear includes chronic sialadenitis, HIV related benign lymphoproliferative lesion, Warthin tumors, lymphoepithelial carcinoma and metastatic tumors. When the FNAC shows the features of lymphoproliferative disorder, the procedure of choice for final diagnosis of parotid lymphoma should be core biopsy along with flow cytometry and immunophenotyping [8].

The treatment options includes radiotherapy and chemotherapy. Surgical excision is advocated only for the diagnosis [4]. Thus FNAC plays a pivotal role in such a setting for an early definitive diagnosis.

## Conclusion

Primary parotid gland extranodal NHLs are extremely rare and the clinical presentation is not classical. The disease is often overlooked and diagnosis is delayed, causing further delay in the treatment. FNAC is a useful diagnostic tool. However, histological confirmation is required for a definitive diagnosis. IHC is essential for categorization and further classification. A complete assessment and staging is mandatory before starting any therapy. The patients who present at an early stage or with low-grade NHL have a better prognosis than the others.

## Conflict of Interest Statement

We have no conflict of interest.

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