Case Report

Diffuse large B-cell lymphoma of the parotid gland: Cytological, histopathological, and immunohistochemical features: A rare case report

ABSTRACT
Primary malignant lymphomas of the salivary glands are rare, accounting for 2-5% of salivary gland tumors and 5% of extranodal lymphomas, frequently seen in the parotid gland. There are single case reports mentioned in the literature. Clinical presentation is not characteristic and the disease is often overlooked with delay in diagnosis and treatment. We are reporting a case of bilateral parotid gland lymphoma in a 55-year-old male, presented with bilateral enlarged parotids. Magnetic resonance imaging (MRI) showed bilateral enlarged parotid glands with multiple well-defined intraparotid lesions. Fine Needle Aspiration Cytology (FNAC) of both showed mixed population of lymphoid cells with large monocytoid cells with scant cytoplasm, anisonucleosis with prominent nucleoli, and numerous mitoses suggestive of non-Hodgkin’s lymphoma (NHL). Histopathology showed sheets of large lymphoma cells destructing the salivary acini and infiltrating the periparotid fat. Immunohistochemistry (IHC) showed diffuse CD20 positivity, B-cell lymphoma 6 protein (Bcl-6) was focally positive and negative for cluster of differentiation (CD) 3, CD5, CD10, and Multiple myeloma oncogene-1 (MUM1) which led to the diagnosis of NHL-Diffuse large B cell type.

Key words: Extranodal lymphoma; large B-cell lymphoma; primary parotid lymphoma

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Diffuse large B-cell lymphoma of the parotid gland: Cytological, histopathological, and immunohistochemical features: A rare case report

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Introduction

Lymphoma is the second most common neoplasm of the head and the neck region after squamous cell carcinoma.[1] Lymphomas primarily in the salivary gland tissue are very rare, the incidence being 0.3% of all tumors, 2-5% of all salivary gland tumors, and 5% of extranodal lymphomas.[2] The first case of mucosa-associated lymphoid tissue (MALT) lymphoma was reported in 1963. Clinical presentation is not characteristic and the disease is often overlooked, resulting in late diagnosis and treatment. Most cases of lymphoma involve the parotid (70%), followed by the submandibular gland.[3]

Diffuse large B-cell lymphoma (DLBCL) is an infiltrative tumor, associated with the destruction of the salivary gland.[4]

Case Report

A 55-year-old male presented with bilateral parotid swelling of a 3-year duration, slowly progressing in size, approximately 5 cm × 4 cm, firm, and painless. Clinical diagnosis of pleomorphic adenoma was made. All investigations were within normal limits and human immunodeficiency virus (HIV) status was nonreactive. Magnetic resonance imaging (MRI): Bilateral (B/L) enlarged parotid glands with multiple well-defined intraparotid focal lesions: Warthin tumor/ tuberculosis/ lymphoma. Ultrasonography (USG): No cervical, mediastinal, or paraaortic lymphadenopathy. The present case had a bilateral enlargement of the parotid gland, seronegative for HIV and no other lymphadenopathy.

Fine Needle Aspiration Cytology (FNAC) revealed heterogeneous population of atypical lymphoid cells consisting of small and intermediate sized lymphocytes with round-to-irregular nuclear borders, finely granular chromatin, prominent nucleoli, and brisk mitoses [Figure 1a]. Plasmacytoid cells with abundant cytoplasm and eccentric nucleus, large monocytoid cells with pale staining cytoplasm, indented nucleus with prominent 1-3 nucleoli were noted [Figure 1b]. Based on these, a diagnosis of non-Hodgkin’s lymphoma (NHL) was offered. Right superficial parotidectomy was done.

Histopathology revealed capsulated nodular mass measuring 5 cm × 4 cm × 3 cm, glistening smooth surface with fatty areas. Cut section (C/S): Tan-brown tumor areas and irregular grey white areas. Microscopy: Capsulated mass with effaced glandular architecture, heterogeneous population of cells in sheets that are small to intermediate sized. Few are large, having scant basophilic cytoplasm, round-oval vesicular, centrally located nucleus, and multiple nucleoli. Few show nuclear angulation. These cells are seen destroying glandular parenchyma and infiltrating periparotid fat. Mitosis were conspicuous [Figure 1c].

Immunohistochemistry (IHC): Lymphoid cells are immunoreactive for CD20 [Figure 1d] and focally immunoreactive for B-cell lymphoma 6 protein (Bcl-6), but immunonegative for cluster of differentiation (CD) 3, CD5, CD10, MUM1.

Postoperatively, the patient underwent local radiotherapy, followed by chemotherapy and was disease-free at the end of 1 year of follow-up.

Discussion

Malignant lymphomas developing primarily in the salivary glands are uncommon. Only case reports are available in the literature. They are more commonly seen in the parotid gland followed by submandibular.[4] The age range is wide, more common in adults and older people, the mean age being 70 years. These lymphomas are usually seen with acquired immunodeficiency syndrome and are disseminated at the time of diagnosis.[5] In the present case, malignant lymphoma is seen in bilateral parotid gland in a 55-year-old male.

Bilateral parotid gland enlargement can occur due to mumps, benign lymphoepithelial lesion (Mikulicz disease), and Sjogren’s syndrome. Mumps is a disease of viral origin, commonly seen in children and present with bilateral painful parotid enlargement, fever, malaise, trismus, and dysphagia. Histopathology shows characteristic viral cytopathic changes and distinctive intranuclear inclusions.[6] Mikulicz disease presents in the fourth to the seventh decade as recurrent, diffuse, firm, often painful swelling of the salivary glands, mainly parotid and lacrimal. Histologically, there is dense lymphocytic infiltrate in periductal areas gradually replacing the whole acinus. Insinuation of lymphocytes into the epithelium gives rise to epimyoepithelial islands.[7] The risk of developing lymphoma in these patients is approximately 40 times higher than the general population.[6] In Sjogren’s syndrome, parotid involvement is bilateral, diffuse, painless, and firm. Biopsy shows lymphoid follicles with a germinal center and characteristic lymphoepithelial islands. These patients show increased risk of developing MALT lymphoma or DLBCL.[8]

Parotid lymphoma most commonly presents as painless mass indistinguishable from other nonmalignant and other more common epithelial tumors.[5] Our case presented with painless, progressive, bilateral parotid enlargement. Bilateral parotid lymphomas have been described in 4-21% of patients,
although not always clear whether these patients actually have bilateral disease or whether a unilateral lymphoma is associated with bilateral benign lymphoepithelial lesion.\textsuperscript{[9]} However, Roh \textit{et al}. reported 20 cases of primary parotid lymphoma out of which two showed bilateral involvement.\textsuperscript{[10]} MRI showed bilateral enlarged parotids with multiple well-defined intraparotid focal lesions. FNAC showed features suggestive of NHL. FNAC alone is often incapable of determining the precise histological subtype for lymphoma.\textsuperscript{[5]} Hence, FNAC was typically followed by an open biopsy. In addition, diagnostic imaging studies indicate whether or not the mass is salivary in origin but do not help in classifying histologically.

Most of the parotid NHL are of B cell lineage including low grade MALT lymphoma, diffuse large B cell lymphoma, and follicular lymphoma. These may arise from intraparotid lymph nodes or the gland itself. In the parotid gland, there are intraglandular lymph nodes and hence, it is difficult to distinguish between lymphoma arising primarily in the salivary gland and those of lymph nodes embedded in the gland. The morphology and prognosis is similar for both origins.\textsuperscript{[2,3]}

Hyman and Wolff proposed criteria for the diagnosis of primary parotid lymphoma:
\begin{itemize}
  \item a. Involvement of the salivary gland as the first clinical manifestation of disease;
  \item b. Histologic proof that lymphoma involves the salivary gland parenchyma, rather than being confined to soft tissue or a lymph node in the area;
  \item c. Architectural and cytological confirmation of the malignant nature of the infiltrate. Based on these criteria, the present case is diagnosed as primary parotid lymphoma.\textsuperscript{[2,3]}
\end{itemize}

IHC showed diffuse positivity for CD20, focal positivity for Bcl-6 and negative for CD3, CD5, CD10, and MUM1 helped in categorizing it as NHL of diffuse large B cell type.

**Conclusion**

Primary parotid gland extranodal NHLs are extremely rare and the clinical presentation is not characteristic. The disease is often overlooked and diagnosis is delayed, further causing delay in the treatment. FNAC will aid in the preliminary diagnosis, followed by histopathologic confirmation. IHC is essential for categorization and classification.

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**Conflicts of interest**

There are no conflicts of interest.

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