Original Article

Primary salivary gland lymphomas: A case series

Rajeev Sen, Divya Srivastava, Mansi Agarwal, Hemant Yadav, Shilpi Bhargava, Aarzoo Jahan

Department of Pathology, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India

ABSTRACT

Background: Primary lymphoma of the salivary gland is not often encountered in routine practice. About 5–10% of Non-Hodgkin's lymphomas (NHLs) are found in the salivary gland, most frequently involving parotid gland. Henceforth, it is necessary to understand the distinct clinical presentations and course of primary salivary gland lymphomas as this may help guide the proper diagnosis and management of patients with these tumors. **Materials and Methods:** We retrospectively reviewed primary NHL diagnosed at our medical institute over a period of 2 years. **Results:** Five cases of primary salivary gland lymphoma were found, two involving parotid gland while other three affecting submandibular gland. None of the cases had a clinical suspicion of lymphoma. However, they were diagnosed as having NHL B-cell type on histopathology. **Conclusion:** Since primary salivary gland NHL is an uncommon finding, it is often overlooked as the differential diagnosis. Methods of diagnosing and treating lymphoma are different from those of other benign pathologies of the salivary gland. Therefore, a high index of suspicion is warranted to provide a quick and efficient diagnosis and treatment without subjecting the patient to unnecessary tests and procedures.

Key words: B-cell, lymphoma, salivary gland

INTRODUCTION

Primary non-Hodgkin's lymphoma (NHL) of the salivary gland is a rare malignancy accounting for only 5% of the extranodal NHL[1] and only 1.7% of the salivary gland malignancies. The most commonly involved salivary gland is parotid, followed by the submandibular gland, minor salivary glands, and sublingual gland. Primary NHLs of the salivary glands have been reported to occur in a background of chronic immune-mediated diseases, such as Sjogren's syndrome and myoepithelial sialadenitis, also called benign lymphoepithelial lesion.[2] Hence, surgeons generally do not anticipate primary NHL in the salivary glands preoperatively, and pathologists too find it difficult to give a definitive and diagnostic report based on either frozen section or fine needle aspiration (FNA) biopsy. Due to this difficulty, patients are subjected to radical surgical procedures before a definite diagnosis is made. Radiotherapy and chemotherapy are effective modes of treatment, often with a favorable prognosis.[3] Therefore, it becomes desirable to provide a quick and efficient diagnosis to prevent unnecessary harm to the patient.

We reviewed all the cases of extranodal lymphomas in our institute in the past 2 years and encountered only five cases of primary salivary gland lymphomas.

MATERIALS AND METHODS

We conducted a retrospective review of five patients aged 35–55 years with salivary gland swelling who were diagnosed with primary salivary gland lymphoma and treated in our Tertiary Medical Center in the years 2013 and 2014. The patients (three males and two females) presented with swellings in salivary gland region, with

Address for correspondence: Dr. Hemant Yadav, 1477/21, Adarsh Nagar, Rohtak - 124 001, Haryana, India.
E-mail: hemantyadav7022@gmail.com

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two patients having parotid region swelling and the other three having submandibular region swellings. None of the patients had B symptoms (i.e., fever, night sweats or weight loss) or lymph node enlargement. No patient suffered complications of facial nerve palsy or Sjogren's syndrome or any other autoimmune disorder. All patients had unilateral involvement and only one, with the parotid mass, complained of pain in the swelling. FNA cytology had been done as an initial investigation in the patient having parotid swelling, and a diagnosis of Warthin's tumor was made. Patient having the submandibular mass was clinically suspected to be a case of chronic sialadenitis. Another two patients with submandibular swelling were suspected as the case of pleomorphic adenoma with the involvement of both superficial and deep lobes and two submandibular lymph nodes involvement on contrast enhanced computerized tomography (CT). Biopsies were sent to the Department of Pathology with no previous clinical suspicion of NHL. All specimens were stained with hematoxylin-eosin and immunohistochemical markers (cytokeratin [CK], leucocyte common antigen [LCA], CD3, CD5, CD10, CD15, CD20, CD30, BCL2, and Cyclin D1).

RESULTS

Excised submandibular swelling, clinically suspected to be a pleomorphic adenoma, showed hypercellular proliferation of small lymphoid cells in darkly staining nodular fashion separated by lightly stained paracortical zones revealing presence of lymphoepithelial structures in some areas [Figure 1]. The periphery of lymphoid tissue near the residual parenchyma of salivary gland showed residual lymphoid follicles.

On immunohistochemistry (IHC), CD3 and 5 were positive in lightly stained areas as well as cells colonizing the darkly stained nodules [Figure 2]. CD10, TdT, Cyclin D1, and BCL6 were negative and CD20 stained outer nodular areas (residual lymphoid follicles) clinching diagnosis in favor of peripheral T-cell lymphoma of the follicular pattern.

Biopsy from parotid swelling showed features of NHL with IHC showing positivity of CD20 and BCL2 in tumor population in one case. This case was finally diagnosed as follicular lymphoma of the parotid gland. Other cases were found to be NHL B-cell type based on histopathology and IHC findings.

These tumors were composed of a diffuse proliferation of lymphoid cells with the destruction of normal architecture of ducts and acini of the salivary gland [Figure 3]. The cells had moderately high mitotic rate [Figure 4]. These cells were positive for LCA and CD20 [Figure 5] and negative for CK and various T-cell markers. CK was found positive in residual salivary gland parenchyma [Figure 6]. Majority of the salivary gland lymphomas (70–80%) arise in the parotid

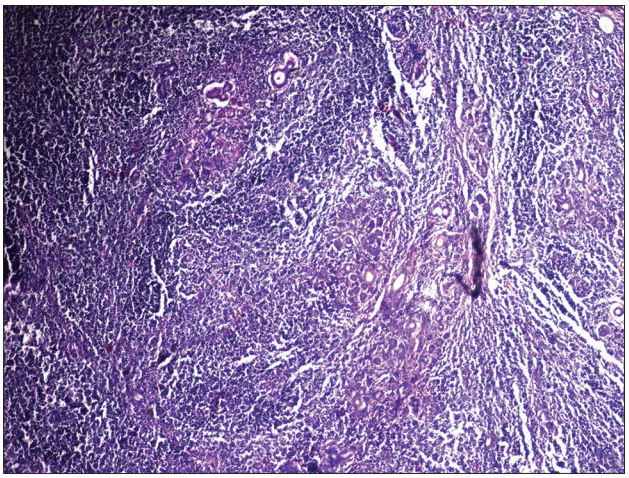

Figure 1: Excised submandibular gland showing proliferation of small lymphoid cells in nodular fashion revealing presence of lymphoepithelial islands in some areas (H and E, ×100)

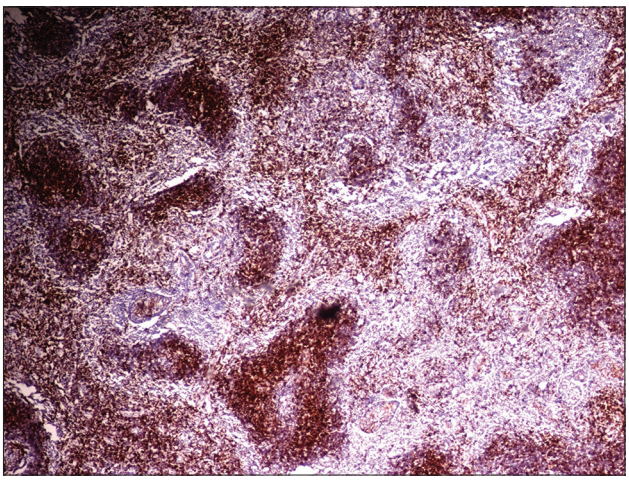

Figure 2: CD5 positivity in nodular areas and light stained areas (CD5, ×200)

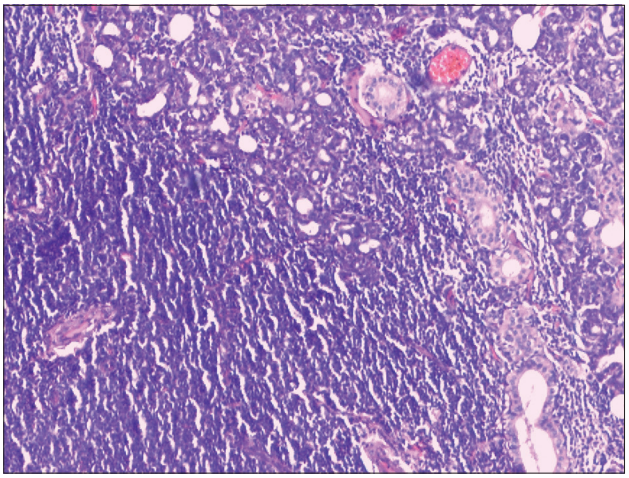

Figure 3: Lymphoid cells causing destruction of normal salivary gland architecture (H and E, ×100)

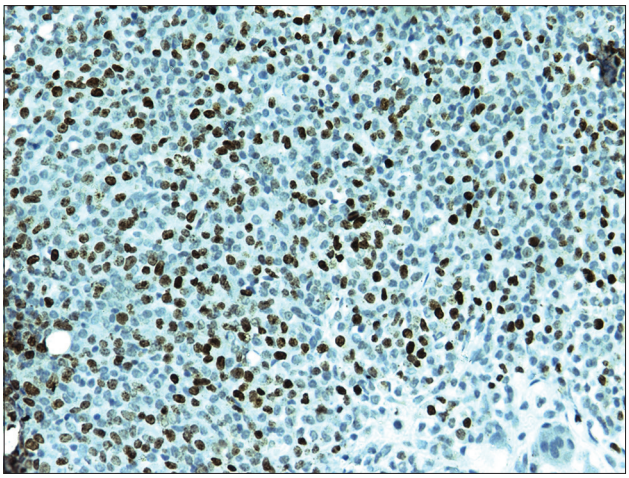

Figure 4: Ki-67 positivity in tumor cells showing a high mitotic activity (Ki-67, ×200)

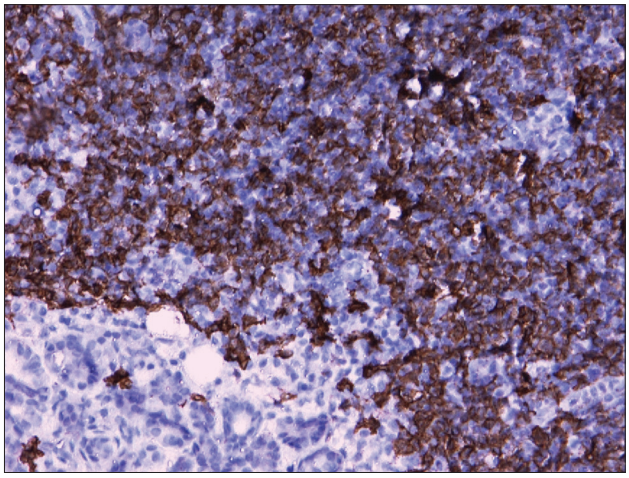

Figure 5: CD20 positivity in tumor cells (CD20, ×400)

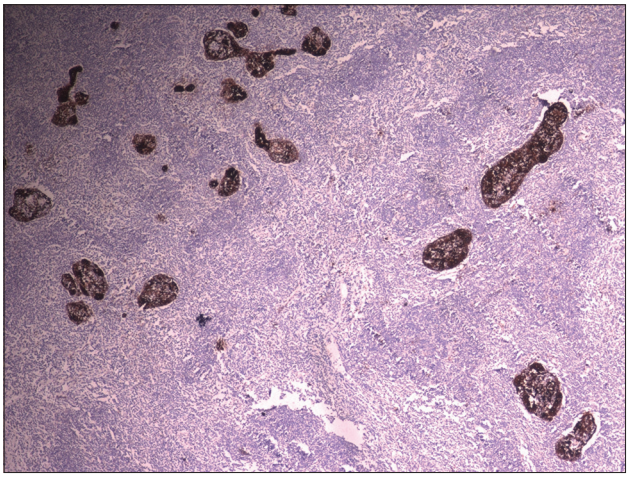

Figure 6: CK positivity highlighting residual salivary parenchyma in lymphoma (CK, ×100)

gland, and most are low-grade NHLs with women having less common involvement than men.[4] However, in this series, the frequency of parotid and submandibular glands involvement was 2:3 and male/female ratio was 1:1. Mean age at presentation was 45. All the patients were diagnosed as lymphomas on the basis of histologic and IHC findings. In general, malignant lymphoma originating in the salivary gland is histologically described as low-grade NHL, B-cell type.[5] In this series, one of the five cases was diagnosed as follicular B-cell lymphoma involving the parotid and the other four as NHLs (B-cell type). The patients were treated with radiotherapy and chemotherapy and are on follow-up with no complications till date.

DISCUSSION

Primary lymphomas of the salivary glands are very uncommon, only a small number of cases have been described in the literature.[1] Most of the NHLs arise primarily in the lymph nodes (71.9%) while only 29.1% are primarily extra-nodal.[4] The major salivary glands are affected in only 5% of all primary extranodal malignant lymphomas.[2] The parotid is the most common salivary gland involved although primary parotid lymphomas account for only 0.87% of all NHL cases.[4] This is the reason it is rarely suspected before biopsy or surgical removal.

It has been reported that 80–85% of parotid gland tumors are benign, and only 15–20% are malignant[5] usually presenting as painless, progressively enlarging swelling. The diffuse lymphoid tissue can increase in some benign conditions which can resemble histologically to NHL, for example, Mikulicz' disease, lymphoepithelial sialadenitis, myoepithelial sialadenitis, and hence, forming the differential diagnosis.[1]

The malignancy seems to be associated with autoimmune diseases, the strongest correlation being with Sjogren syndrome.[4] Warthin's tumor and malignant lymphomas are only rarely associated. Follicular lymphoma is the most common lymphoma presenting as a collision tumor with Warthin's.[3] Even though we had a diagnosis of Warthin's in the preoperative FNA, it was not confirmed in the final histology.

Salivary gland lymphomas have a better survival rate as compared with nodal and other extranodal lymphomas.[6] Most salivary gland NHLs tend to remain localized and relapse locally. As per literature, FNA is not diagnostic and, therefore, should be avoided whenever a high index of suspicion for lymphoma arises in the differential diagnosis. CT scan may add information regarding the malignant nature of the disease, with signs such as irregular borders and extraparotid extension. Currently, there is still no pathognomonic findings indicative of lymphoma on CT. The procedure of choice for the diagnosis of lymphoma in the parotid gland should be core biopsy. Therapeutically complete tumor resection and

irradiation constitute a suitable treatment modality for early stage tumors, with the addition of chemotherapy in patients with advanced disease.[4] The chemotherapeutic agent may be MACOP-P or VEPA. Patients showing relapse can be treated with additional radiotherapy combined with chemotherapy.

CONCLUSION

Lymphoma rarely presents as a mass in the salivary gland region and must be considered in the differential diagnosis of salivary gland swellings whether unilateral or bilateral, painless or painful. Because of the rarity and indistinct radiological features, the diagnosis is overlooked, and patients are often subjected to unnecessary procedures and a delay in diagnosis. However, the prognosis for a well-evaluated and appropriately treated patient with lymphoma presenting in the salivary glands is excellent.

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Conflicts of interest
There are no conflicts of interest.

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