Nodular Lymphocyte-Predominant Hodgkin's Lymphoma of the Parotid Gland: A Case Report

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Abstract

Introduction. Parotid lymphoma is a rare occurrence, let alone a diagnosis of nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Salivary gland tumors commonly affect the parotid gland, although a primary malignant lesion rarely occurs, with an incidence of 0.5 to 3.0/100,000 population/year worldwide. This case report describes the presentation of this rare lymphoma. This also demonstrates the efficacy of standard of care chemotherapy with doxorubicin, vincristine, bleomycin, and dacarbazine with an anti-CD20 monoclonal antibody, rituximab (R-ABVD).

Case. This is a case of a 44-year-old male with a gradually enlarging right preauricular mass. Biopsy and immunohistochemical staining confirmed a diagnosis of NLPHL Stage IIA. A total of six cycles of chemotherapy with R-ABVD was given. Follow-up PET CT showed resolution of FDG avid nodes localized near the surgically removed parotid gland, confirming complete remission.

Discussion. Parotid malignancy only accounts for 5% of all head and neck tumors. NLPHL is even more rare, with an incidence of 1.5/1,000,000 population per year. The rarity of the case limits clinical trials for its treatment. Because of this, R-ABVD has been employed as a treatment of choice for intermediate-staged NLPHL. Overall response showed an 85% five-year progression-free survival and 99% overall survival.

Conclusion. This case report highlights the significance of early lymphoma detection despite its rarity among parotid tumors and prompt initiation of chemotherapy.

Keywords: Parotid gland mass, Parotid gland malignancy, Parotid gland lymphoma, Nodular lymphocyte-predominant Hodgkin's Lymphoma, NLPHL

Introduction

Parotid lymphoma is a rare occurrence, let alone a diagnosis of nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Although the parotid gland is the most affected salivary gland by tumors, a primary malignant lesion rarely occurs with an incidence of 0.5 to 3.0/100,000 population/year worldwide [6]

NLPHL is a rare subtype of Hodgkin's lymphoma, constituting only 5% of cases. This is derived from the malignant transformation of germinal center B cells within an inflammatory background.[4] NLPHL is commonly diagnosed at early stages of the disease and presents with peripheral adenopathy localized to the neck, axilla, or inguinal region. Primary parotid involvement is rare. Treatment is stage-dependent, with earlier stages favoring limited field radiation therapy, while intermediate- and late-stage disease favor combined modality treatment or chemotherapy, respectively.[2]

This case report describes the presentation of this rare type of lymphoma and the significance of considering this as a differential diagnosis among patients presenting with parotid tumors. It also demonstrates the efficacy of standard of care chemotherapy with doxorubicin, vinblastine, bleomycin, and dacarbazine (ABVD) with the addition of an anti-CD20 monoclonal antibody, rituximab (R).

Case Report

This is a case of a 44-year-old male who noticed a palpable mass at the right preauricular area since November 2020. The mass was firm, nontender, and non-erythematous, with regular smooth borders, measuring approximately 1 cm. There were no other symptoms, such as fever, weight loss, and night sweats. He is a

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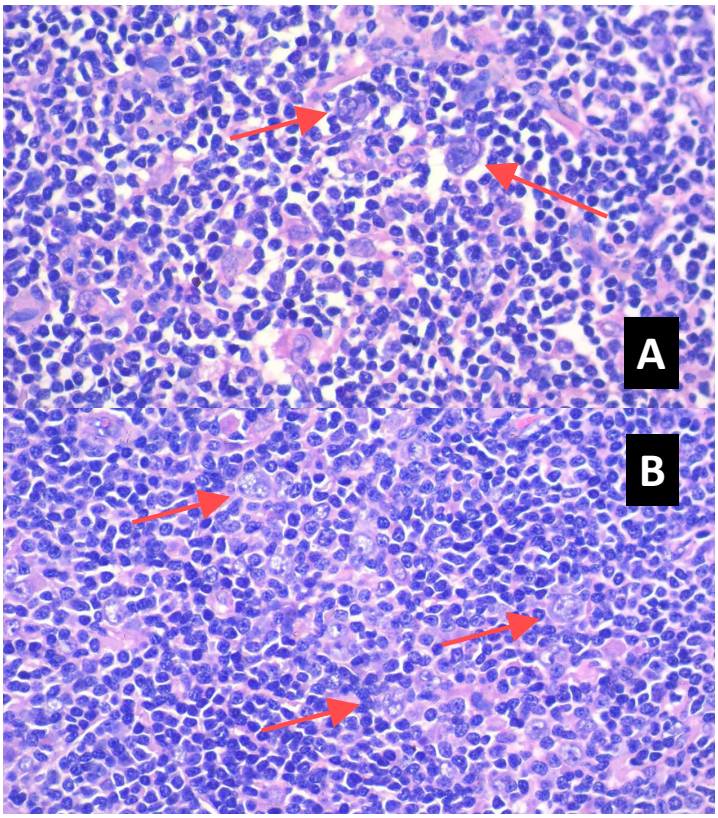

Figure 1 A and B. Seen here are LP cells or "popcorn" cells (red arrows) admixed with small lymphocytes and epithelioid histiocytes. These cells have multilobulated or extremely folded (like popcorn) or round nuclei with thin nuclear membranes, finely granular chromatin, and variable small nucleoli.

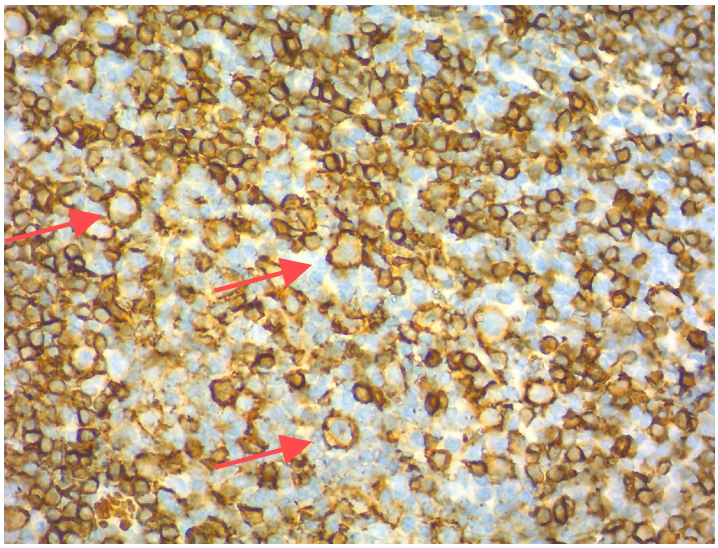

Figure 2. LP cells *(red arrows)* and B-lymphocytes in nodular areas stain positive for CD20

known hypertensive and is maintained on losartan. Family history revealed malignancy (bone and lung) on both paternal and maternal sides, respectively.

The mass was observed to be gradually enlarging to approximately 2-3 cm; hence, the patient sought consultation with a surgeon last March 2021. Ultrasound of the mass showed a predominantly cystic mass at the right preauricular region, which may have been parotid in origin. Other findings include a prominent thyroid gland and an echogenic right level III cervical lymph node. A superficial parotidectomy with frozen section biopsy was done last April 28, 2021.

Diagnosis. Parotid biopsy showed a macronodular pattern with pushing borders. The macronodules have several scattered, large, round, to popcorn-like cells surrounded by numerous small lymphocytes. Immunohistochemical staining revealed the following results: CD3 negative in the cells of interest but forms T cell rosetting around CD3 negative cells of interest; negative for CD10 and Cyclin D1; BCL2 positive in both small and large lymphocytes; 15-45% Ki-67 positive, highlighting both large and small B cells. The large, round to popcorn-like cells were positive for CD20, CD79a, PAX5, BCL6, and lambda light chains and were generally negative for CD30 antigens. A diagnosis of nodular lymphocyte-predominant Hodgkin's lymphoma was made.

The staging was done through PET-CT, which revealed a hypermetabolic enhancement of soft tissue density along the lateral margin of the right parotid gland and preauricular region, with overlying subcutaneous fat stranding densities representing post-surgical changes. Additional findings include hypermetabolic enhancing nodules in the remaining right parotid gland (*Deauville 5*), prominent to enlarged lymph node inferior to the right parotid gland and at level II, right (*Deauville 5*) and sub-centimeter bilateral inguinal mesenteric, aortocaval, paraaortic, and bilateral external iliac lymph nodes with low-grade metabolic activity (*Deauville 2-3*). With extranodal involvement in the absence of symptoms, the patient was staged as IIA (intermediate-stage disease).

Treatment. Chemotherapy with doxorubicin 25mg/m^2, bleomycin 10,000 u/m^2, vinblastine 6mg/m^2 and dacarbazine 375mg/m^2 on Day 1 and 15 of each cycle was given together with an anti-CD20 monoclonal antibody rituximab at 375mg/m^2 every Day 1 of the cycle for four cycles. Tests done prior to chemotherapy showed normal complete blood count levels, creatinine, and bilirubin levels. The patient is non-reactive for hepatitis work-up. Liver transaminases were, however, elevated. 2D echo showed concentric LV remodeling (LV mass index 98.53g/m^2) with normal wall motion and contractility with a computed ejection fraction of 66%. Doses for doxorubicin, vinblastine, and dacarbazine were adjusted to address elevated liver transaminases.

After four cycles of R-ABVD, an interim PET-CT scan was done, which revealed a slight decrease in the enhancing soft tissue density/thickening along the lateral margin of

the right parotid gland and preauricular region with overlying subcutaneous fat stranding densities but no significant metabolic activity, suggestive of a post-surgical change. There was a decrease in the sizes and number of enhancing nodules in the remaining right parotid gland, which are now too small for PET-CT to characterize. There was also a decrease in the sizes of the previously seen prominent enlarged lymph nodes inferior to the right parotid gland and at right level II. One of the smaller lymph nodes had interval metabolic regression, which now has low-grade metabolic activity (*Deauville 2*). In contrast, interval metabolic resolution was seen in the other nodes mentioned above. The bilateral external iliac LN (*Deauville 2*) still has low-grade metabolic activity, while the rest do not have significant FDG activity. Additional two cycles of R-ABVD therapy were given. Limited-field radiotherapy was not employed.

After six cycles of chemotherapy, a repeat PET-CT shows no significant change in the right parotid gland nodules. Post-surgical changes remained stable. There was no significant change in the sizes of the previously described prominent to enlarged lymph nodes but with interval regression of metabolic activity in the lymph nodes inferior to the right parotid gland (*Deauville 2*). There was an interval note of mild metabolic activity in the left aspect of the nasopharynx, which was probably inflammatory. There was no significant change in the size of the right hilar lymph node with interval metabolic regression and interval decrease in the size of the small para-aortic lymph node. This confirms complete remission. The patient is now on periodic follow-up check-ups.

Discussion

In the rule of 80, salivary gland tumors affect the parotid gland in 80% of cases, with 80% of these cases as benign and 80% of the benign tumors diagnosed as pleomorphic adenoma. Parotid malignancy only accounts for 5% of all head and neck tumors. This is a rare encounter with an incidence rate of 0.5-3.0/100,000 population per year.[6] NLPHL comes rarer with an incidence of 1.5/1,000,000 population per year.[4] Incidence peaks in childhood and among young adults.

NLPHL has a rather more indolent course, and 75% are diagnosed in the early stages. They commonly present peripheral adenopathy localized to the neck, axilla, or inguinal region. However, involvement of the parotid gland is rare, with few cases reported.[1]

Diagnosis is confirmed through a biopsy of the affected lymph node or organ showing enlarged nuclei with lobular contours and prominent multiple nucleoli, termed malignant LP cells ("popcorn cells") in a background of B-cell-rich lymphoid follicles associated with follicular dendritic cell meshwork.[4] LP cells consistently express CD20 but lack CD30 as opposed to its counterpart classical Hodgkin Lymphoma.[2] It also expresses strong PAX5, OCT2m, and BOB1 and lacks expression of CD15 and EBV. These LP cells are derived from the malignant transformation of germinal center B cells within an inflammatory background. It is characterized by constitutive activation of NF-KB and aberrant kinase signaling.

In this case, the patient presented with a gradually enlarging right preauricular mass without B symptoms, with biopsy and immunohistochemical staining results consistent with NLPHL.

The rarity of the case limits clinical trials for its treatment. Because of this, treatment for classical Hodgkin's Lymphoma is used. ABVD has been employed as the treatment of choice for intermediate-stage NLPHL.[5] This is combined with anti-CD20 monoclonal antibody rituximab. Overall response showed an 85% five-year progression-free survival and 99% overall survival.[4]

Early-stage disease in the absence of risk factors benefitted from limited-field radiotherapy alone rather than active surveillance or rituximab monotherapy.[2] Active surveillance showed no difference in overall survival compared to treatment groups, but a shorter progression-free survival was found.[4] Based on recent studies, advance staged NLPHL have a better response with a more aggressive chemotherapy regimen such as BEACOPPesc (escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) or R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).[2] NLPHL has a propensity for late relapse or transformation to an aggressive form of B-cell non-Hodgkin Lymphoma (NHL) emphasizing the need for close follow-up check-up even after response to treatment.

We have found only two cases of parotid gland NLPHL reported in literature. The first case was of a 32-year-old Caucasian male who presented with a one-year right cheek tumor. Surgical removal and radiotherapy resulted in complete excision of the mass and towards remission. No chemotherapy was given.[1] The other is a case of NLPHL in the progressive transformation of germinal centers (PTGC). This was a case of a 39-year-old female presenting with right lymphadenopathy and an ipsilateral parotid mass. The diagnosis was confirmed through a biopsy of the excised parotid mass. PTGC precedes NLPHL, and both may be present in one lymph node. PTGC can be differentiated pathologically from NLPHL by nonneoplastic small mantle B cells. There was no mention of treatment in this paper.[3]

Conclusion

Parotid gland NLPHL is a rare disease entity, but treatment provides good response and outcome. Early detection and biopsy of a growing mass are significant in treatment. Diagnosis should not be limited to the common findings of a parotid gland tumor. Lymphoma, though a rare entity affecting the parotid gland, should still be considered, especially since early initiation of treatment using a stage-based treatment regimen provides good response rates. Close follow-up and surveillance, as clinically indicated, are well emphasized

to detect relapse early and transform into a more aggressive form of NHL.

Ethical Considerations. This report was written in compliance to the following local and international ethical guidelines for research ethics: Declaration of Helsinki 2015, International Conference on Harmonization on Good Clinical Practice (ICH-GCP), Council for International Organizations for Medical Sciences 2016, Good Research Practice (GRP), Philippine National Ethical Guidelines for Health and Health-Related Research of 2017, Philippine Data Privacy Act of 2012 and its Implementing Rules and Regulations (IRR) of 2016.

Conflict of Interest. No external funding was used for this study. The authors declare that they have no conflict of interest regarding the publication of this paper.

Informed Consent Process. Informed consent was obtained from the patient himself. The patient is a doctor of Medicine specializing in Dermatology. He has a competent grasp of English; hence, the informed consent form written in Tagalog was no longer used. The contents of the consent form were explained in detail, and the patient was given ample time to make decisions. Consent was voluntarily signed by the patient, a witness, and the principal investigator.

Risks and Benefits. The patient and his family did not directly benefit from participating in this case report. The patient was not compensated for participating in this report. However, the information that can be shared with other healthcare professionals may improve the care received by others with the same case in the future. There is no untoward effect expected from participating in this case report.

Data Privacy and Confidentiality. Identifying descriptors were removed from the manuscript to preserve the patient's right to privacy. There is, however, a limited risk of losing confidentiality by virtue of the uniqueness of the case. The patient's chart, consent forms, and result printouts that contain personal identifying information are stored securely in locked file cabinets when not in use and are handled only by the investigators. All electronic data is stored in private computers that require password access. The data will be kept for three years for verification and publication purposes. Then, physical copies of data will be destroyed via paper shredder, while electronic files will be permanently deleted.

Vulnerability. Informed consent was obtained from the patient. He was not forced to provide information for this case report. There is no expected untoward effect from participating in the conduction of this case report.

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