A 23-year-old white Caucasian male reported a 3-month history of an asymptomatic lump in the right submandibular region. An ultrasound scan and a magnetic resonance imaging (MRI) demonstrated a large and well-defined hypercellular mass in the right level Ib/submandibular region. A fine needle aspiration (FNA) and excision biopsy were performed. Fluorescence in situ hybridization (FISH) confirmed a diagnosis of a diffuse large B-cell lymphoma, non-germinal center type. The patient was treated with a 12-week chemotherapy regime (R-CHOP). A pre- and post-chemotherapy PET-CT was performed, the latter of which showed only normal physiological uptake and no recurrence or signs of distant metastasis.

**Conclusion:** Submandibular lymphomas are a well-documented yet rare presentation, particularly in the young adult. This case report highlights the successful diagnosis, treatment, and follow-up of an extremely rare finding in a 23-year-old patient and highlights the importance of considering a diffuse B-cell lymphoma in a patient presenting with a lump in the submandibular gland.

**Keywords:** Diffuse B-cell lymphoma, Head and neck cancer, MRI, Submandibular gland
submandibular gland lacks presence of intraglandular lymph nodes and, therefore, the incidence of extranodal parenchymal lymphomas of the submandibular glands is very rare [4–7]. This case report highlights the first documented example of a primary diffuse B-cell lymphoma originating from the parenchymal tissue of a submandibular gland.

CASE REPORT

A 23-year-old white Caucasian male was referred to the maxillo-facial department for investigations of a painless lump in the right submandibular region. The patient reported an asymptomatic lump that had been present over a 3-month period with no prior symptoms, particularly no B-symptoms (fever, night sweats, and weight loss). The patient was otherwise fit and well with no past medical history.

The patient underwent an ultrasound scan and an MRI scan which demonstrated a large and well-defined mass in the right level Ib/submandibular region with modest heterogenous enhancement. The patient went on to have a FNA and a core biopsy, the latter of which was inconclusive. The fine needle aspiration showed morphology suggestive of a high grade non-Hodgkin lymphoma and a further biopsy was advised. The patient underwent an excision biopsy. Histopathological analysis of the biopsied specimen was suggestive of a high grade B-cell lymphoma. Fluorescence in situ hybridization (FISH) further confirmed a diagnosis of a diffuse large B-cell lymphoma, non-germinal center type.

Post-operatively, the patient underwent a PET-CT scan showing high uptake posterior to the right hemimandible and no distant metastasis. The patient was referred to the oncology team and was treated with multiple rounds of chemotherapy after which a PET-CT scan was performed showing only normal physiological uptake and no recurrence or signs of distant metastasis.

Presentation

Macroscopic

The patient presented with a 3-month history of a right-sided submandibular lump (Figure 1). Following a core biopsy and a FNA the patient underwent a surgical excision that revealed a creamy, cheesy textured lymphoma like mass.

Imaging modalities

Ultrasound neck demonstrated a well-defined hypoechoic lesion in the right submandibular region (Figure 2). This was difficult to distinguish as discrete from the submandibular gland. The patient also underwent a FNA for cytology.

An MRI of the neck revealed a large and well-defined mass in the right level 1b submandibular region. A T2-weighted image demonstrated intermediate signal while a T1-weighted post-contrast image demonstrated modest heterogenous enhancement (Figure 3). Axial diffusion-weighted imaging with a b1000 image and apparent diffusion coefficient (ADC) map demonstrated diffusion restriction compatible with a hypercellular lesion (Figure 4). This finding on axial diffusion-weighted scan was highly suggestive of a malignant cause.
Cytology

Four air-dried samples were processed for cytology from the FNA revealing a population of lymphoid cells with a marked increase in nuclear to cytoplasmic ratio, irregular nuclear outlines, and nuclear hyperchromasia. Scattered mitotic figures were also seen. No germinal center fragments were noted and only occasional small lymphocytes were seen scattered in the background (Figure 5). The findings were suggestive of a high grade non-Hodgkin lymphoma.

Histology

An irregular multilobulated cream/hemorrhagic nodule $55 \times 40 \times 20$ mm weighing 21.4 g was analyzed. Microscopically, most of the salivary glands were within normal limits. An enlarged lymph node which was partially replaced by a vaguely nodular infiltrate of centroblasts with scattered tingible macrophages was seen. No necrosis was observed. Part of the same lymph node showed normal germinal centers. Several smaller lymph nodes showed reactive changes only.

Immunostains showed that the large cells were B-lymphocytes; CD20+, BCL6+, and bc12+ (weak) with high proliferation rate, MIB1 60–70%. There was an underlying moth eaten follicular dendritic cells (FDC) meshwork on CD21. Staining for CD30, CD5, and EBER was negative. The features were those of high grade B-cell lymphoma, likely diffuse large B-cell lymphoma (DLBCL), non-germinal center type. Some features suggest that this might have arisen from an underlying low grade lymphoma, either follicular lymphoma or marginal zone lymphoma. Fluorescence in situ hybridization (FISH) was negative for c-myc and bc12 translocation and positive for BCL6 translocation (Figure 6). This was entirely in keeping with diffuse a large B-cell lymphoma, non-germinal center type.

Follow-up

Post-operatively, the histology of the surgically excised neck lump confirmed a DLBCL. The patient was referred to the oncology team for further management where a 12-week chemotherapy regime (R-CHOP) was arranged. The therapy consisted of Rituximab, Cyclophosphamide, Doxorubicin Hydrochloride, Vincristine, and Prednisolone. To assess for response to chemotherapy, the patient underwent a PET-CT scan showing only normal physiological uptake and no area of concern at the site of the excision and no concerns of recurrence or distant metastasis (Figures 7 and 8).
DISCUSSION

Common differentials for a neck lump arising from the submandibular gland are divided into two categories, non-neoplastic, and neoplastic. Non-neoplastic differentials include sialadenitis and sialolithiasis. Neoplastic differentials include pleomorphic adenoma, mucoepidermoid carcinoma, adenocarcinoma, and lymphoma. Often the history of presentation and examination of the neck lump can help clinicians determine the nature of the lump (infective, obstructive, or malignant). Sialadenitis and sialolithiasis commonly present with a shorter history of a warm, erythematous tender submandibular neck lump accompanied with malaise and pyrexia. In the case of a hematological malignancy presenting as a neck lump, patients commonly present with B-symptoms suggestive of a neoplastic cause. B-symptoms commonly include unexplained pyrexia, night sweats, and unexplained weight loss.

In this particular case, the patient presented with a three month history of a non-tender neck lump in the absence of infective symptoms, raising suspicion for a neoplastic lump. Absence of B-symptoms in this patient’s presentation would suggest a non-hematological malignancy.

As per local and national guidance, the least invasive form of imaging was arranged under a 2-week wait and the patient underwent an ultrasound scan with a FNA and core biopsy. An MRI scan was also performed and the hypercellular findings on the diffusion weighted images were highly suggestive of a malignant cause. This highlights the importance of MRI scanning in the workup of head and neck masses.

Although the results of the core biopsy were inconclusive, the high level of suspicion for a malignant cause led to an early excision rather than a repeat biopsy. The cytology from FNA samples was highly suggestive of lymphoma which was later confirmed on histology of the surgically excised mass. An early referral was made to an oncological department where a chemotherapy regime had been advised for the patient. After 12 weeks (four 3-week cycles) of chemotherapy, a post-treatment PET-CT scan was performed. This showed a normal physiological uptake and no evidence of recurrence at the site of the excision and of distant metastasis.

This case demonstrates a rare occurrence of DLBCL in a submandibular gland and the first of its kind to be documented in a young and otherwise healthy adult of only 23 years of age. It highlights the importance of considering lymphoma in the set of differentials when working up a neck lump in an otherwise young and healthy adult. Current literature suggests that lymphomas are more commonly seen in parotid glands as compared to submandibular glands [8]. However, this case suggests that lymphoma within the submandibular gland is a possibility despite the lack of intraglandular lymph nodes. Furthermore, the diagnosis of DLBCL highlighted the need for further work up to assess for local or distant spread. As mentioned earlier, post-operative PET-CT in this case did not show any signs of distant metastasis and patient was classified as having DLBCL stage 1a.

Diffuse large B-cell lymphoma is one of the more aggressive forms of NHL and makes up 40% of all NHL cases in adults [9]. It is more common in men compared to females [9]. Oncological management is based around chemotherapy, immunotherapy, and radiotherapy. Early stage DLBCL is typically treated with three to four cycles (each cycles lasts three weeks) of chemoimmunotherapy. In our case a surgical excision of the tumor was undertaken followed by four 3-week cycles of R-CHOP chemotherapy leading to complete metabolic remission. The case also highlights the importance of a multi-disciplinary approach to a very rare presentation.

CONCLUSION

Lymphomas originating in the submandibular salivary glands are a rare but well-documented occurrence. This case report emphasizes the importance of including lymphoma in the differentials of young patients being investigated for a suspicious neck lump. This case highlights the successful diagnosis, treatment, and follow-up of an extremely rare finding.

REFERENCES

1. Hashimoto K, Ikebe T, Ozeki S. Diffuse large B-cell lymphoma in the submandibular gland. Asian Journal of Oral and Maxillofacial Surgery 2008;20(1):41–5.
2. Takahashi H, Tsuda N, Tezuka F, Fujita S, Okabe H. Non-Hodgkin’s lymphoma of the major salivary
gland: A morphologic and immunohistochemical study of 15 cases. J Oral Pathol Med 1990;19(7):306–12.
3. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer 1972;29(1):252–60.
4. Zhu L, Wang P, Yang J, Yu Q. Non-Hodgkin lymphoma involving the parotid gland: CT and MR imaging findings. Dentomaxillofac Radiol 2013;42(9):20130046.
5. Gleeson MJ, Bennett MH, Cawson RA. Lymphomas of salivary glands. Cancer 1986;58(3):699–704.
6. Hyman GA, Wolff M. Malignant lymphomas of the salivary glands. Review of the literature and report of 33 new cases, including four cases associated with the lymphoepithelial lesion. Am J Clin Pathol 1976;65(4):421–38.
7. Faur A, Lazăr E, Cornianu M, et al. Primary malignant non-Hodgkin’s lymphomas of salivary glands. Rom J Morphol Embryol 2009;50(4):693–9.
8. Ellis G, Auclair P. Atlas of tumor pathology. Washington: Armed Forces Institute of Pathology Tumors of the salivary glands. Malignant Lymphoma of the Major Salivary Glands 1996. P. 387–402.
9. https://www.cancerresearchuk.org/about-cancer/non-hodgkin-lymphoma/types/diffuse-large-B-cell-lymphoma

**********

**Author Contributions**

Farooq Hassan Afzaal – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Basil Zia Khan – Conception of the work, Design of the work, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Karim Kassam – Conception of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ashok Adams – Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Guarantor of Submission**

The corresponding author is the guarantor of submission.

**Source of Support**

None.

**Consent Statement**

Written informed consent was obtained from the patient for publication of this article.

**Conflict of Interest**

Authors declare no conflict of interest.

**Data Availability**

All relevant data are within the paper and its Supporting Information files.

**Copyright**

© 2021 Farooq Hassan Afzaal et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.
Submit your manuscripts at
www.edoriumjournals.com