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CASE REPORT

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Spontaneous resolution of untreated diffuse large B-cell lymphoma of maxillary bone after incisional biopsy

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Abstract

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group of lymphomas which require multiagent therapy for remission induction and are associated with relapse in more than 40% of patients. Spontaneous remission of diffuse large B-cell lymphoma (DLBCL) is a rare occurrence.

KEYWORDS

chemotherapy, diffuse large B-cell lymphoma, non-Hodgkin lymphoma, spontaneous remission

1 | INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) among adults and requires treatment with cytotoxic combination chemotherapies. Spontaneous remission of DLBCL is an extremely rare phenomenon and to date has only been described in case reports.

2 | CASE HISTORY/EXAMINATION

A 61-year-old woman with history of diabetes mellitus presented to her dentist with a painful loose tooth in right upper jaw and underwent a root canal and treatment with antibiotics. Three months later, she developed another tooth infection that required treatment with oral antibiotics. Due to her recurrent infections and significant bone loss around the tooth by radiography, an underlying malignancy was suspected. Four months after her initial presentation, an incisional biopsy of the maxillary bone was performed by an oral maxillofacial surgeon and initial pathology showed a fibro-osseous lesion, which was later amended to germinal center DLBCL following additional pathology review. The patient was referred to the University of New Mexico where on initial evaluation she was found to be asymptomatic and without evidence of lymphadenopathy on physical exam. Hematopathology review of her previous biopsy revealed multiple areas of soft tissue and bone infiltration by dense lymphoid infiltrates. These were comprised of large atypical cells with round to oval nuclei, slightly irregular nuclear contours, vesicular chromatin, inconspicuous to prominent nucleoli, and scant cytoplasm. There were many apoptotic bodies and a few mitotic figures intermixed within the large atypical cells. A background population of small mature lymphocytes was also present. The bony fragments showed new bone formation with extensive osteoblastic activity, fibrovascular connective tissue, and

fibrosis. By immunohistochemical stains (IHC), CD3 highlighted only few small, mature background T-cells whereas CD20 highlighted back-to-back sheets of large B cells supportive of the diagnosis of DLBCL. These cells expressed BCL-6 (>30%). The nuclear proliferation index (Ki-67) was elevated in the cells of interest, around 90%. MUM1 highlighted rare large cells (overall < 30%). BCL-2 expression was variable and positive in less than 50% of the neoplastic cells. The cells of interest were negative for CD5, CD10, cyclin D1, MYC, and EBER by in-situ hybridization. CD3 and CD5 highlighted background small T-cells. The expression pattern of CD10, BCL6, and MUM1 supported the diagnosis of germinal center subtype (Figure 1).

At presentation, laboratory data were largely unremarkable, with normal complete blood counts, LDH (154 Unit/L), and renal and hepatic function. Human immunodeficiency virus (HIV) was also negative. A computed tomography (CT scan) with contrast of the neck showed nonpathologically enlarged level 2 lymph nodes, measuring up to 8 mm (Figure 6). An 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) CT, which was performed six weeks after the incisional biopsy, showed only very minimal activity in the right maxillary canine, most likely postprocedural inflammation, without any significant lymphadenopathy (Figures 7 and 8).

The patient's pain has resolved after the initial biopsy. Systemic chemotherapy followed by local radiation was recommended but the patient declined both and opted for active surveillance. Twenty-two months after the diagnosis, she still has no signs or symptoms of clinical recurrence.

2.1 | Pathology images

See Figures 1-8.

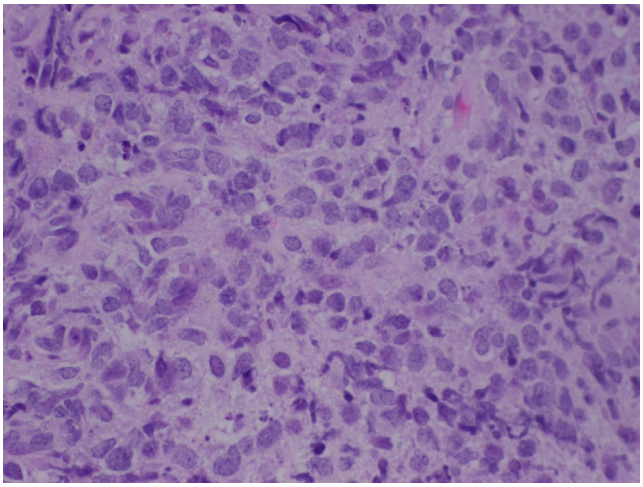

FIGURE 1 Maxillary bone biopsy. Sheets of large atypical cells by H&E stain

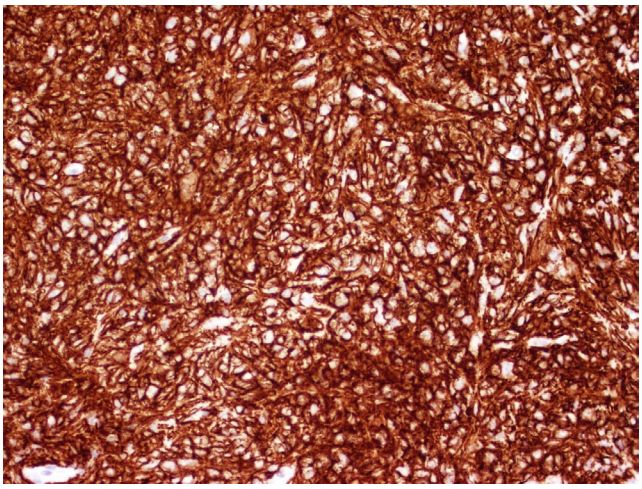

FIGURE 2 Large atypical cells that strongly express CD20

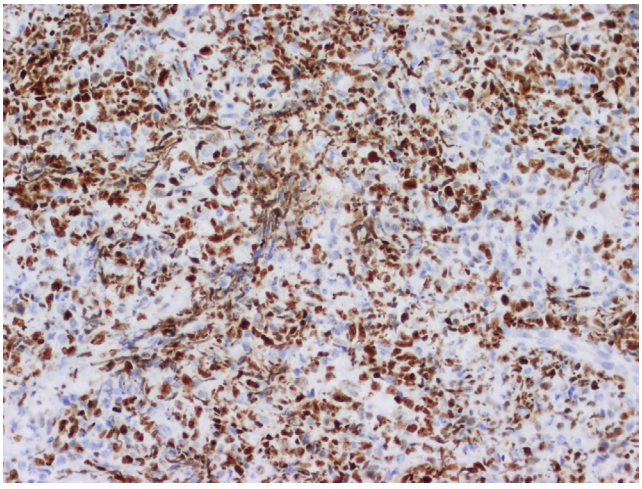

FIGURE 3 Neoplastic B-cells express BCL-6 in ≥30% of cells

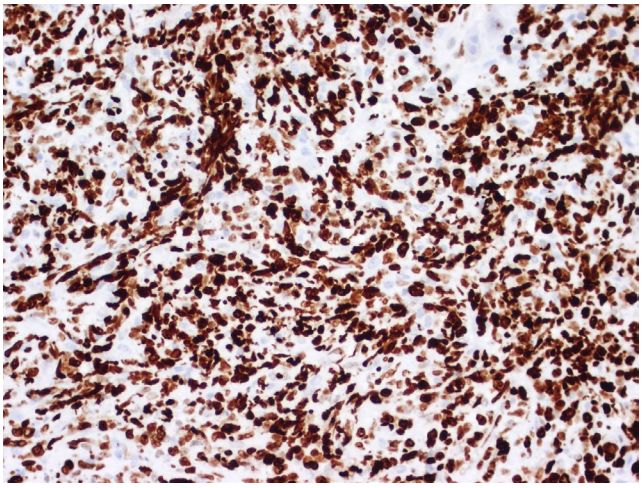

FIGURE 4 High Ki-67 proliferation index, ~90%

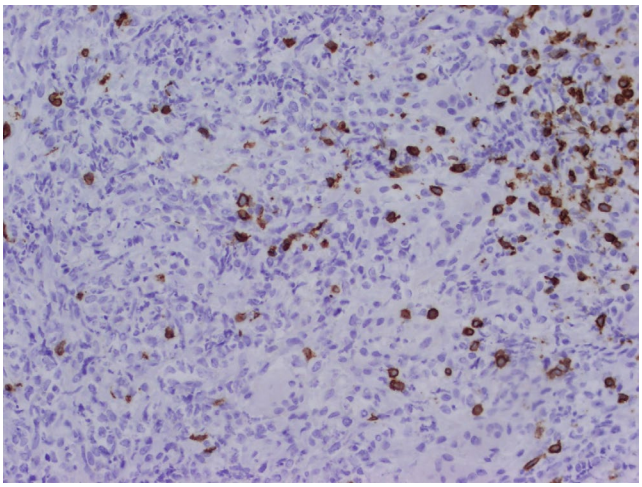

FIGURE 5 Few small, mature T-cells

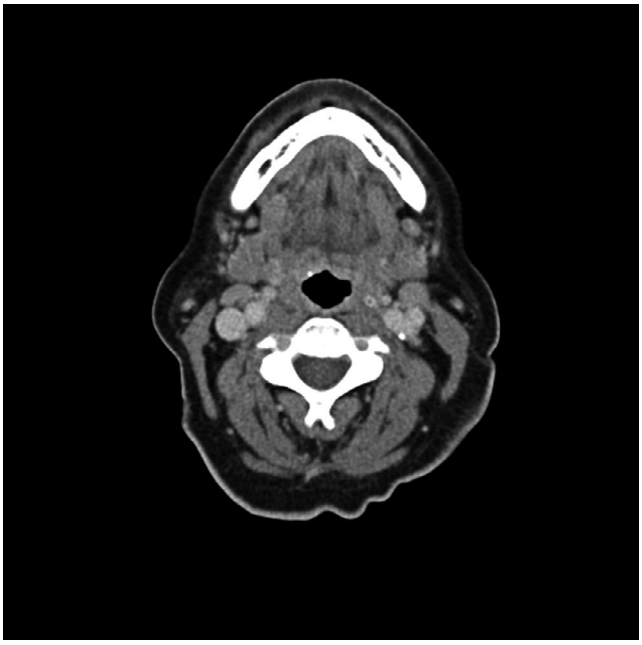

FIGURE 6 Neck CT scan. 8 mm nonpathologically enlarged cervical lymph nodes

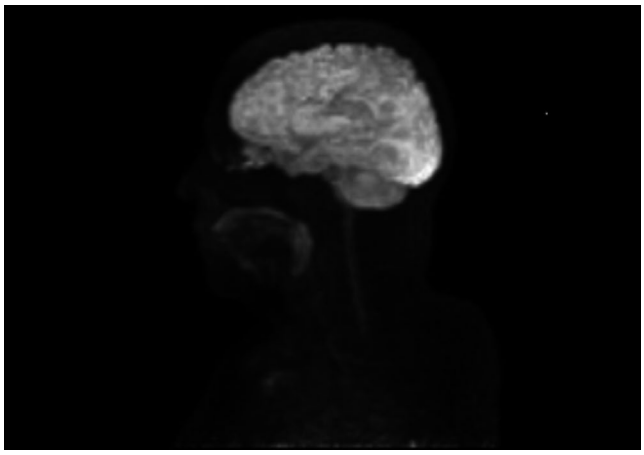

FIGURE 7 Positron emission tomography CT scan. No standardized uptake value (SUV) activity detected in lateral view

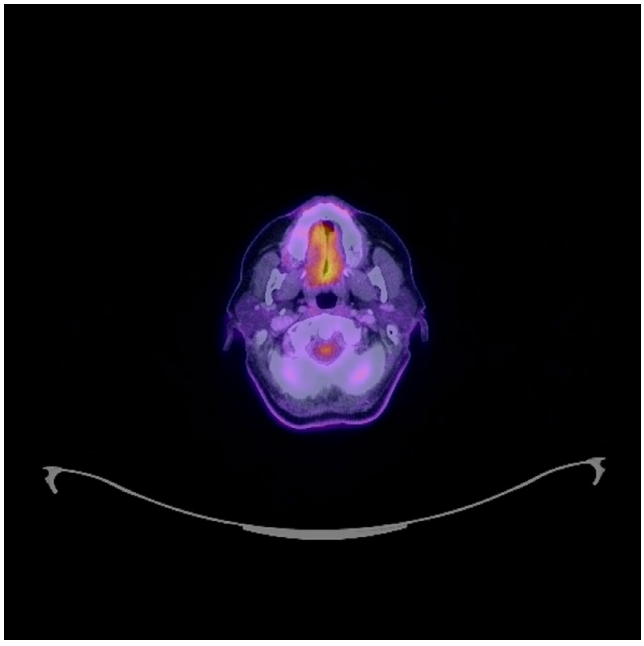

FIGURE 8 Minimal standardized uptake value (SUV) activity in the right maxillary canine, postprocedural

3 | DISCUSSION

Diffuse large B-cell lymphoma (DLBCL) comprises a heterogeneous group of lymphoma that can be cured in 60%-70% of patients with immunochemotherapy. In addition to WHO morphological subtypes, current molecular classification divides DLBCL into germinal center B-cell-like (GCB) or activated B-cell-like (ABC) with different prognoses. Next-generation sequencing (NGS) has expanded the classification of DLBCL patients into four groups: MCD, BN2, N1, and EZB.[1]

Although commonly seen in nodal areas, DLBCL can occur in essentially any tissue of the body and is typically lethal within two years of diagnosis without treatment.[2] Spontaneous regression is a rare but documented phenomenon that is more common in low grade phenotypes [3] Primary non-Hodgkin lymphoma of the bone is also rare, accounting for 5% of extranodal lymphoma and less than 1% of non-Hodgkin's lymphoma.[4] The usual management involves combined modality therapy with chemotherapy and in some cases radiation; surgery does not play a therapeutic role.[4] R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, and prednisone only) is the regimen of choice in the absence of high-risk features such as double or triple hit or double expressor DLBCL.[5] Of the subtypes, diffuse large B cell is the most common subtype of primary bone lymphoma.[4]

Primary bone diffuse large B-cell lymphoma (PB-DLBCL) is a rare and favorable prognosis lymphoma, with

PFS and OS rates of 80% and 93%, respectively. Gene expression profile and microRNA showed a distinct profile compared to GCB-DLBCL in the centroblast-origin (CB) subtype and had higher levels of miR-125a-3p, miR-34-3p, miR-155-5p and lower levels of miR-17-5p and miR-17-3p.[6]

The mechanism of regression in lymphoma is postulated to be immune-mediated secondary to activation from viruses like Epstein-Barr virus versus local trauma from a biopsy.[7-9] This has been documented in primary cutaneous DLBCL of the leg,[7,9,10] as well as DLBCL of the bladder,[11] breast,[12] and conjunctiva.[13] Extranodal onset may confer a greater likelihood of spontaneous regression.[2,7] One case series found that regression is more likely to occur if there is a decrease in the size of the mass within the first two weeks after biopsy, which may be a predictor of spontaneous regression.[14]

Per our literature review, there has been only one documented case of spontaneous regression of a primary bone lymphoma. Brachet et al describe a case of a submucosal mass of lymphoma found in the right posterior hard palate which regressed spontaneously within fifteen days of a biopsy without further therapy.[15] Their patient, however, did receive R-CHOP for hypermetabolic nodes throughout the body.[16] Koga et al, describe a case of gingival lymphoma that underwent spontaneous regression after biopsy but did not have bone involvement.[9] Hiroshima et al, reported on a case of regression of sphenoid and ethmoid sinus diffuse large B-cell lymphoma with metastases in an 85-year-old woman with advanced dementia treated with loxoprofen.[16] Their patient had spontaneous regression over the course of two months and a biopsy was positive for COX-2 which lead them to theorize that inhibition of the COX-2 receptor by loxoprofen resulted in regression of the tumors but did not comment on the role the biopsy might have played in stimulating the immune system.[15] This is distinct from our case in that our patient continued her diabetes medications but was not treated with anti-inflammatory agents. Also, in their case the mass was not from the bone itself but rather the surrounding mucosa. Armstrong et al describe a case of HIV-associated plasmablastic lymphoma of the oral cavity.[8] Plasmablastic lymphoma often arises in the oral cavity with invasion into the soft tissue and bone and is not CD20 positive.[17] This case is similar to ours as the patient presented with an oral lesion originally thought to be due to an infection and had spontaneous regression after sampling. The authors hypothesized that immune reconstitution occurred following initiation of antiretroviral therapy and this played a role in the regression of the tumor, which has been demonstrated in other case reports.[8] Our patient had no evidence of either a compromised immune system or immune reconstitution. Our case is a unique example of primary bone DLBCL without nodal involvement which demonstrated spontaneous regression after incisional biopsy leading to a stable remission without adjuvant therapies. This remission occurred via an unknown mechanism but was possibly related to immune system activation. It is also one of the first examples of primary bone lymphoma regression and the first example in which the patient was not given any additional systemic therapy. The patient elected for surveillance and has shown no evidence of disease recurrence at eight months following her biopsy. This case provides further evidence that immunotherapy could play a role in the initial treatment of DLBCL. Also, in rare circumstances where spontaneous regression has occurred, watchful waiting is a viable alternative to chemotherapy if the patient does not desire treatment and has no evidence of disease.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

LFT, KW: Completed the background research, drafted, and edited the manuscript, AJ drafted the pathology data and edited manuscript, LA edited the manuscript, CAY edited the manuscript and approved the final manuscript.

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REFERENCES

1. Thieblemont C, Bernard S, Meignan M, Molina T. Optimizing initial therapy in DLBCL. *Best Pract Res Clin Haematol*. 2018;31(3):199-208.
2. Tamás L, Sári E, Répássy G, et al. Spontaneous remission in localized diffuse large B-cell lymphoma. *Pathol Oncol Res*. 2011;17(3):779-784.
3. Kumar R, Bhargava P, Zhuang H, Yu JQ, Schuster SJ, Alavi A. Spontaneous regression of follicular, mantle cell, and diffuse large B-cell non-Hodgkin's lymphomas detected by FDG-PET imaging. *Clin Nucl Med*. 2004;29(11):685-688.
4. Mikhaeel NG. Primary bone lymphoma. *Clin Oncol*. 2012;24(5):366-370.
5. Ramadan KM, Shenekier T, Sehn LH, Gascoyne RD, Connors JM. A clinicopathological retrospective study of 131 patients with primary bone lymphoma: a population-based study of successively treated cohorts from the British Columbia cancer agency. *Ann Oncol*. 2007;18(1):129-135.
6. Li X, Xu-Monette ZY, Yi S, et al. Primary bone lymphoma exhibits a favorable prognosis and distinct gene expression signatures resembling diffuse large b-cell lymphoma derived from centrocytes in the germinal. *Center. Am J Surg Pathol*. 2017;41(10):1309-1321.
7. Marrero-Alemán G, Montenegro-Dámaso T, Peñate Y. Primary cutaneous diffuse large B-cell lymphoma, leg type, with spontaneous regression after biopsy. *Am J Dermatopathol*. 2017;39(10):785-787.

8. Armstrong R, Bradrick J, Liu YC. Spontaneous regression of an HIV-associated plasmablastic lymphoma in the oral cavity: a case report. *J Oral Maxillofac Surg*. 2007;65(7):1361-1364.
9. Koga M, Kusukawa J, Hayabuchi N. Spontaneous regression of extranodal malignant lymphoma occurred in the gingiva. *Oral Oncol*. 2003;39(3):323-324.
10. Alcántara-González J, González-García C, Fernández-Guarino M, Jaén-Olasolo P. Spontaneous regression of primary diffuse large B-cell lymphoma, leg type. *Actas Dermosifiliogr*. 2014;105(1):78-83.
11. Yamada M, Kuroda H, Sato K, et al. Spontaneous regression of methotrexate-related diffuse large B-cell lymphoma following bladder lesion resection. *Rinsho Ketsueki*. 2017;58(4):287-291.
12. Iwatani T, Kawabata H, Miura D, Ota Y, Ohashi K. Complete spontaneous regression of primary diffuse large B-Cell lymphoma of the breast. *J Clin Oncol*. 2011;29(5):e113-e115.
13. Chang YC, Chang CH, Liu YT, Tsai KB, Liu TC, Lin YN. Spontaneous regression of a large-cell lymphoma in the conjunctiva and orbit. *Ophthalmic Plast Reconstr Surg*. 2004;20(6):461-463.
14. Abe R, Ogawa K, Maruyama Y, Nakamura N, Abe M. Spontaneous regression of diffuse large B-cell lymphoma harbouring Epstein-Barr virus: a case report and review of the literature. *J Clin Exp Hematop*. 2007;47(1):23-26.
15. Brachet P, de Leval L, Chantrain G, Loeb I, Saussez S. [Hard palate B cell lymphoma with spontaneous regression]. *Rev Stomatol Chir Maxillofac*. 2011;112(3):180-182. French. Erratum. In: Rev Stomatol Chir Maxillofac. 2012 Jun; 113(3):199. Deleval, L [corrected to de Leval, L].
16. Hiroshima Y, Kato T, Tajima K. Regression of diffuse large B-cell lymphoma in sphenoid and ethmoid sinuses following treatment with loxoprofen. *Leuk Lymphoma*. 2016;57(3):721-723.
17. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lymphoma. *Blood*. 2015;125:2323-2330.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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