

Case study**Mandibular swelling revealing a rare disease of Non-Hodgkin's Lymphoma-a clinical dilemma****Abstract**

Mandible remains a site of swelling for number of diseases including infection, cyst & tumors. Although the frequency of such lesions is variable, a few lesions with rarest occurrence without any pathognomic, clinical & radiological features may cause diagnostic predicament. Although the list of various swellings of mandible mostly inflammatory, odontogenic and occasionally salivary gland lesions, but such list is not limited to those diseases alone & may be kept open to incidence of some other diseases such as diffuse large B-cell lymphoma as in our case which is a rare form of extranodal non-Hodgkin's lymphoma that account for 0.1 – 0.2% of cases in oral cavity, and occasionally appears in the mandible. We report a case of diffuse large B-cell lymphoma in a 77-year-old male patient. The patient presented with firm, mild painful swelling on the left lower face with history of non-healing extraction socket and enlarged left submandibular lymph nodes leading to a provisional diagnosis of chronic dental infection or dentoalveolar abscess. Incisional biopsy from the lesion and immunohistochemistry study confirmed the diagnosis of diffuse large B-cell lymphoma of left mandible.

Keys word: Diffuse large B-cell lymphoma, immunohistochemistry and mandible.

22 **Introduction**

23 Lymphomas are a diverse group of neoplasms affecting the lympho-reticular system. It is
24 divided into Hodgkin's disease and Non-Hodgkin's disease. Hodgkin's type commonly
25 presented as nodal disease, often involving cervical, axillary and inguinal nodes. Whereas
26 non-Hodgkin's disease have extra-nodal presentation and can occur in stomach, salivary
27 glands and rarely in oral cavity and jaw [1]. Primary non-Hodgkin's lymphomas (NHL) of bone
28 are quite rare, but among jaw lesions, they more frequently arise in the maxilla than in the
29 mandible [1].

30 NHL of bone formerly referred to as reticulum cell sarcoma of bone, represents 7% of
31 primary bone tumours and 5% of all primary extranodal NHL [2,3]. The most common
32 histologic type is diffuse large B-cell lymphoma (DLBCL) accounting for approximately 30% of
33 all NHL [4]. Most of DLBCL arises in lymph nodes. However, 40% of these malignancies arise
34 in extranodal sites, most commonly the gastrointestinal tract, skin, and Waldeyer's ring
35 [5]. Lymphomas arising within the oral cavity accounts for less than 5% of all oral
36 malignancies and approximately 85% of the lesions involve the tonsils and palate [6]. Here,
37 we reported a case of primary DLBCL of the mandible, presenting as diffuse swelling on the
38 left body of the mandible.

39 **Case report**

40 A 77-year old male patient presented with firm and mild painful swelling on the left lower
41 face with duration of two months. The swelling was gradual in onset and increases to
42 present size with facial asymmetry. The patient had past history of loosening of left side

43 tooth with extraction of 36 mobile teeth and received antibiotics for one month without any
44 significant clinical improvement.

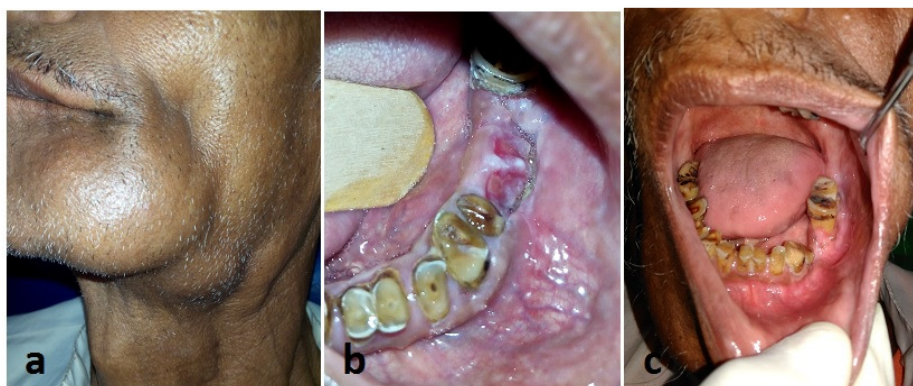
45 Extraoral examination revealed a solitary swelling extending from left parasymphysis region
46 to body of mandible measuring 2.5×2cm in size, firm to hard in consistency with smooth,
47 normal overlying skin surface and left submandibular lymphadenopathy (figure-1a).

48 On intra oral examination the swelling was extended from 32 to 37 tooth regions
49 obliterating buccal vestibule, with non-healing 36 socket region and lateral expansion of
50 buccal cortical plate (figure-1b). Patient had history of smoking (10years), poor oral hygiene,
51 generalized attrition, and calculus deposit. Orthopantomogram showed radiolucency with
52 irregular destruction of bone extending 32-37 tooth regions (figure-2a). Indurated non-
53 healing extraction socket, smoking history and atypical clinical finding raised a suspicion of
54 malignancy. Incisional biopsy from the lesion was performed which showed diffuse sheets of
55 round to oval tumor cells with scanty cytoplasm, vesicular nuclei with prominent nucleoli revealing
56 features of round cell tumor possibly NHL with differential diagnosis of other round cell
57 tumors (poorly differentiated squamous cell carcinoma, small cell osteosarcoma,
58 neuroblastoma, ewing sarcoma) (figure-3a).

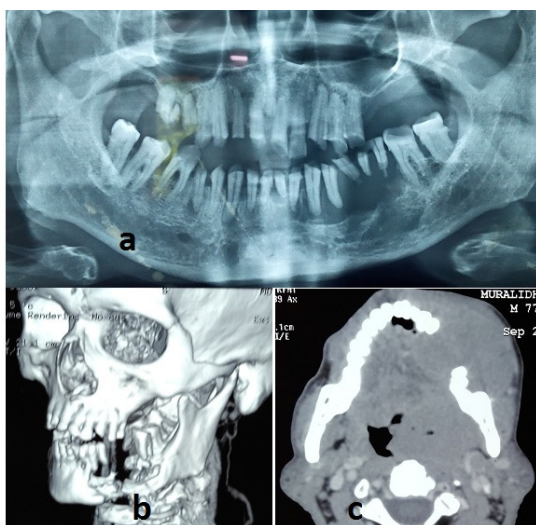
59 Immunohistochemistry study showed positivity for LCA, CD20, negative for CK, S100, HMB
60 45, Vimentin and a high proliferative index (MIB1 = 60%) confirming the diagnosis of DLBCL
61 (figure-3b, -3c).

62 Due to communication breach patient reported after 2months and contrast enhanced CT
63 (CECT) scan showed complete destruction of both buccal and lingual cortical plates with
64 enlargement of ulcerative growth (figure-2b, -2c). Serum lactate dehydrogenase (LDH), CECT
65 scan of thorax, abdomen and pelvis, and bone marrow biopsy were found to be normal. The

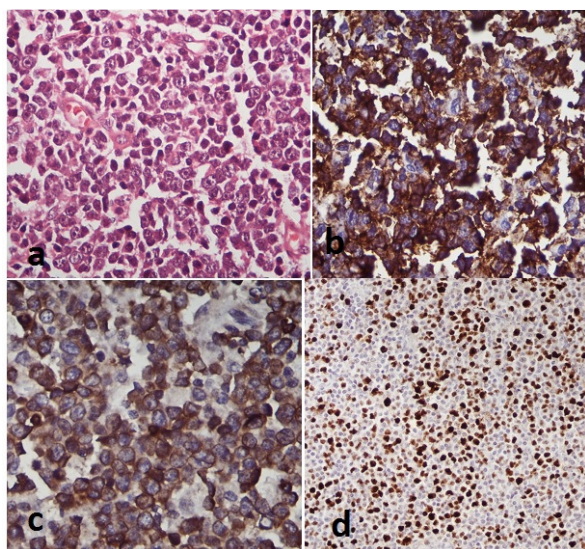
66 patient was treated with radical chemotherapy followed by radiotherapy. Patient had
 67 received six cycles of chemotherapy R-CHOP regimen (Rituximab, Cyclophosphamide,
 68 doxorubicin, vincristine and Prednisolone) with proper dose schedule. After that, patient
 69 had received involved field radiotherapy (IFRT) of 40 GY in 20 fractions. The patient was
 70 disease free with clinically normal healthy oral mucosa (figure-1c) after one year follow-up.



72 Figure-1: Showing a) Swelling over left side body of mandible, b) Non-healing socket with
 73 respect to 35-36 tooth region, and swelling of left vestibule, and c) Post-treatment normal
 74 healthy mucosa.



76 Figure-2: a) Orthopantogram showing ill-defined radiolucency extending from 32 -37 tooth
77 region, b) and c) CECT scan showing bicortical bone destruction with extension of the lesion.



78

79 Figure-3: Showing a) histopathology (H & E stain 400X): Diffuse sheets of round to oval
80 tumor cells with scanty cytoplasm, vesicular nuclei with prominent nucleoli
81 Immunohistochemistry study showing b) CD20 positive, c) BCL-2 positive, d) MIB1 (60%)

82 Discussion

83 NHL is broadly classified into two broad groups: B-cell lymphoma and T-cell lymphoma.
84 According to WHO classification (2001), DLBCL is a special entity placed under mature
85 peripheral B-cell neoplasm group [7].

86 Extra nodal presentation is seen in 40% of NHL [8] and 2-3% of these found as oral cavity
87 and jaw primary. Majority presents in the age group of 6th and 7th decades of life and
88 commonly seen in maxilla [9]. Present case was presented at age of 77 years with a
89 diagnosis of DLBCL at a rare site of location as mandible primary. To our knowledge, there
90 are only a few cases were reported.

91 DLBCL is a high-grade B-cell NHL and present case is without any significant aggressiveness
92 of the tumour. Due to little incidence and non-specific symptoms, primary NHL of the
93 mandible or jaws is often misdiagnosed for a dental infection [10,11]. Biopsy is performed
94 after poor response to antibiotic treatment, non-healing ulcer or extraction socket.

95 WHO diagnostic criteria for primary lymphoma of bone are a primary focus in a single bone
96 with no evidence of distant soft tissue or lymph node involvement. According to Coley
97 (1950), the criteria for diagnosis of bone primary is lymphoma presenting in an osseous site
98 with no evidence of disease elsewhere for at least 6 months after diagnosis [10].

99 Parrington et al. have discussed a case of primary lymphoma of the mandible presenting
100 after tooth extraction [12]. Leva Djavonmardi et al. have reviewed 16 cases of NHL of the
101 jaws and found that diagnosis was usually difficult and often misleading and delayed before
102 the first bone biopsy [13]. The present case also misdiagnosed by many dentist and
103 physician treated as dento-alveolar abscess. Gusenbauer et al. emphasized that malignant
104 lymphoma must be considered in the differential diagnosis of unexplained dental pain and
105 Comment [p18]: Grammatical error swelling of the mandible [14]. In non-healing extraction
106 socket with irregular bone destruction NHL is one of the differential diagnosis.

107 Bone swelling is the frequent clinical presentation in jaw lymphoma, often associated with
108 teeth mobility, pain and neurological disturbance as in the present case. Histopathology
109 usually shows sheets of chronic inflammatory cells, especially lymphocytes, mimicking an
110 inflammatory reaction. Careful examination by a skillful pathologist is necessary. In DLBCL
111 careful microscopic examination showed presence of particular types of large cancerous
112 lymphocytes spread diffusely throughout the biopsy specimen, cells are spread about rather
113 than in clusters and should be confirmed by immunohistochemistry study.

114 Localized low-grade lymphomas are treated with radiotherapy, while aggressive
115 chemotherapy is used for diffuse high-grade ones. A combination of chemotherapy and
116 radiotherapy is used to treat patients with localized high-grade lymphomas. The surgical
117 approach is limited to obtain a specimen sufficient for a complete histological examination
118 [15]. As DLBCL is an aggressive, rapidly growing neoplasm, a combination of chemotherapy
119 and radiotherapy would be the most appropriate choice and this chemo-radiotherapy was
120 adopted in our case with disease free for one year follow-up. The prognosis is excellent in
121 localized disease, whereas in disseminated disease, it is less favorable [9].

122 **Conclusion**

123 Lymphoma of the mandible being a rare disease and may be considered in the differential
124 diagnosis of long-standing, unhealed extraction wound. Early diagnosis and treatment for
125 such disease result in improved survival outcome. With the rising incidence of extra-nodal
126 lymphomas, clinician may not take laxity on any oro-facial swellings at their face values; on
127 the contrary the histopathology consideration may be given priority to plan an appropriate
128 treatment to yield improving results.

129 **Reference**

- 130 1. Bidokhty HA, Mohtasham N, Pazouki M, Babakoochi S. Primary diffuse large B-cell
131 lymphoma
132 of the mandible: A case report. J Oral Maxillofac Surg Med Pathol, 2014;26: 98–100
- 133 2. Baar J, Burkes RL, Bell R, Blackstine M, Fernandes B, Langer F. Primary non-Hodgkin's
134 lymphoma of bone: A clinicopathologic study, Cancer, 1994; 73:1194 – 1199.

- 135 3. Zucca E, Ruggiero E, Bertoni F, Conconi A, Cavalli F. Primary extranodal non-Hodgkin's
136 lymphomas. *Ann. Oncol*, 1999; 10: 1023 – 1033.
- 137 4. The Non-Hodgkin's Lymphoma Pathologic Classification Project, A clinical evaluation of
138 the
139 International Lymphoma Study Group classification of non-Hodgkin's lymphoma, *Blood*,
140 1997; 89: 3909 – 3918.
- 141 5. Groves FD, Linet MS, Travis LB, Devesa SS. Cancer surveillance series: non-Hodgkin's
142 lymphoma incidence by histologic subtype in the United States from 1978 through
143 1995. *J. Natl. Cancer Inst*, 2000; 92: 1240 – 1251.
- 144
145 6. Epstein JB, Epstein JD, Le ND, Gorsky M. Characteristics of oral and paraoral malignant
146 lymphoma: A population-based review of 361 cases. *Oral Surg Oral Med Oral Pathol Oral*
147 *Radio Endod*, 2001; 92: 519-25.
- 148 7. Robert E, Marx, Diane Stern. *Oral and Maxillofacial Pathology: a rational for diagnostic and*
149 *treatment*. 2nd ed.: Quintessence pub co, Inc: 2012. p. 931
- 150 8. Regezi JA, Sciubba JJ, Jordan RCR. *Oral pathology: clinical pathologic correlations*. China:
151 Elsevier; 2008: p. 223.
- 152 9. Kini R, Saha A, Naik V. Diffuse large B-cell lymphoma of mandible: a case report. *Med Oral*
153 *Patol Oral Cir Bucal*, 2009; 14: e421–4.
- 154 10. Rahmat K. Primary bone lymphoma - a case report with multifocal skeletal involvement.
155 *Biomed Imaging Interv J*, 2008; 3: e52.

- 156 11. Beal K, Allen L, Yahalom J. Primary bone lymphoma. *Cancer* 2006; 106:2652-6.
- 157 12. Parrington SJ, Punnia-Moorthy A. Primary non-hodgkin's lymphoma of the mandible
158 presenting following tooth extraction. *Br Dent J.* 1997; 187:468–7.
- 159 13. Djavanmardi L, Oprean N, Alantar A, Bousetta K, Princ G. Malignant non-hodgkin's
160 lymphoma of the jaws - a review of 16 cases. *J Craniomaxillofac Surg.* 2008; 36:410-4.
- 161 14. Gusenbauer AW, Katsikeris NF, Brown A. Primary lymphoma of bone. *J Oral Maxillofac*
162 *Surg.*1990; 48:409–15.
- 163 15. Longo F, De Maria G, Esposito P, Califano L. Primary non-Hodgkin's lymphoma of the
164 mandible. Report of a case. *Int J Oral Maxillofac Surg* 2004; 33:801–3.