Case study

Diffuse large B cell lymphoma of the maxilla. A rare case report emphasizing differential diagnosis of maxillary involvement

ABSTRACT

Aims: Report a rare case of Diffuse large B cell lymphoma (DLBCL) of the maxilla which is difficult to diagnose clinically and radiographically with a wide array of differential diagnosis lists.

Presentation of case: A case of a 16-year male with well-defined swelling in the posterior region of the palate associated with pain, paraesthesia, and loosening of teeth which mimicked the localized periodontal abscess. The clinical diagnosis of DLBCL poses a challenge opening a wide array of false diagnostic impressions.

Discussion: Traditionally lymphoma is classified into Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL) and NHL involves the extranodal site including the gastrointestinal tract, central nervous system, and skin while in the head and neck area involving waldeyer's ring, buccal mucosa, tongue, maxilla, and mandible

Conclusion: The diagnosis of DLBCL may get delayed with a wide range of differentials in the jaw. A false diagnosis like periapical pathology or other benign lesions would delay the treatment plan. Clinically any lesion suspicious of malignancy in the jaw requires the attention of clinicopathological and radiographic correlation with special diagnostic techniques like immunohistochemistry.

Keywords – *B cell lymphoma, diagnosis, non-Hodgkin's lymphoma, swelling*

INTRODUCTION

Lymphomas are 2nd most common malignant tumors and are categorized into Hodgkin's and non-Hodgkin's lymphoma (NHL). It represents 3.5% of all intraoral malignancies and is commonly seen in the sixth to the seventh decade with men's predilection.[1] Diffuse large B cell lymphoma is the most common tumor of NHL and it can be subcategorized by gene expression profiling into germinal center B cell-like (GCB) and activated B cell-like (ABC type or non-GCB) subtypes.[2] Our case was documented in the non-GCB subtype of DLBCL. In the oral cavity, the non-NHL is relatively very rare and most commonly occurs in the gingiva followed by the hard palate, and in the head-neck region in the palatine tonsil followed by the parotid gland.[3] The etiology of DLBCL is still uncertain but associated predisposing factors include human T cell lymphotropic virus (HTCL-1), Epstein-Barr virus (EBV), human immunodeficiency virus (HIV), human herpes virus (HHV-8), and hepatitis B and C. microorganism including chlamydia and helicobacter pylori.[4]

Genetic mutation with overexpression B cell surface markers like CD45, CD20, CD3, and KI67 along with genetic rearrangement of c-MYC and BCL-2 and/or BCL-6 have DLBCL and BCL-2 and /or BCL- 6 are considered as double hit or triple hit hypothesis.[5] In this case overexpression B cell surface markers i.e., CD45, CD20, CD3, and KI67 were observed. DLBCL, a diagnostic workup is aided by cell surface marker expression. Also, 60% of DLBCL patients can be cured by using R-CHOP therapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).[2] Early diagnosis of lymphoma in the jaw gives prognostic treatment value with an increased disease-free survival rate. But clinician faces a challenge in the diagnosis of DLBCL, as benign odontogenic and non-odontogenic cyst and tumor, periapical pathology, and salivary gland tumor pose a wide scale of the differential ladder. This differential list is ruled out by histopathological and immunohistochemistry techniques in clinicopathological correlation.[3] Here we discuss clinical and radiographical features which mimic the cyst and tumor of DLCBCL.

CASE REPORT

A 16-year-old male presented in the oral medicine and radiology department with complaints of pain, swelling, and loosening of teeth in the upper right

posterior region of the jaw over fifteen days. The history had revealed that swelling was insidious at the onset and gradually increases, so the patient reported to the local dentist and got prescribed antibiotics and analgesics. But the patient did not get relief instead the patient noticed a loosening of teeth in the 14,15,16,17 regions. There was no trauma history and family history, medical history, and personal history were non-contributory.

On general examination, there were no significant findings. On extra oral examination, no gross facial asymmetry was seen or facial palsy was seen, on palpation, tenderness was present in the right malar region, and no lymph node was palpable. (Figure -1A)

Intraoral examination revealed, diffuse swelling in the palatal region on the right side associated with grade 2 mobility of teeth 14,15,16,17. On palpation, the swelling was soft to firm in consistency and tender. (Figure-1B) The provisional diagnosis was a periodontal abscess with 14,15,16,17, region and the differential diagnosis was a pleomorphic adenoma, mucoepidermoid carcinoma, ossifying fibroma, periapical abscess, and other cyst and tumors

To rule out pathology the patient has advised computed tomography (CT) and orthopantomogram (OPG) and OPG was revealed that ill-defined radiolucency was seen in apical regions of the 14,15,16,17 regions which extend superoinferiorly from the infraorbital margin to the alveolar process on the right side and mesiodistally from the apical region distal surface of 14 to mesial surface 18 regions.

The effect of surrounding structure includes loss of lamina dura in premolars and molars regions and loss of inferior, medial, and posterior borders of the maxillary sinus. Internally the lesion was partially a radiolucent-looking mix of radiopaque and radiolucent structures. (Figure -2A)

CT revealed that a well-defined hypodense lesion was present in the right maxillary sinus with the destruction of the anterior and posterior walls. Medially thinning and medial displacement of the medial wall of the sinus in the right nasal cavity and compression of the middle and inferior turbinate. Superiorly, eroding floor right orbit, anteriorly extending into the premaxillary subcutaneous tissue, posteriorly retro antral and pterygopalatine fossa, inferiorly eroding the upper alveolar arch in premolar and molar region and nasal septum deviated to the left side. (Figure-2B)

Radiographically, an impression was suggestive of Ewing sarcoma and the differential diagnosis list was Langerhans cell histiocytosis, osteomyelitis, osteolytic osteosarcoma, fibrosarcoma another benign lesion including fibro-osseous lesion, adenomatoid odontogenic tumor, and calcifying odontogenic tumor.

Histopathological examination revealed the presence of many bone trabeculae showing lacunae with osteocytes and sheets of small uniform, basophilic neoplastic round cells separated by fibrovascular septae. Diffuse chronic inflammatory cell infiltrate chiefly that of lymphocytes and plasma cells are seen. Suggestive of small round cell tumor.(Figure3)

Due to aggressive lesions at a younger age, the sample sent for immunohistochemistry, revealed positive markers found including CD20, CD45,

CD3, Ki67, BC2, and BCL6 with genetic rearrangement. (Table-1) The final diagnosis of DIFFUSE LARGE B CELL LYMPHOMA was made on immunohistochemistry and clinicopathological correlation.

This case was treated surgically with curettage of the right maxillary sinus region, and the patient was sent for radiotherapy. The patient recalled after six months, there was no postsurgical complication seen with good healing of tissue. (Figure-4A, Figure-4B)

DISCUSSION

Lymphomas are malignant neoplasms of lymphocytes and their precursor cell. Freeman et al reported 28% of extranodal sites of NHL in the head and neck area and 2% in the oral cavity.[6] Traditionally lymphoma is classified into Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL) and NHL involves the extranodal site including the gastrointestinal tract, central nervous system, and skin while in the head and neck area involving waldeyer's ring, buccal mucosa, tongue, maxilla, and mandible.[7]

The DLBCL of the jaw is difficult to diagnose due to clinical and radiographic features that are not specific to NHL. The clinically differential diagnosis of palatal swelling includes salivary gland tumor, pyogenic granuloma, periapical abscess, fibroma, lymphoid hyperplasia, and peripheral osteoma.[8]

In the salivary gland tumor: pleomorphic adenoma is most commonly seen on the palate, slow growing, asymptomatic, soft to firm in consistency, in a female patient with 4th to 6th decade commonly, in our case possibility to rule this pleomorphic adenoma due to highly aggressive, symptomatic, with mobility of teeth, in younger age.[9]

Pyogenic granuloma has the presence of nodular or sessile lobulated swelling which is in gingival origin and is most commonly seen in pregnant women due to high levels of estrogen, in our case swelling was diffuse.[10] A palatal abscess is typically seen as a palatal diffuse swelling originating from the source of pulpal and periodontal tissue associated with a nonvital tooth and it is a purely odontogenic origin.[11] In our case possibility, all teeth were vital and the swelling was of bony origin.

Fibroma of the palate typically is asymptomatic slow growing sessile or pedunculated swelling commonly on gingiva associated with local irritation or history of trauma, in our presented case showing painful diffuse swelling without a history of trauma.[12]

Peripheral osteoma shows firm to bony hard swelling usually asymptomatic sessile growth with facial asymmetry seen, in our case the swelling was painful and soft to firm in consistency to easily rule out peripheral osteoma.[13]

World health organization (WHO) 2022 5th edition made diagnostic criteria, the diagnosis of DLBCL can be ruled out by differentiating the benign odontogenic and non-odontogenic tumor based on age, gender, and location of lesions. Calcifying odontogenic the tumor in the 4th decade, no gender predilection, the body of the mandible. Adenomatoid odontogenic tumor, 2nd to 3rd decade, anterior maxilla. Complex odontoma posterior body of the mandible and compound odontoma anterior region of maxilla, both 2nd 3rd common, no gender predilection. A radicular cyst is commonly seen in the e 4th to 5th decade, slightly in the male in the anterior maxilla associated with h non-vital teeth.[14]

We exclude all, presenting the case using the above diagnostic criteria, as diffuse swelling in the posterior region of the hard palate at a younger age has the radiographical feature of malignant lymphoma. The radiographical picture characteristically was showing ill-defined radiolucency with severe bone resorption if involved in the maxilla and mandible. It extends into the maxillary sinus and the alveolar process leads to the mobility of teeth if mandible involvement is seen, the resorption is mostly seen in buccal cortical bone.[15]

Radiographically diagnosis met a challenge from other lesions including Ewing sarcoma, and osteomyelitis of the jaw. Ewing sarcoma shows mottled and ill-defined radiolucency expansile bony destructive lesion with onion skin periosteal reaction, sometime Ewing sarcoma shows a mix of radiopaque and radiolucent lesions in the maxilla and mandible.[16]

Osteomyelitis also mimics the lesion and extensive destruction of the maxilla and mandible. our presented case shows radiographically extensive destruction

of the maxillary sinus associated with radiopacity internally and bony expansion extending up to the infraorbital margin.[17]

The diagnosis of DLBCL meets unmet variables based on clinical, morphological, radiographic, and histopathological examination. The first line therapy of treatment of DLBCL is CHOP (cyclophosphamide, hydroxy doxorubicin, oncovin, and prednisolone). The early stage of DLBCL is managed by both combinations of chemotherapy and radiotherapy.[6]

CONCLUSION- The diagnosis of DLBCL may get delayed with a wide range of differentials in the jaw. A false diagnosis like periapical pathology or other benign lesions would delay the treatment plan. Clinically any lesion suspicious of malignancy in the jaw requires the attention of clinicopathological and radiographic correlation with special diagnostic techniques like immunohistochemistry.

References

1. Liu K, Gao Y, Han J, Han X, Shi Y, Liu C, et al. Diffuse Large B-Cell Lymphoma of the Mandible Diagnosed by Metagenomic Sequencing: A Case Report. Front Med (Lausanne). 2021;8:752523.

2. Sehn LH, Salles G. Diffuse Large B-Cell Lymphoma. N Engl J Med. 2021 Mar 4;384(9):842–58.

3. Bugshan A, Kassolis J, Basile J. Primary Diffuse Large B-Cell Lymphoma of the Mandible: Case Report and Review of the Literature. Case Rep Oncol. 2015 Dec;8(3):451–5.

4. Jayapalan CS, Pynadath MK, Mangalath U, George A, Aslam S, Hafiz A. Clinical diagnostic dilemma in an uncharacteristic rapidly enlarging swelling of the anterior maxilla: extranodal diffuse large B cell lymphoma. BMJ Case Rep. 2016 Mar 30;2016:bcr2015213141.

5. Liu Y, Barta SK. Diffuse large B-cell lymphoma: 2019 update on diagnosis, risk stratification, and treatment. Am J Hematol. 2019 May;94(5):604–16.

6. Coskunses FM, Cilasun Ü, Celik Topcu P, Tokuc B. Primary diffuse large B-cell lymphoma of the mandible: A case report. Gerodontology 2020 Sep;37(3):307-311DOI: 10.1111/ger.12470

7. Zou H, Yang H, Zou Y, Lei L, Song L. Primary diffuse large B-cell lymphoma in the maxilla: A case report. Medicine (Baltimore). 2018 May;97(20):e10707.

8. Ozden B, Bas B, Duran H, Celenk P, Gunhan O. Arteriovenous malformations in the differential diagnosis of palatal swellings. J Istanb Univ Fac Dent. 2016; 50(1): 55–58 doi: 10.17096/jiufd.86859

9. Yousra Z, Saliha C. Pleomorphic adenoma of hard palate: a case report. Pan Afr Med J. 2021;38:146.

10. Amirchaghmaghi M, Falaki F, Mohtasham N, Mozafari PM. Extragingival pyogenic granuloma: a case report. Cases J. 2008 Dec 3;1(1):371.

11. Sumer A, Celenk P. Palatal Abscess in a Pediatric Patient: Report of a Case. European journal of dentistry. 2008 Nov 1;2:291–3.

12. Tsikopoulos A, Festas C, Fountarlis A, Sidiropoulou V, Chaitidis N, Symeonidis A, et al. Large irritation fibroma of hard palate: a case report of a rare clinical entity. Pan Afr Med J. 2021; 38: 61 doi: 10.11604/pamj.2021.38.61.27662

13. Cincik H, Gungor A, Ertugrul E, Cekin E, Dogru S. Peripheral osteoma of the mandible mimicking a parotid mass. Eur Arch Otorhinolaryngol. 2007 Apr;264(4):429–31.

14. Soluk-Tekkesin M, Wright JM. The World Health Organization Classification of Odontogenic Lesions: A Summary of the Changes of the 2022 (5th) Edition. Turk Patoloji Derg. 2022;38(2):168–84.

15. Yasuyuki Michi, Hiroyuki Harada, Yu Oikawa, Kohei Okuyama, Takuma Kugimoto, Takeshi Kuroshima et al.Clinical manifestations of diffuse large B-cell lymphoma that exhibits initial symptoms in the maxilla and mandible: a single-center retrospective study - BMC Oral Health. 2022; 22: 20. doi: 10.1186/s12903-022-02056-x

16. Ahuja US, Puri N, Gupta D, Singh S, Kumar G. Ewing's Sarcoma of Mandible: A Case Report with Review. International Journal of Clinical Pediatric Dentistry, Volume 12 Issue 5 (September–October 2019) doi: 10.5005/jp-journals-10005-1665

17. Nilesh K. Extensive maxillary osteomyelitis following tooth extraction in a patient with osteopetrosis. BMJ Case Rep 2020;13:e235091. doi: 10.1136/bcr-2020-235091

Tables

Table -1 immunohistochemistry markers and result

IMMUNOHISTOCHEMISTRY MARKERS	RESULT
CD45	Immunoreactive, score +4 in lesional cells
CD3	Immunoreactive, score +1 in reactive T cell
CD 20	Immunoreactive, score+3 in neoplastic b cell
KI67	60 to 70% proliferation index
BCL2	Immunoreactive, score+3 in neoplastic b cell
BCL6	Immunoreactive, score+3 in neoplastic b cell
MUM1	Immunoreactive, score+3 in neoplastic b cell
INTERPRETATION	
RESULT	SCORE
NON IMMUNOREACTIVE	0
IMMUNOREACTIVE IN 1-25% CELL	1+
IMMUNOREACTIVE IN 26-50% CELL	2+
IMMUNOREACTIVE IN 51-75% CELL	3+

IMMUNOREACTIVE IN 76-100% CELL	4+

FIGURES AND LEGENDS

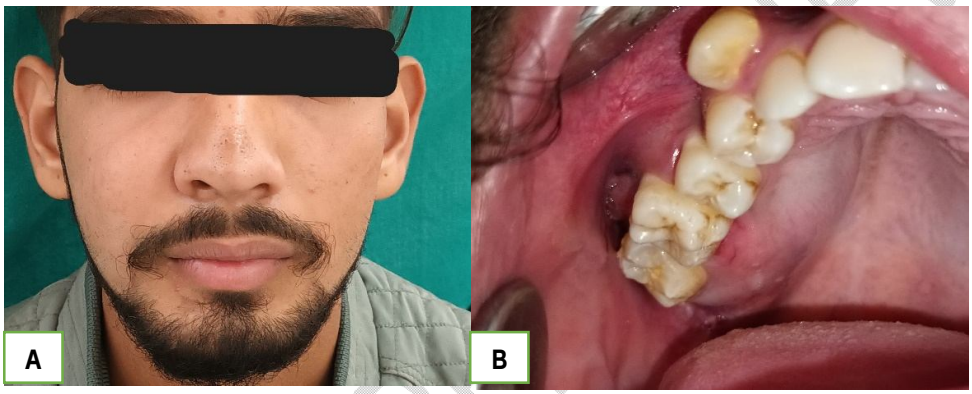

Figure 1: A – The image shows no gross facial asymmetry or any erythematous surface seen on the right malar region. **B**- Diffuse swelling with obliteration of buccal vestibule and mild erythematous surface in the palatal region on the right side associated 14,15,16,17 teeth regions of the maxillary jaw

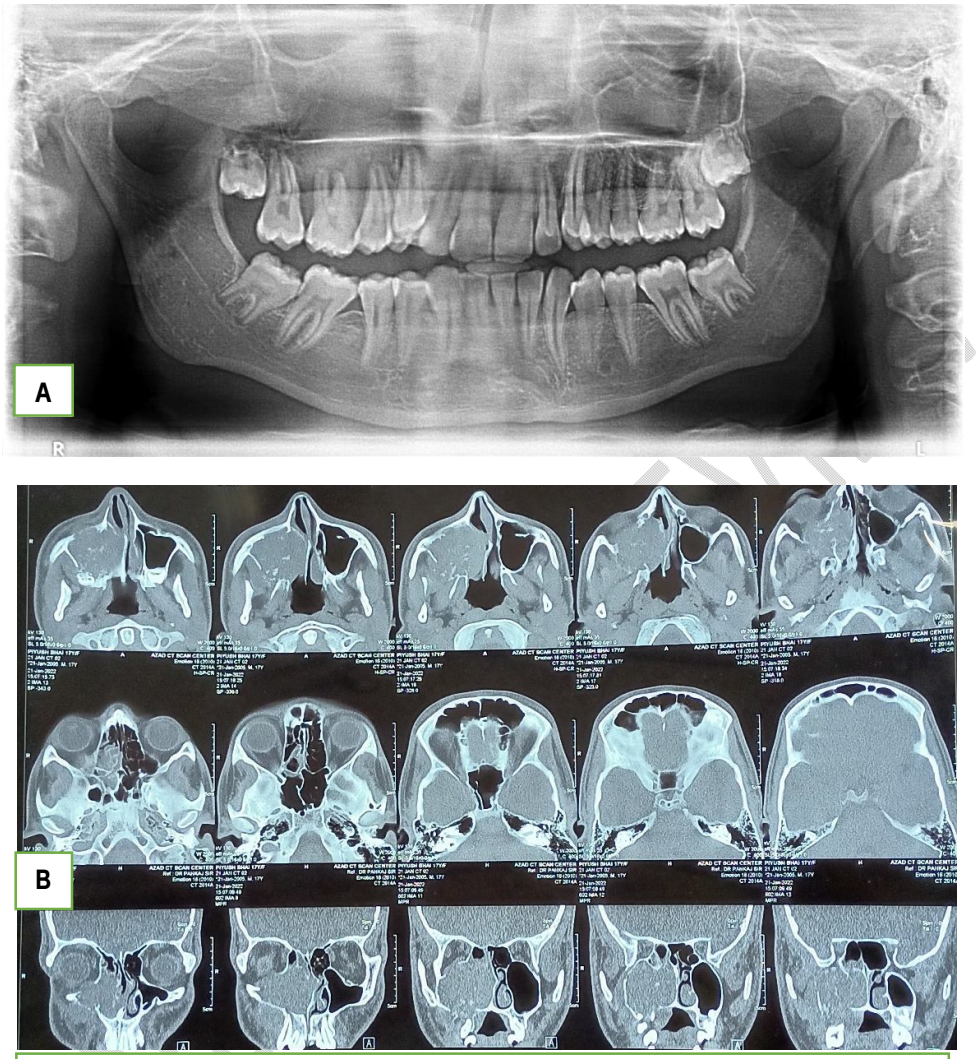

Figure 2: A- The image shows ill-defined radiolucency with the apex of 14,15,16,17 teeth regions. extend superoinferiorly from the infraorbital margin to the alveolar process and mesiodistally from the apical region distal surface of 14 to mesial surface 18 regions. The effect of surrounding structure includes loss of lamina dura in premolars and molars regions and loss of inferior, medial, and posterior borders of the maxillary sinus. **B**- Well-defined hypodense lesion was present in the right maxillary sinus with the destruction of the anterior and posterior walls. Medially thinning and medial displacement of the medial wall of the sinus in the right nasal cavity and compression of the middle and inferior turbinate. Superiorly, eroding floor right orbit, inferiorly eroding the upper alveolar arch in premolar and molar region and nasal septum deviated to the

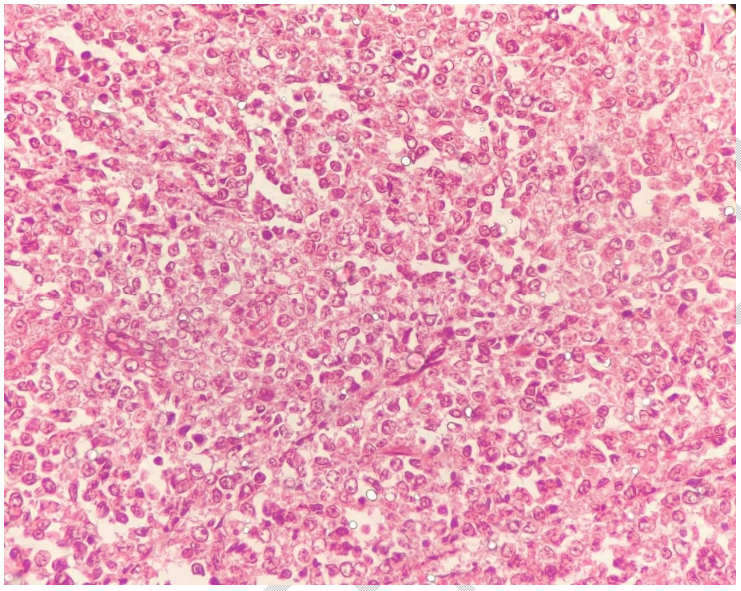

Figure 3 -Histopathological examination revealed the presence of many bone trabeculae showing lacunae with osteocytes and sheets of small uniform, basophilic neoplastic round cells separated by fibrovascular septae. Diffuse chronic inflammatory cell infiltrate chiefly that of lymphocytes and plasma cells are seen. Suggestive of small round cell tumor

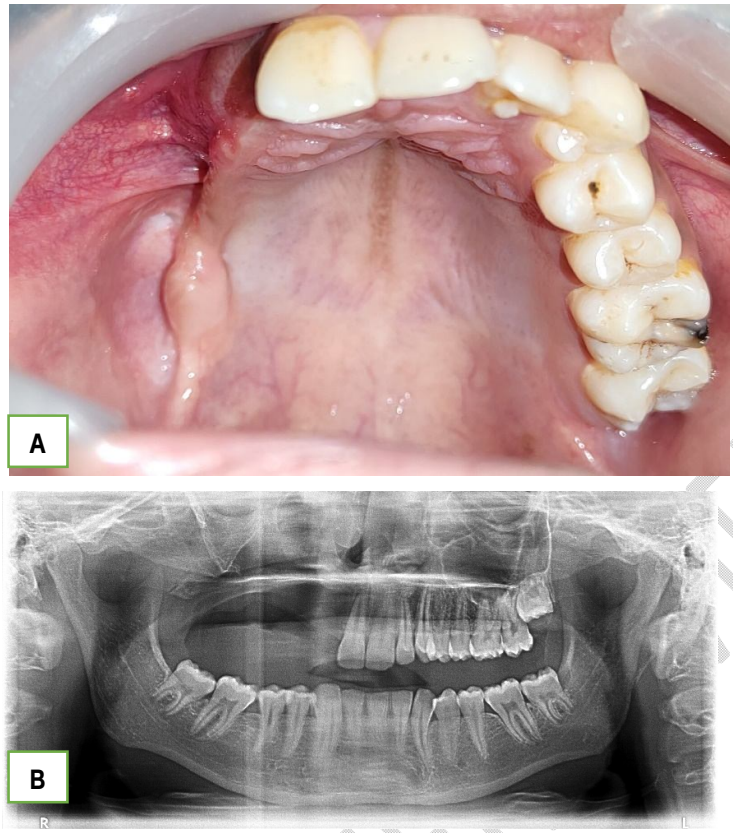

Figure 4: A- Image shows post-surgical with good healing of tissue on the right side of the palate **B** – Post-surgical OPG images show good healing of bone