



Differential diagnosis of hematopoietic malignancies of head and neck: Report of six cases

Reshma Poothakulath Krishnan^{1*}, Deepak Pandiar¹, Pratibha Ramani¹

¹Oral Pathology and Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India

*Corresponding Author: Reshma Poothakulath Krishnan, Email: reshmakpai@gmail.com

Abstract

Background: Lymphoma and multiple myeloma account for a small but significant proportion of all oral malignancies. Oral manifestations of hematopoietic malignancies are sometimes diagnosed with delay as most of them mimic various other diseases like osteomyelitis and periodontal diseases. We present five unusual, challenging cases of head and neck lymphomas and one case of oral myeloma.

Methods: In this article, we report six cases, five cases of oral lymphomas, and one oral multiple myeloma case. All cases were initially diagnosed by oral histopathologists and then referred to specialists for further treatment.

Results: We report these cases to understand these lesions better, as we saw some worrisome delays in their diagnoses. We aim to raise awareness about these hematopathological diseases among general dentists.

Conclusion: It is crucial for the multidisciplinary team members to thoroughly examine the oral cavity for any worrisome lesions like these, as they might be an initial sign of a systemic disease. Pathologists must also be aware of the pitfalls in the interpretation of immunohistochemical sections and the immune profile of a tumor.

Keywords: Lymphoma, Multiple myeloma, Oral malignancies, Hodgkins' lymphoma, Neoplasm

Citation: Krishnan RP, Pandiar D, Ramani P. Differential diagnosis of hematopoietic malignancies of head and neck: report of six cases. *J Oral Health Oral Epidemiol.* 2024;13(1):31–35. doi: [10.34172/johoe.2302.1533](https://doi.org/10.34172/johoe.2302.1533)

Received: May 6, 2023, **Accepted:** August 17, 2023, **ePublished:** March 27, 2024

Introduction

Several systemic diseases, like Crohn's disease, myelomas, and lymphomas, show oral manifestations; however, these symptoms are not pathognomonic and might be the initial signs of the disease. Lymphoma, a malignant hematopathological disease, shows clonal proliferation of lymphoid cells or their precursors.¹ The lymphoid tissue in the oral cavity can potentially undergo malignant transformation and cause systemic diseases, such as lymphoma.² They account for 14% of head and neck cancers, and 97% of these are reported to be non-Hodgkin's lymphomas.³ Multiple myeloma shows monoclonal proliferation of plasma cells and is rarely reported in the oral cavity.⁴ These account for only 10% of hematological cancers.⁵ Multiple myeloma exhibits varied clinical presentations; therefore, awareness of suspicious lesions of the oral cavity is critical for proper diagnosis and treatment.

In this article, we report six cases: five cases of lymphomas and one multiple myeloma case that presented initially in the oral cavity. This article also highlights the various clinical symptoms of these hematopathological diseases,

the diagnostic challenges faced, and the role of general dentists in diagnosing these diseases.

Methods

From 2008 to 2021, five patients with oral lymphoma and one with multiple myeloma presented to the Department of Oral Pathology of a private dental college and hospital in Chennai, Tamil Nadu. Four patients presented with diffuse B cell lymphoma and one patient with Hodgkin's lymphoma. Oral pathologists diagnosed all the above cases and then referred them to the specialists for further treatment. Clinical presentation (Figure 1), histopathological features (Figure 2), and immunohistochemical findings are provided in Table 1.

Results

We report these cases to improve practitioners' understanding of these lesions, as we saw some worrisome diagnosis delays. Various diagnostic procedures were performed due to the wide variety of differential diagnoses. Biopsy procedure was also found to be delayed in a few cases.



Discussion

Hematological malignancies like lymphomas and myelomas present as the proliferation of lymphoid and plasma cells, respectively. Lymphoma and multiple myeloma comprise a small but significant proportion of oral cancers, and these lesions have various presentations in the oral cavity.⁶ The data for the above malignancies in India is limited. In this case series, we report six cases of lymphoma and myeloma for a better understanding of these lesions.

Hematological malignancies like lymphomas and myelomas show varied clinical presentations, which mimic diseases like osteomyelitis, sarcomas, and common conditions such as periodontitis. In our case series, all

the patients, including those with Hodgkin’s and non-Hodgkin’s lymphoma, complained of swelling, and two patients reported pain. The patient with Hodgkin’s lymphoma showed multiple swellings along the course of lymph nodes. None of the clinical features mentioned above are specific to lymphoma. Moreover, the patient with Hodgkin’s lymphoma had been treated with antibiotics, suspecting a bacterial infection, and there was a delay in performing a biopsy. Differentiating these malignancies from infectious diseases like cytomegalovirus and Epstein-Barr virus infections is also important. Multiple myeloma is less common in the oral cavity and might present as swelling in the jaw with tooth mobility, paresthesia, and cortical destruction of bone.⁷ Our case also had swelling and a mobile tooth in the upper front tooth region. None of these symptoms are particularly specific to multiple myeloma and can lead to a misdiagnosis in their initial stages. The clinical symptoms of oral lymphoma (both Hodgkin’s and non-Hodgkin’s lymphoma) and multiple myeloma were heterogeneous in our case series. A wide range of differentials can be given for these lesions.

Lymphoma and myeloma diagnosis is one of the most complicated tasks in histopathology, and the exact classification greatly affects the patient’s treatment and overall prognosis. An invasive diagnostic procedure like a biopsy should be taken if the clinical or radiographic findings are doubtful and do not match the patient’s history and symptoms. Adequate tissue sampling and auxiliary pathologic tests are necessary for an accurate diagnosis. In our case series, an incisional biopsy was done in five cases, and a true-cut biopsy was done for the Hodgkin’s lymphoma case. As it was a true cut biopsy specimen, further subtyping of Hodgkin’s lymphoma was impossible. Improper biopsy techniques with insufficient tissue will further hinder the diagnosis and delay the

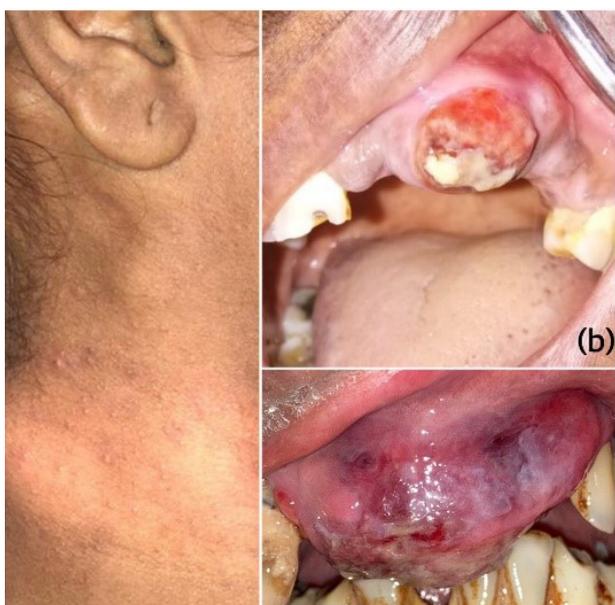


Figure 1. Photomicrograph shows clinical presentation of (A) Hodgkin’s lymphoma, (B) non-Hodgkin’s lymphoma, (C) multiple myeloma

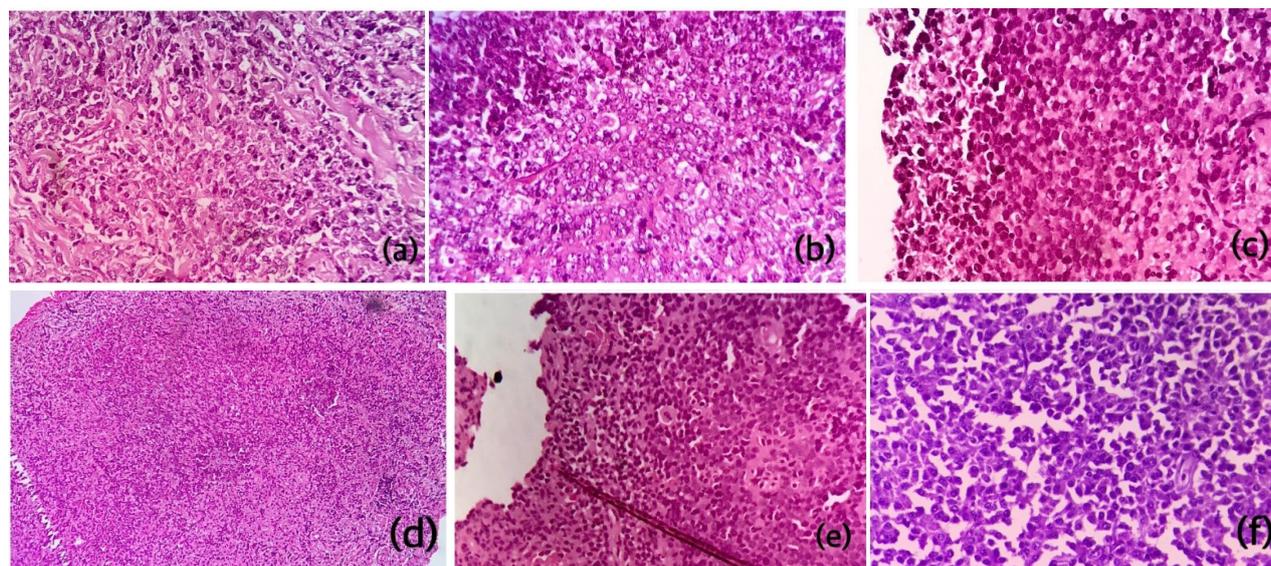


Figure 2. Photomicrograph shows histopathological features of lymphomas and myeloma (a, b, c, e, f: 400× and d: 40×)

Table 1. Clinical presentation, histopathological features, and IHC findings of the lymphoma and myeloma cases

No.	Age	Sex	Site	Duration	Clinical features	Differential diagnosis	Diagnostic methods	Histopathological finding	IHC	Diagnosis	Additional findings
1	29	F	Right and left side neck (Figure 1A)	3 months	Multiple swellings on both sides of the neck Dull aching pain H/O pruritis (past 3 months) H/O treatment with antibiotics expecting an infectious cause.	Infection Granulomatous lesions Lymphoma	True cut biopsy	Small lymphocytes showing irregular nuclei Few large binucleated cells resembling Reed-Sternberg cells and lacunar cells	CD15-+ve for Reed-Sternberg cells	Lymphoproliferative disorder Hodgkin's lymphoma. The patient was advised to have a CT scan.	CT scan: Multiple enlarged submandibular, bilateral axillary, paraaortic, upper and lower paratracheal and prevascular nodes Multiple enlarged inguinal and femoral nodes were noted on either side. The spleen was mildly enlarged. Diagnosis of Hodgkin's lymphoma was confirmed.
2	37	F	Swelling in the left maxillary back tooth region	20 days	Swelling expanded bucco-palatally from the 24–27 region The swelling was a reddish, soft, raised lesion with a smooth surface.	Squamous cell carcinoma Soft tissue sarcomas Hematological malignancy Squamous cell carcinoma Metastasis	Incisional biopsy	Large tumor cells exhibiting round to oval-shaped vesicular nuclei with prominent nucleoli Few large cleaved cells and numerous mitotic figures were evident.	CD 45, CD 20-+ve for tumor cells.	Lymphoproliferative disorder Diffuse Large B-cell lymphoma.	
3	60	F	Growth in the maxillary anterior tooth region (Figure 1B)	2 months	The swelling was 2 × 3 cm in size with a reddish-white color and firm consistency (Figure 2). An area of necrosis was seen on the swelling.	Odontogenic tumor Intraosseous malignancy Metastasis Soft tissue sarcomas	Incisional biopsy	Numerous monomorphous round cells, seemingly of lymphoid origin, arranged in sheets with large round nuclei, showing vesicular chromatin patterns with prominent nucleoli along with pale scanty cytoplasm, were seen (Figure 3). Numerous mitotic figures	CD 45 (Figure 4) and CD 20 showed strong positivity for tumor cells.	Lymphoproliferative disorder Large Non-cleaved diffuse B-cell lymphoma.	
4	44	M	Swelling in the left mandible	2 months	Diffuse swelling was evident, extending from the 34–48 region. Soft in consistency with mild tenderness on palpation. On radiographic examination, multilocular radiolucency was evident in the left body of the mandible.	Odontogenic tumor Intraosseous malignancy Metastasis Soft tissue sarcoma	Incisional biopsy	Atypical lymphoid cells arranged in sheets and scattered cells (Figure 5). Their cells were monotonous and round, with scanty cytoplasm, vesicular nuclei, and prominent nucleoli. Numerous mitotic figures (4-5/10 hpf) were also evident.	CD 45 and CD 20-+ve among tumor cells	B cell lymphoma, possibly diffuse large B-cell lymphoma.	
5	40	F	Swelling in the left maxillary back tooth region	2 months	Swelling was evident in relation to the 25, 26, and 27 regions showing buccal and palatal expansion. CT scan revealed an expanding lesion in the sinus.	Odontogenic tumor Sinus pathology Intraosseous malignancy Soft tissue sarcoma	Incisional biopsy	Few small round cells with round to ovoid nuclei, irregular or cleaved nuclear contours, and scanty cytoplasm suggestive of centrocytes intermixed with numerous large round cells with round to ovoid nuclei, open nuclear chromatin, several nucleoli and a modest amount of cytoplasm suggestive of centroblasts. Monotonous sheets of variably differentiated pleomorphic round cells with many cells showing eccentrically placed hyperchromatic vesicular nuclei, increased nuclear-cytoplasmic ratio, and few mitotic figures were evident. Numerous oval-shaped cells with eccentrically placed nuclei resembling plasma cells	CD 20, BCL2 - showed strong positivity among the tumor cells. CD 45 showed diffuse focal positivity for tumor cells.	Lymphoproliferative disorder Diffuse large B-cell lymphoma.	
6	54	M	Swelling and mobile tooth in the upper front tooth region History of exfoliation of tooth 20 days back. (Figure 1C).	15 days	A growth was seen in the upper front teeth region, reddish-white in color and firm in consistency.	Metastasis Oral squamous cell carcinoma Hematopoietic lesion	Incisional biopsy		CD 45-+ve	Malignancy of hematopoietic origin. The patient was advised to have a CT scan and flow cytometry.	CT scan: A well-defined heterogeneously enhancing lesion in the anterior maxilla and upper lip with extension and erosion of adjacent bones. A few small lytic lesions in the D1 vertebral body and frontal bone were evident. Correlating radiographically and comparing the flow cytometric results, a final diagnosis of multiple myeloma was made.

treatment.⁸ We recommend an incisional biopsy to ensure sufficient tissue for further diagnostic procedures, such as immunohistochemistry and molecular diagnostic tests. This prevents delays in diagnosis and treatment. Oral pathologists should communicate with the surgeons in case of doubts regarding the symptoms and inform them about the adequate tissue requirement.

Pathologists must be aware of the pitfalls in the interpretation of immunohistochemical sections and the immune profile of a tumor. Immunohistochemistry must be used with knowledge of the sensitivity and specificity of each marker. In our case of multiple myeloma, CD45 was positive. CD45, a common leukocyte antigen, is a transmembrane protein found on all nucleated hematopoietic cells. Most myeloma cases are not positive for CD45. However, it has been reported that immature proliferating myeloma cells are positive for CD45.⁹ According to Kumar S et al., myeloma patients with CD45 positivity have an increased overall survival.¹⁰ Knowledge of the immunohistochemical markers and their staining patterns is critical in diagnosing a disease. As CD45 was positive in our case, other than lymphoma, we had a differential diagnosis of multiple myeloma, and the patient was sent for flow cytometry. Flow cytometry can be used when immunohistochemical techniques fail to identify the antibodies in FFPE (formalin-fixed paraffin-embedded sections). These diagnostic methods should be implemented in the routine diagnosis of hematopathological diseases.

This article describes various clinical presentations of patients with hematopathological diseases affecting the oral cavity and raises awareness among general dentists. The main cause of misdiagnosis or delay in these types of lesions could be lack of access to specialists, poor compliance, and similarity of pathological manifestations. In our experience, if a patient presents with an unusual swelling and is not responding to the primary treatment modality, other rare lesions should be considered, and a biopsy should be performed.

Strengths and limitations

This case series provides the demographic data, clinical symptoms, and diagnostic procedures performed on six patients with lymphoma and myeloma referred to our department. Furthermore, the article also explains the importance of the judicious use of diagnostic techniques like immunohistochemistry and flow cytometry in diagnosing these lesions.

Conclusion

General dentists must be aware of these rare conditions as they play an important role in diagnosing and treating these hematological lesions. The entire oral cavity should

be thoroughly examined, and the pitfalls in interpreting immunohistochemical sections should also be considered before the final typing of these lesions.

Authors' Contribution

Conceptualization: Reshma Poothakulath Krishnan, Deepak Pandiar.

Data curation: Reshma Poothakulath Krishnan, Deepak Pandiar.

Investigation: Reshma Poothakulath Krishnan, Deepak Pandiar.

Formal analysis: Reshma Poothakulath Krishnan, Deepak Pandiar.

Methodology: Reshma Poothakulath Krishnan.

Project administration: Reshma Poothakulath Krishnan.

Supervision: Deepak Pandiar, Pratibha Ramani.

Software: Reshma Poothakulath Krishnan.

Resource: Pratibha Ramani.

Validation: Reshma Poothakulath Krishnan, Deepak Pandiar.

Visualization: Reshma Poothakulath Krishnan.

Writing—original draft: Reshma Poothakulath Krishnan.

Writing—review & editing: Deepak Pandiar, Pratibha Ramani.

Competing Interests

Nil.

Data Availability Statement

Nil.

Ethical Approval

Institutional Ethics Committee number was obtained (IHEC number: SRB/SDC/FACULTY/22/OPATH/053).

Funding

Nil.

References

1. Mawardi H, Cutler C, Treister N. Medical management update: non-Hodgkin lymphoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107(1):e19-33. doi: [10.1016/j.tripleo.2008.08.054](https://doi.org/10.1016/j.tripleo.2008.08.054).
2. Allsobrook OF, Bakri I, Farthing PM, Morley NJ, Hegarty AM. Oral lymphoma: a case series. *Dent Update.* 2018;45(7):641-4. doi: [10.12968/denu.2018.45.7.641](https://doi.org/10.12968/denu.2018.45.7.641).
3. Iguchi H, Wada T, Matsushita N, Oishi M, Yamane H. Anatomic distribution of hematology malignancies in the head and neck: 7 years of experience with 122 patients in a single institution. *Acta Otolaryngol.* 2012;132(11):1224-31. doi: [10.3109/00016489.2012.694474](https://doi.org/10.3109/00016489.2012.694474).
4. Vieira-Leite-Segundo A, Lima Falcão MF, Correia-Lins Filho R, Marques Soares MS, López López J, Chimenos Küstner E. Multiple myeloma with primary manifestation in the mandible: a case report. *Med Oral Patol Oral Cir Bucal.* 2008;13(4):E232-4.
5. Rajkumar SV. Multiple myeloma: 2011 update on diagnosis, risk-stratification, and management. *Am J Hematol.* 2011;86(1):57-65. doi: [10.1002/ajh.21913](https://doi.org/10.1002/ajh.21913).
6. Deb Barma M, Indiran MA, Kumar RP, Balasubramaniam A, Kumar MPS. Quality of life among head and neck cancer treated patients in South India: a cross-sectional study. *J Oral Biol Craniofac Res.* 2021;11(2):215-8. doi: [10.1016/j.jobcr.2021.02.002](https://doi.org/10.1016/j.jobcr.2021.02.002).
7. Epstein JB, Voss NJ, Stevenson-Moore P. Maxillofacial manifestations of multiple myeloma. An unusual case and review of the literature. *Oral Surg Oral Med Oral Pathol.*

- 1984;57(3):267-71. doi: [10.1016/0030-4220\(84\)90182-8](https://doi.org/10.1016/0030-4220(84)90182-8).
8. Li X. Pitfalls in the pathological diagnosis of lymphoma. *Chin Clin Oncol*. 2015;4(1):3. doi: [10.3978/j.issn.2304-3865.2014.11.04](https://doi.org/10.3978/j.issn.2304-3865.2014.11.04).
9. Fujii R, Ishikawa H, Mahmoud MS, Asaoku H, Kawano MM. MPC-1-CD49e- immature myeloma cells include CD45+subpopulations that can proliferate in response to IL-6 in human myelomas. *Br J Haematol*. 1999;105(1):131-40. doi: [10.1111/j.1365-2141.1999.01281.x](https://doi.org/10.1111/j.1365-2141.1999.01281.x).
10. Kumar S, Rajkumar SV, Kimlinger T, Greipp PR, Witzig TE. CD45 expression by bone marrow plasma cells in multiple myeloma: clinical and biological correlations. *Leukemia*. 2005;19(8):1466-70. doi: [10.1038/sj.leu.2403823](https://doi.org/10.1038/sj.leu.2403823).