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

Reshma Poothakulath Krishnan1*, 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, Hodgkin's lymphoma, Neoplasm

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

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

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Duration</th>
<th>Clinical features</th>
<th>Differential diagnosis</th>
<th>Diagnostic methods</th>
<th>Histopathological finding</th>
<th>IHC</th>
<th>Diagnosis</th>
<th>Additional findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>F</td>
<td>Right and left side neck</td>
<td>3 months</td>
<td>Multiple swellings on both sides of the neck</td>
<td>Infection Granulomatous lesions Lymphoma</td>
<td>True cut biopsy</td>
<td>Small lymphocytes showing irregular nuclei Few large binucleated cells resembling Reed-Sternberg cells and lacunar cells</td>
<td>CD15- + ve for Reed-Sternberg cells</td>
<td>Lymphoproliferative disorder Hodgkin’s lymphoma. The patient was advised to have a CT scan. CT scan: Multiple enlarged submandibular, bilateral axillary, paracoracic, 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.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>37</td>
<td>F</td>
<td>Swelling in the left mandible</td>
<td>20 days</td>
<td>Swelling expanded bucco-palatally from the 24–27 region The swelling was a reddish, soft, raised lesion with a smooth surface.</td>
<td>Squamous cell carcinoma Soft tissue sarcoma Hematological malignancy</td>
<td>Incisional biopsy</td>
<td>Large tumor cells exhibiting round to oval-shaped vesicular nuclei with prominent nucleoli Few large cleaved cells and numerous mitotic figures were evident.</td>
<td>CD 45, CD 20- + ve for tumor cells.</td>
<td>Lymphoproliferative disorder Diffuse Large B-cell lymphoma.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>F</td>
<td>Growth in the left maxillary back tooth region</td>
<td>2 months</td>
<td>The swelling was 2 × 3 cm in size with a reddish-white color and firm consistency (Figure 1). An area of necrosis was seen on the swelling.</td>
<td>Squamous cell carcinoma Metastasis Odontogenic cyst/tumor Soft tissue sarcoma</td>
<td>Incisional biopsy</td>
<td>Numerous monomorphic 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 were evident.</td>
<td>CD 45 (Figure 4) and CD 20 showed strong positivity for tumor cells.</td>
<td>Lymphoproliferative disorder Large Non-cleaved diffuse B-cell lymphoma.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>M</td>
<td>Swelling in the left mandible</td>
<td>2 months</td>
<td>Diffuse swelling was evident, extending from the 34–48 region. Soft in consistency with mild tenderness on palpation. On radiographic examination, multinodular radiolucency was evident in the left body of the mandible.</td>
<td>Odontogenic tumor Intrasosseous malignancy Metastasis Soft tissue sarcoma</td>
<td>Incisional biopsy</td>
<td>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.</td>
<td>CD 45 and CD 20- + ve among tumor cells</td>
<td>B cell lymphoma, possibly diffuse large B-cell lymphoma.</td>
<td></td>
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<tr>
<td>5</td>
<td>40</td>
<td>F</td>
<td>Swelling in the left maxillary back tooth region</td>
<td>2 months</td>
<td>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.</td>
<td>Odontogenic tumor Sinus pathology Intrasosseous malignancy Soft tissue sarcoma</td>
<td>Incisional biopsy</td>
<td>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.</td>
<td>CD 20, BCL2 - showed strong positivity among the tumor cells. CD 45 showed diffuse focal positivity for tumor cells.</td>
<td>Lymphoproliferative disorder Diffuse large B-cell lymphoma.</td>
<td></td>
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<tr>
<td>6</td>
<td>54</td>
<td>M</td>
<td>Swelling and mobile tooth in the upper front tooth region History of exfoliation of tooth 20 days back. (Figure 1C).</td>
<td>15 days</td>
<td>A growth was seen in the upper front teeth region, reddish-white in color and firm in consistency.</td>
<td>Metastasis Oral squamous cell carcinoma Hematopoietic lesion</td>
<td>Incisional biopsy</td>
<td>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.</td>
<td>CD 45- + ve</td>
<td>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.</td>
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</table>
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**

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**References**


Lymphoma and myeloma of head and neck

