Case Report

Early diagnosis of an isolated primary peripheral T-cell lymphoma masquerading as massive gingival enlargement in a pediatric patient

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Abstract

Lymphomas are malignant neoplasm of the lymphocyte cell lines, classified as either Hodgkin's or non-Hodgkin's lymphoma (NHL). NHL comprises a heterogeneous group of lymphoid neoplasm arising from B-cell, T-cell or natural killer cell with a spectrum of behavior ranging from relatively indolent to highly aggressive and potentially fatal. Peripheral T-cell lymphoma, a variant of NHL, is a disease characterized by the presence of diffuse lymphadenopathy, extranodal involvement, classical B symptoms such as fever (>100.4°F) for 3 consecutive days, weight loss exceeding 10% of body weight in 6 months and drenching night sweats with a tendency for recurrence. Among NHLs, extranodal presentations are relatively common. Extranodal presentation particularly in the oral cavity is very rare and may misinterpret the diagnosis. Lesions of this type should be cautiously dealt especially in pediatric patients and young adolescents. The present case report is about an atypical presentation of disease process in a 15-year-old male patient, which was diagnosed early with the help of a combination of histopathology and immunohistochemistry techniques.

Keywords: CD20, CD3, gingiva, lymphoma, peripheral, T-cell

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INTRODUCTION

Pediatric non-Hodgkin's lymphoma (NHL) accounts for 8%–10% of all childhood malignancies, and malignant clonal proliferation can occur at any stage during lymphocyte proliferation. About 90% of these lymphomas are Burkitt's lymphoma, diffuse large B-cell lymphoma, lymphoblastic lymphoma and anaplastic large-cell lymphoma. Marginal zone lymphoma, cutaneous T-cell lymphoma, follicular lymphoma and peripheral T-cell lymphomas (`s) constitute the remaining 10% of the NHLs.[1]

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PTCLs are a diverse group of lymphoproliferative disorders with different biological and clinical behaviors. The cell of origin is the mature T-cell, derived from the postthymic T-cells.[2] Primary sites of involvement in oral cavity include palate, gingiva, tongue, buccal mucosa, floor of the mouth and lips, accounting for approximately 2% of all extranodal sites.[3,4] A diffuse gingival enlargement of maxilla and mandible in extranodal NHL is an atypical presentation often presenting as a diagnostic challenge to the clinicians. Accurate diagnosis and timely intervention often help in reducing the mortality.

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CASE HISTORY

A 15-year-old male reported to the outpatient department with a chief complaint of swelling in the gingiva of upper and lower jaws for the past 45 days. He reported that the swelling was painless and progressive in nature associated with symptoms such as fever, fatigue and difficulty in breathing on severe exhaustion. Extraoral examination revealed the presence of incompetent lips [Figure 1a] and rashes on the neck that developed concomitantly with fever. On intraoral examination, gingival enlargement involving the free, marginal and attached gingiva of the complete set of maxillary and mandibular teeth was noticed [Figure 1b and c]. The marginal and interdental gingivae were erythematous, bulbous and tender associated with bleeding on probing [Figure 1d]. There was no lymph node involvement.

Based on the clinical features, a provisional diagnosis of conditioned gingival enlargement was considered, with a set of possible differential diagnoses such as inflammatory gingival enlargement, drug-induced gingival enlargement, gingival fibromatoses and neoplastic gingival enlargement. Chest X-ray and hematological investigations revealed no significant abnormalities. After a thorough oral prophylaxis, an incisional biopsy was performed and was sent for histopathological examination.

Hematoxylin and eosin-stained tissue sections showed a parakeratinized stratified squamous epithelium with an underlying connective tissue showing sheets of monotonous round lymphoid cells. [Figure 2a]. Epithelioid histiocytes interspersed among malignant lymphocytes were found in the areas of necrosis [Figure 2b]. Invasion of tumor cells into the blood vessels is also noticed [Figure 2d]. The tumor cells showed nuclear hyperchromatism along with cellular and nuclear pleomorphism [Figure 2c]. A diagnosis of primary extranodal NHL was made based on the abovementioned findings.

Immunohistochemical analysis revealed a positive staining for CD3 marker [Figure 3a] and negative for CD20 [Figure 3b-d], thus confirming a final diagnosis of isolated extranodal PTCL.

DISCUSSION

PTCLs comprise a diverse group of uncommon and aggressive malignant lymphomas thought to derive from peripheral T-lymphocytes in lymph nodes and other nonlymphoid sites. They include a broad spectrum of lymphocyte morphology, but in all instances, they express T-cell markers admixed with epithelioid histiocytes, plasma cells and eosinophils. Clinical presentation of the aggressive T-cell lymphomas can include cutaneous, nodal, extranodal and leukemic groups.[5]

According to the International T/natural killer cell lymphoma study, the most common subtype of mature T-cell lymphoma is PTCL not otherwise specified comprising of 26% of cases, followed by angioimmunoblastic lymphoma (18%) and anaplastic large-cell lymphoma (13%).[6]

A study on pediatric and adolescent NHLs conducted in South Indian population compared the frequency and distribution of major subtypes. Of 467 patients, only six

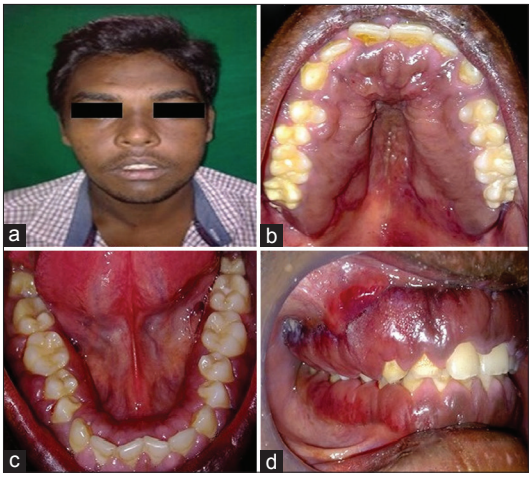

Figure 1: (a) Extraoral photograph showing incompetent lips, (b) marked diffuse gingival enlargement with respect to maxillary arch, (c) marked diffuse gingival enlargement with respect to mandibular arch, (d) erythematous swelling noticed in right buccal vestibule of maxilla and bulbous interdental papillae

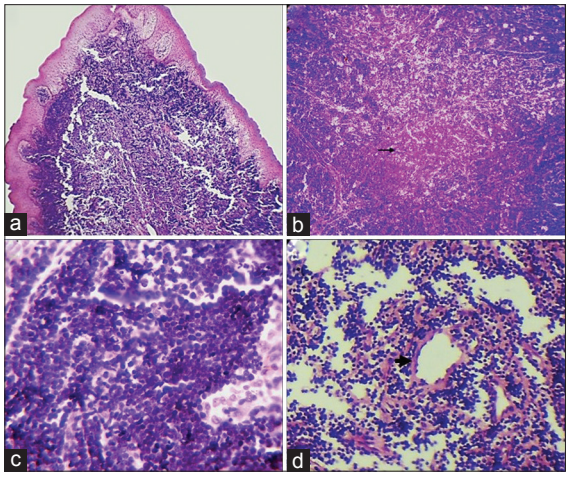

Figure 2: (a) Parakeratinized stratified squamous epithelium with underlying diffuse infiltrate of lymphoid cells (×100), (b) areas of necrosis inside the tumor mass, (c) monotonously arranged round lymphoid cells with hyperchromatic nuclei (×400), (d) invasion of tumor cells around the blood vessels (×400)

cases (2.4%) with PTCL with a mean age of 11.33 years (range: 2–18 years) were recorded.[7] These figures imply the rare occurrence of the lesion in the pediatric age groups.

According to the analysis of International Peripheral T-cell Lymphoma Project, the median age of the patients diagnosed with PTCL was found to be 60 years and the male-to-female ratio was 1.9:1. Majority of patients (69%) presented with advanced-stage (III/IV) disease. Nodal disease was present in 38%, nodal and extranodal in 49% and extranodal in 13% of the patients.[8]

Shah *et al*.'s study of 15 cases of primary oral NHLs reported that the gingivobuccal complex was the most common site of involvement in oral cavity.[4] Oral extranodal NHLs clinically present as soft-tissue swellings that are relatively nontender, soft to firm in consistency and seldom with an overlying ulceration associated with pseudomembrane formation.[4,9]

A PubMed search of extranodal NHLs of T-cell origin involving oral cavity especially gingiva as the primary site was performed and the details are depicted in Table 1. None of the cases were reported in the pediatric age group.

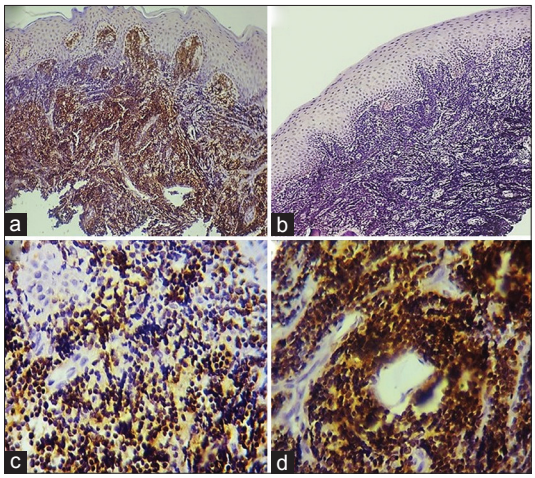

Figure 3: (a) IHC staining with CD3 marker showing positivity for malignant cells (×100), (b) IHC staining with CD20 marker showing negativity for malignant cells (×100), (c) CD3-positive tumor cells (×400), (d) tumor cells infiltrating around the blood vessel (×400)

In contrast to the previously mentioned cases, the present case occurred in an adolescent of 15 years with a clinical presentation that is deceptive of a lymphoma.

Vinoth *et al*.[16] reported a case presenting with multiple gingival masses in the maxillary anterior region of a 14-year-old girl who was diagnosed as diffuse large B-cell lymphoma.

The causes of the PTCL are uncertain; however, the risk factors include immunosuppression, autoimmune diseases or viral infections such as Epstein–Barr virus, HIV infection and human T-cell lymphotropic virus-1.[5] The systemic signs and symptoms of T-cell neoplasms can include fever of unknown origin, inexplicable weight loss, night sweats and malaise, skin rashes and pain in abdomen for no reason (known as classic B symptoms).[5] In the present case, the patient typically presented with a history of fever and malaise accompanied with rashes in the neck region.

Histopathologically, the lesions exhibit connective tissue infiltrated by numerous round cells containing scanty cytoplasm, vesiculated nucleus and prominent nucleoli. Atypical mitotic figures can sometimes be seen. T-cell-associated antigens such as CD3, CD5 and CD7 are variably expressed on immunohistochemical analysis, although one of the mature T-cell antigens such as CD5 or CD7 is usually lost.[17] Ki-67 is often used in the assessment of prognosis and staging of tumor. In the present case, CD3 marker showed strong positivity for tumor cells, suggesting the origin of lymphoma from mature T-cells excluding the B-cell origin as CD20 was negative.

In children and adolescents with NHL, there has been a significant improvement in the overall survival (OS) rate. Independent of the subtype of NHL, the disease-free survival rate is currently ~80%.[1] However, it largely depends on prognostic factors of tumor and host such as the extent of the disease and medical condition.

Guevara-Canales *et al*. in their study of 151 subjects with malignant lymphomas of oral cavity found an OS of 60% at 2 years and 45% at 5 years. In patients with single

Table 1: Demographics of previously reported cases of T-cell lymphoma affecting gingiva

Author	Age	Sex	Site and duration	Histological subtype of T-cell lymphoma
Rana *et al*.[10]	55	Male	Gingival swelling of right side of the lower jaw since 3 months	T-cell lymphoma
Argyris *et al*.[11]	35	Male	Gingival swelling of the right maxillary lateral incisor and canine	Angioimmunoblastic T-cell lymphoma
Matsumoto *et al*.[12]	76	Female	Gingival swelling of maxilla and mandible	Anaplastic large T-cell lymphoma
Milenović *et al*.[13]	68	Female	Extensive ulcerations and necrotic tissue on the left mandibular gingiva	Anaplastic large T-cell lymphoma
Buddula and Assad[14]	66	Male	Gingival swelling in the area of 13–15 for 1-month duration	Peripheral T-cell lymphoma
Rosenberg *et al*.[15]	75	Female	Maxillary gingiva	Anaplastic large T-cell lymphoma

extranodal site involvement, the 5-year survival rate was 73% and in patients with more than one extranodal site it was 38%.[18] The present case falls into Principal Stage I with modification category 'E' of Ann Arbor staging system with a relatively good prognosis. Treatment for such indolent lymphomas constitute radiotherapy alone.

CONCLUSION

Pediatric extranodal lymphomas have diverse clinical presentations, and those occurring in the oral cavity can mimic an inflammatory lesion, reactive lesion or a carcinoma. In the present case, the proliferative growth clinically resembled a conditioned gingival enlargement. In the event of absence of confirmation by histopathology and immunohistochemistry, the patient would have been treated for a nonspecific lesion with an inappropriate treatment strategy. Therefore, every general practice dentist must be aware of such atypical clinical presentations and should be careful enough in accurately diagnosing lesions of this type. With the scarcity of data that are existing in the literature illustrating the behavior of T-cell neoplasms among the pediatric age group, the present case report is aimed to expose the unusual variant of NHL occurring at unusual site and in the unusual age group.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parents have given consent for images and other clinical information to be reported in the journal. The patient's parents understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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