

## Case Report

### Metastatic anaplastic large cell lymphoma of the oral cavity

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#### ABSTRACT

Lymphoma is a malignant neoplasm of lymphoid tissue which is divided into 2 groups: Hodgkin and non-Hodgkin. About 85% of non-Hodgkin lymphomas are B-cell lymphomas, and T-cell lymphomas are unusual. Anaplastic large cell lymphoma (ALCL) is a kind of non-Hodgkin lymphoma with T or NK cell origin that is rarely seen in the oral cavity and only 10 cases have been reported up to now. Here we present a case of ALCL metastasized to the oral cavity in a 32-year-old man with previous history of ALCL which caused an ulceration in the posterior area of the hard palate. Radiography showed irregular resorption of alveolar bone. Histopathologic examination of the incisional biopsy revealed neoplastic proliferation of large and bizarre cells with hyperchromatic nuclei and numerous giant cells and atypical mitoses. Immunohistochemistry markers (CK, LCA, CD3, CD30, CD20) confirmed the diagnosis of ALCL.

**Key Words:** Anaplastic, large cell, lymphoma, non-hodgkin, oral cavity

#### INTRODUCTION

Malignant neoplasm of lymphoid cell is lymphomas which is divided into 2 groups: Hodgkin and non-Hodgkin. Primarily Hodgkin's Lymphoma is lymph nodes's disease, which has been known with the presence of two nuclear cells called Reed-sternberg cells and lymphoid stroma composed of many non-neoplastic cells.<sup>[1]</sup>

Non-Hodgkin's Lymphomas are a group of prevalent neoplasms that originate primarily from lymph nodes, but also extranodal non-Hodgkin's lymphomas are found that constitute 20-40% of Non-Hodgkin's Lymphomas in USA and approximately half of those in Asian countries.<sup>[2]</sup>

The majority of head and neck Maxillofacial lymphomas arise in lymphoid tissue, especially the

cervical group of lymph nodes and Waldeyer's ring, followed by the vestibule and gingiva, mandible, palatal soft tissue, maxilla, and tongue.<sup>[3-5]</sup>

Non-Hodgkin lymphoma generally originates from the two groups B and T lymphocytes<sup>[1,2]</sup> 85% of non-Hodgkin lymphoma derived from B lymphocytes but T-cell origin tumors are less common.<sup>[2,6]</sup>

Anaplastic large-cell lymphoma (ALCL) is a subgroup of non-Hodgkin malignant lymphoma (ML), originated from T or NK cells that initially described by Stein *et al.* in 1985.<sup>[2,6]</sup>

The lesion is characterized by proliferation of anaplastic large lymphoid cells with abundant cytoplasm that strongly express CD30 antigen.<sup>[7]</sup> Primary ALCL in the oral cavity is extremely rare, with only 10 other cases known to have been reported.<sup>[6]</sup>

We report a male patient with oral involvement (posterior of the hard palate) as the first sign of systemic ALCL.

We also discuss the clinicopathologic and immunohistochemical profiles compared with those in previously reported cases.

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## CASE REPORT

A 32-year-old man was referred to the Department of Oral Surgery, Dental School of Isfahan in 2010. Patient's chief complaint was swelling and scarring of the posterior hard palate about three weeks before visiting and after the extraction of maxillary left second and third molars.

On physical examination, the patient had scar with raised edges and a yellow - white membrane in posterior of the hard palate [Figure 1]. The patient declared a history of lymphoma from 1.5 years ago in the neck lymph nodes which diagnosis was Anaplastic larg cell lymphoma, that had been receiving chemotherapy.

Severe alveolar ridge resorption with irregular border were found in left maxilla by an X-ray examination [Figure 2].

The clinical signs and symptoms of patient raised probability of diagnosis of ulcers caused by chemotherapy and tumor's metastasis. After that, incisional biopsy was done and was sent to Oral and Maxillofacial Pathology Department after embedding in 10% formalin fixative.

Microscopically, the proliferation of large and bizarre form neoplastic cells with hyperchromatic and angular nuclei, and numerous bizarre tumor giant cells with atypical mitotic figures which had been located between necrotic tissue and degenerated minor salivary glands as seperated foci was seen. Surface of this lesion had been covered with the fibrinoleukocyter membrane [Figure 3].

The histologic findings suggested an ALCL, and differential diagnoses included metastasis of

lymphoma, poorly differentiated carcinoma and malignant melanoma.

Immunohistochemical staining was carried out on formalin-fixed paraffin-embedded tissues. The antibodies used to determine the definitive diagnosis were included: LCA, CK, CD20, CD30 and CD3. The following results were obtained [Figure 4]:

CK = -

LCA = 4+

CD3 = 4+

CD20 = 1+

CD30 = 3+

Based on the immunohistochemical findings, the lesion was diagnosed as an Metastatic ALCL.

The patient was transfered to Omid's hospital of Isfahan. Despite consecutive follow-up, unfortunately the patient didn't corporate about presenting treatment plan and refused from referring to oral pathology department.

## DISCUSSION

Non-Hodgkin's lymphomas are a group of lymphoid neoplasms with a wide range of behavior (some are indolent, some are very aggressive and if untreated can be fatal). This neoplasms may originate from lymph nodes or extranodal lymphoid tissue.

Head and neck area, especially waldeyer's ring is second common site of non-Hodgkin's lymphoma.<sup>[1]</sup>

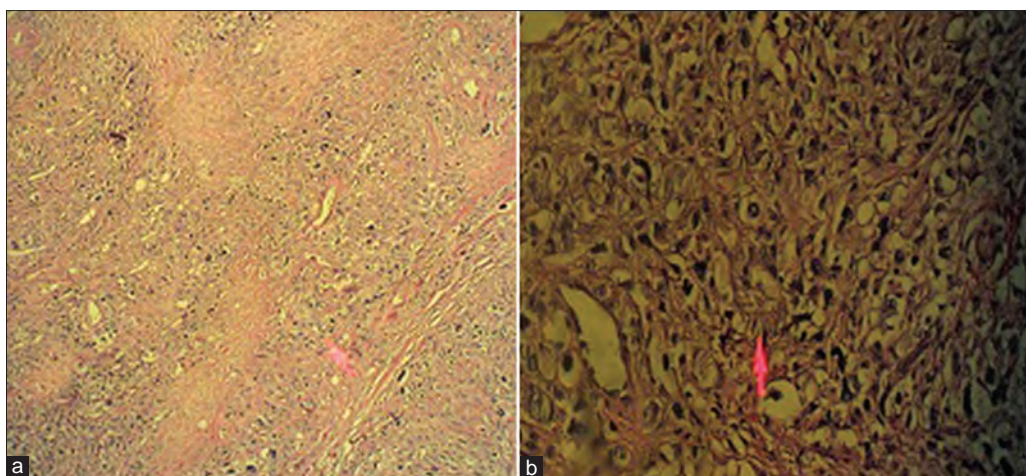
In 1985 Stein *et al.* described a series of 45 diffuse large-cell lymphoma strongly expressing the Ki-1 antigen (CD30) and exhibiting prominent sinusoidal invasion, most of which had previously been diagnosed as malignant histiocytosis or anaplastic carcinoma.<sup>[8]</sup>



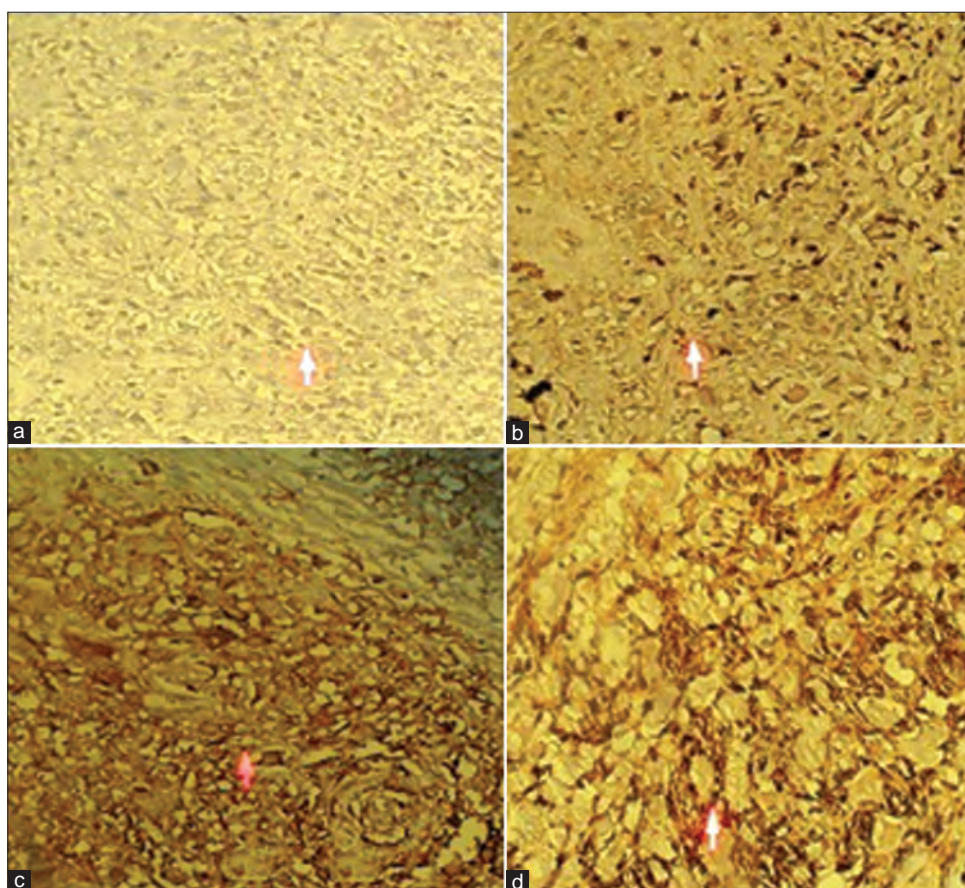
Figure 1: Clinical view of the lesion



Figure 2: Panoramic view of patient



**Figure 3:** Histopathological view: proliferation of large and bizarre form neoplastic cells (H and E, staining  $\times 100$  (a),  $\times 400$  (b))



**Figure 4:** Immunohistochemical staining: cyokeratin (a), leukocyte common antigen (b), CD30 (c), CD3 (d)

As Hodgkin's disease (HD) is also characterized by strong expression of CD30, a common origin of these two entities was initially proposed. However any relationship between these two entities was then disproved in several different studies.<sup>[9-11]</sup> In 1988, the CD30 positive tumours described by Stein *et al.*, were included as a new clinicopathological entity in the revised Kiel classification under the denomination of 'large cell anaplastic lymphoma'.<sup>[8]</sup>

The ALCLs are further subdivided into 3 categories according to clinical criteria and immunohistochemistry: (1) primary systemic anaplastic lymphoma kinase (ALK) positive ALCL; (2) primary systemic anaplastic lymphoma kinase (ALK) negative ALCL; and (3) primary cutaneous ALCL. The ALK expression is predominantly caused by a t(2;5) translocation genetic abnormality, in which the nucleophosmin (NPM) gene at 5q35 is

translocated with the ALK gene at 2p23, resulting in the formation of p80NPM/ALK fusing protein.<sup>[12]</sup>

The ALK(+) ALCLs usually occur in the first decades of life and are more prevalent in males. They response to chemotherapy and have a good prognosis, whereas the ALK(-) ALCLs occur in elderly individuals (most common in 6 decade and male predominance) and have a comparably poor prognosis.<sup>[7,12]</sup> Therefore it is suggested that this neoplasms should be considered an independent pathological entity.<sup>[9]</sup>

Primary systemic ALCL frequently involves both lymph nodes and extranodal sites. Common involved extranodal sites include skin (21%), bone (17%), soft tissues (17%), lung (11%), and liver (8%), and involvement of the gut and central nerve system is rare.<sup>[8-17]</sup>

Involvement of bone marrow in ALCL can be varied from 10 to 40% and depends on a methods of Immunohistochemical and morphological study. Patients with bone marrow involvement have poor prognosis.

In addition, in about 50% of extranodal systemic ALCL, 2 or more sites are involved.<sup>[16]</sup>

Several oral ALCL cases have been reported, although some were the B-cell phenotype that now are classified as an anaplastic type of diffuse large B-cell lymphoma, We found only 9 cases of oral ALCL reported in the English-language literature,<sup>[17-20]</sup> The mean age of the patients was 54.6 years old (range 12 to 77 years) that in comparison with our patient (32 years) were considerably higher and the gender distribution was equal.

Most reported cases have been occurred in the gingiva and in addition of our patient only one case of oral ALCL have been reported in the hard palate. All of the reported patients with oral ALCL complained from swelling occasionally combined with ulceration and pain as a first symptom, which made it difficult to distinguish from other oral inflammatory disorders.

ALCL typically shows a broad spectrum of morphologic features, ranging from small-cell neoplasms to cases with very large and anaplastic cells predominance but almost all the cases, share a common feature, which is the presence of a variable number of so called 'hallmark cells'. These are large cells with abundant cytoplasm and eccentric lobulated 'horse shoe' or 'kidney shaped' nuclei; an intense eosinophilic region corresponding to the Golgi

apparatus is seen near the nucleus, and this region is often surrounded by the nucleus itself. The size of the hallmark cells is usually large, but in small-cell variant cases, smaller elements with the same morphologic features can be present. Along with these highly characteristic and almost diagnostic hallmark cells, neoplastic elements with different morphology are usually seen. In some cases nuclei are round to oval and relatively monomorphic. Multinucleated cells may be present, but cells resembling typical Reed-Sternberg cells are uncommon. Moreover, in ALCL nucleoli are smaller than in HD diagnostic cells.<sup>[8,21]</sup>

In our case, we observed the proliferation of large and bizarre form neoplastic cells with hyperchrome and angular nuclei associated, with numerous bizarre tumor giant cells and atypical mitotic figures which had been located between necrotic tissue and degenerated minor salivary glands as seperated foci. Surface of this had been covered with the fibrinoleukocyter membrane.

The histologic appearance of an ALCL can sometimes be problematic and so confuse with that of a poorly differentiated carcinoma, amelanotic melanoma, or Hodgkin's disease. Therefore, immunohistochemical experiments can be helpful.<sup>[6]</sup>

Various immunohistochemical markers have been studied in this neoplasm, including positive staining for CD3 in 57%, CD30 in 100%, and LCA in 75% of all cases.

In this case, reactivity of tumor cells for LCA, CD3, CD30, and to a lesser degree CD20 was observed.

ALCL should be differentiated from other CD30 positive lesions such as malignant melanoma, Hodgkin's lymphoma, anaplastic large B-cell lymphoma. For example, tumor cells in melanoma are positive for S-100 and HMB45 unlike ALCL. So histologic and immunohistologic evaluation together can lead to a correct diagnosis.<sup>[6,12,14,15]</sup>

Although ALCL is an aggressive tumor, it is responsive well to single or combined chemotrphy with 77% having 5 year survival rate.<sup>[2]</sup>

## REFERENCES

1. Regezi J, Sciubba J. Oral pathology. 5<sup>th</sup> ed. St Louis: WB. Saunders Co; 2008. p. 220-9.
2. Neville BW, Dam DD, Allen CM, Bouqyot JE. Oral and maxillofacial pathology. 3<sup>rd</sup> ed. Philadelphia: Saunders; 2009. p. 592-8.

3. Takahashi H, Fujita S, Okabe H, Tsuda N, Tezuka F. Immunophenotypic analysis of extranodal non-Hodgkin's lymphomas in the oral cavity. *Pathol Res Pract* 1993;189:300-11.
4. Fukuda Y, Ishida T, Fujimoto M, Ueda T, Aozasa K. Malignant lymphoma of the oral cavity: Clinicopathologic analysis of 20 cases. *J Oral Pathol* 1987;16:8-12.
5. Handlers JP, Howell RE, Abrams AM, Melrose RJ. Extranodal oral lymphoma. Part I. A morphologic and immunoperoxidase study of 34 cases. *Oral Surg Oral Med Oral Pathol* 1986;61:362-7.
6. Matsumoto N, Amano Y, Komiyama K. Anaplastic large cell lymphoma in gingiva: Case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;106:e29-34.
7. Ralfkiaer E, Delsol G, Willemze R, Jaffe ES. Primary cutaneous CD30-positive T-cell lymphoproliferative disorders. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. World health organization classification of tumors. Pathology and genetics tumors of haematopoietic and lymphoid tissues. Lyon: IARC Press; 2001. p. 221-2.
8. Fornari A, Piva R, Chiarle R, Nover D, Inghirami G. Anaplastic large cell lymphoma: One or more entities among T-cell lymphoma? *Hematol Oncol* 2009;27:161-70.
9. Wellmann A, Otsuki T, Vogelbruch M, Clark HM, Jaffe ES, Raffeld M. Analysis of the t(2;5)(p23;q35) translocation by reverse transcription-polymerase chain reaction in CD30 anaplastic large-cell lymphomas, in other non-Hodgkin's lymphomas of T-cell phenotype, and in Hodgkin's disease. *Blood* 1995;86:2321-8.
10. Ladanyi M, Cavalchire G, Morris SW, Downing J, Filipa DA. Reverse transcriptase polymerase chain reaction for the Ki-1 anaplastic large cell lymphoma-associated t(2;5) translocation in Hodgkin's disease. *Am J Pathol* 1994;145:1296-300.
11. Elmberger PG, Lozano MD, Weisenburger DD, Sanger W, Chan WC. Transcripts of the npm-alk fusion gene in anaplastic large cell lymphoma, Hodgkin's disease, and reactive lymphoid lesions. *Blood* 1995;86:3517-21.
12. Stein H, Foss HD, Durkop H, Marafioti T, Delsol G, Pulford K, *et al.* CD30 (+) anaplastic large cell lymphoma: A review of its histopathologic, genetic, and clinical features. *Blood* 2000;96:3681-95.
13. Kagami Y, Suzuki R, Taji H, Yatabe Y, Takeuchi T, Maeda S, *et al.* Nodal cytotoxic lymphoma spectrum: A clinicopathologic study of 66 patients. *Am J Surg Pathol* 1999;23:1184-200.
14. Mechtersheimer G, Möller P. Expression of Ki-1 antigen (CD30) in mesenchymal tumors. *Cancer* 1990;66:1732-7.
15. Takeshita M, Akamatsu M, Ohshima K, Kobari S, Kikuchi M, Suzumiya J, *et al.* CD30 (Ki-1) expression in adult T-cell leukaemia/lymphoma is associated with distinctive immunohistological and clinical characteristics. *Histopathology* 1995;26:539-46.
16. Falini B, Pileri S, Zinzani PL, Carbone A, Zagonel V, Wolf- Peeters C, *et al.* ALK\_ lymphoma: Clinico-pathological findings and outcome. *Blood* 1999;93:2697-706.
17. Bitter MA, Franklin WA, Larson RA, McKeithan TW, Rubin CM, Le Beau MM, *et al.* Morphology in Ki-1(CD30)-positive non-Hodgkin's lymphoma is correlated with clinical features and the presence of a unique chromosomal abnormality, t(2;5)(p23;q35). *Am J Surg Pathol* 1990;14:305-16.
18. Fraga M, Brousset P, Schlaifer D, Payen C, Robert A, Rubie H, *et al.* Bone marrow involvement in anaplastic large cell lymphoma. Immunohistochemical detection of minimal disease and its prognostic significance. *Am J Clin Pathol* 1995;103:82-9.
19. Morris SW, Kirstein MN, Valentine MB, Dittmer KG, Shapiro DN, Saltman DL, *et al.* Fusion of a kinase gene, ALK, to a nucleolar protein gene, NPM, in non-Hodgkin's lymphoma. *Science* 1994;263:1281-4.
20. Shiota M, Fujimoto J, Takenaga M, Satoh H, Ichinohasama R, Abe M, *et al.* Diagnosis of t(2;5)(p23;q35)-associated Ki-1 lymphoma with immunohistochemistry. *Blood* 1994;84:3648-52.
21. Pulford K, Lamant L, Morris SW, Butler LH, Wood KM, Stroud D, *et al.* Detection of anaplastic lymphoma kinase (ALK) and nucleolar protein nucleophosmin (NPM)-ALK proteins in normal and neoplastic cells with the monoclonal antibody ALK1. *Blood* 1997;89:1394-404.

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