SIMULTANEOUS PRESENTATION OF ORAL AND SKIN ANAPLASTIC LARGE T-CELL LYMPHOMA

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SUMMARY – We present case of oral and skin anaplastic T-cell lymphoma in a 68-year-old woman. The patient presented with extensive ulcerations and necrotic tissue on the left mandibular gingiva. Orthopantomogram finding showed extensive necrolytic lesions of the adjacent mandible. Biopsy finding of oral lesions and subsequently of the skin confirmed the diagnosis of anaplastic T-cell lymphoma. The bridge on the teeth 35-37 was taken out. After three cycles of chemotherapy, oral lesions subsided, unlike skin lesions. Dentists should be aware that differential diagnosis when dealing with oral ulcerations might be the result of certain malignant hematologic diseases.

Key words: *Lymphoma; T cell, cutaneous; Oral ulcer; Case report*

Introduction

According to the World Health Organization (WHO) definition, lymphomas are classified as non-Hodgkin's lymphomas (NHL) and Hodgkin's lymphomas (HL). The majority of malignant lymphomas, of which more prevalent are B-cell NHL, arise in lymphoid tissue, especially in cervical lymph nodes and Waldeyer's ring, followed by the vestibule and gingiva, mandible, palatal soft tissue, maxilla and tongue[1].

Extranodal sites affected with NHL frequently include skin (21%), bone (17%), soft tissues (17%), lungs (11%) and liver (8%). In general, oral manifestations of NHL occur secondary to a more widespread distribution throughout the body. Clinical presentation is variable. Additionally, simultaneous existence of oral and skin T-cell lymphoma has been described in about thirty case reports so far[1].

Head and neck involvement accounts for 8%-13% of all extranodal lymphomas. Oral manifestations of NHL are present in 2%-5% of all lymphomas and are the third most common malignancy in the oral cavity[2].

Case Report

A 68-year-old female patient was referred to Department of Oral Medicine for evaluation of the extensive ulceration on the gingiva extending from 35-38 in the left mandible (Fig. 1). No lymphadenopathy was noted. The orthopantomogram finding showed extensive mandibular bone loss in the region 34-38 (Fig. 2). She was also suffering from intense pain. At the same time, the patient had skin nodules all over the body. Most of them were firm, some of them pruritic and some painful, while others had erythematous

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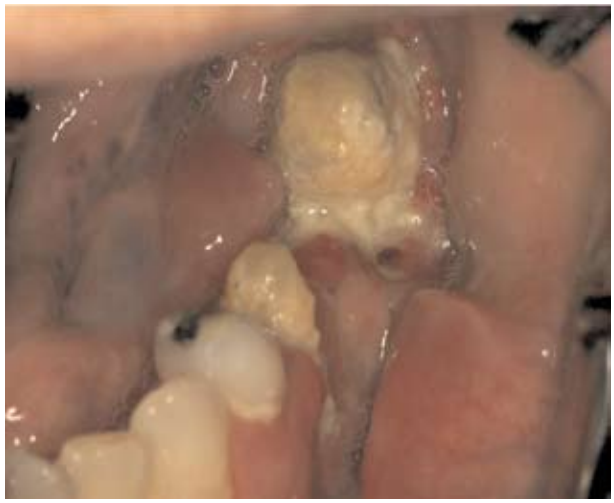

Fig. 1. Extensive ulceration in the region 35–37.

and ulcerative surface (Figs. 3 and 4). Detailed medical history showed to have suffered the patient to from gastritis and osteopenia 15 years before, however, she was not treated with bisphosphonates. Furthermore, several years before, she had undergone uterine and bile duct operation. Three months before eruptions on the skin and oral lesions, she had undergone surgical operation for para-aortic paraganglioma (suprarenal adenoma which was hormonally inactive) as a coincidental finding. The patient was non drinker and non smoker. Biopsy specimens of the oral mucosa and skin nodules were taken. Histologic examination of oral lesions showed medium sized atypical lymphocytes, some with kidney shaped nuclei, together with

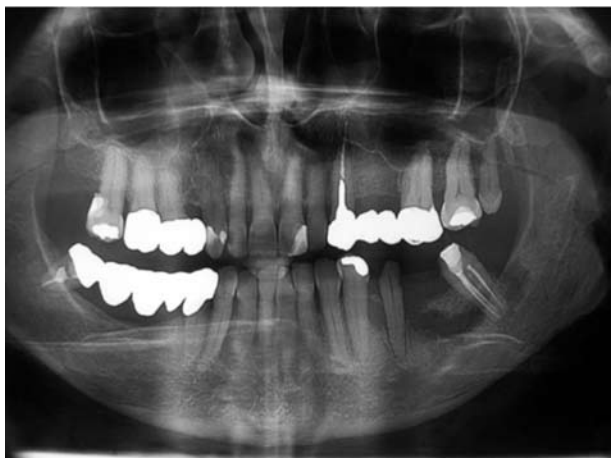

Fig. 2. Orthopantomogram showing extensive bone resorption.

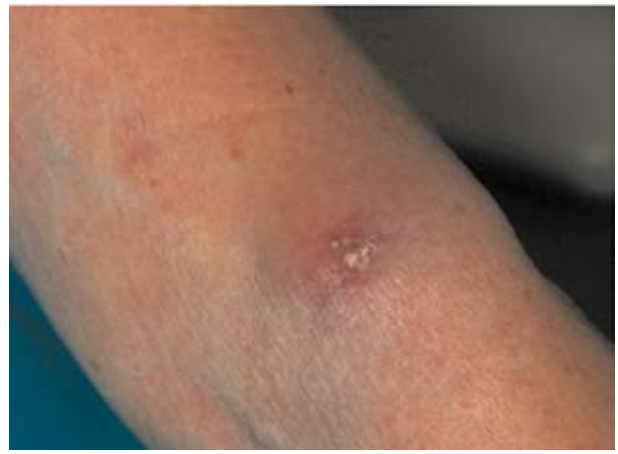

Fig. 3. Skin lesions on the patient's left arm.

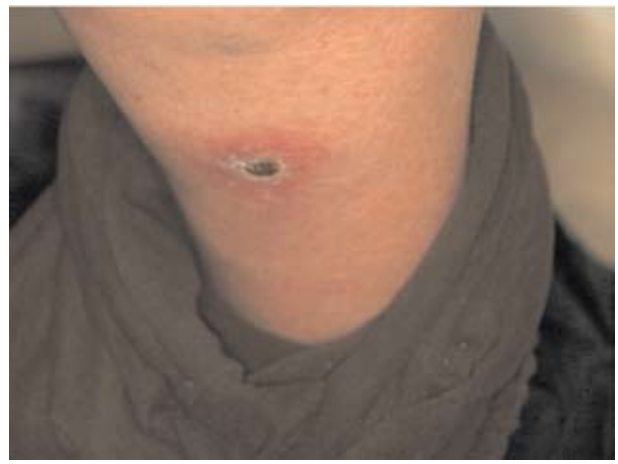

Fig. 4. Leg lesions in our patient.

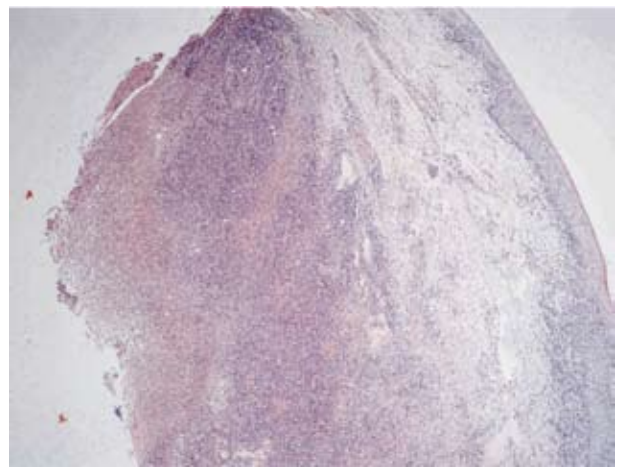

Fig. 5. Infiltration of the mucosa by atypical lymphoid cells (HE, original magnification X40).

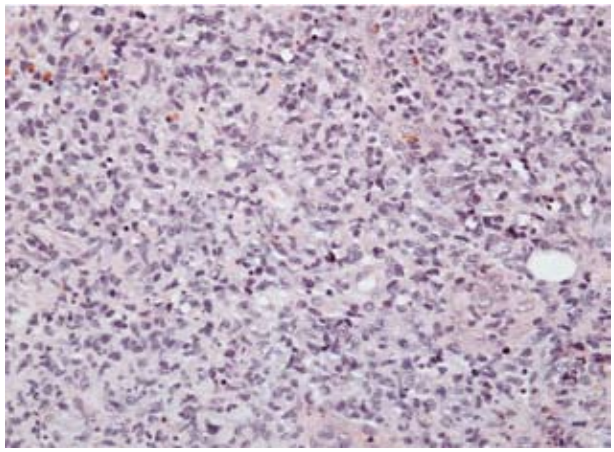

Fig. 6. Atypical lymphoid cells (HE, original magnification X400).

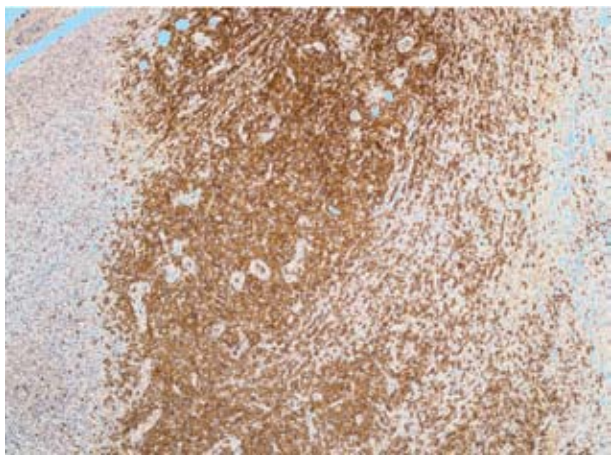

Fig. 7. CD3 positivity (original magnification X100).

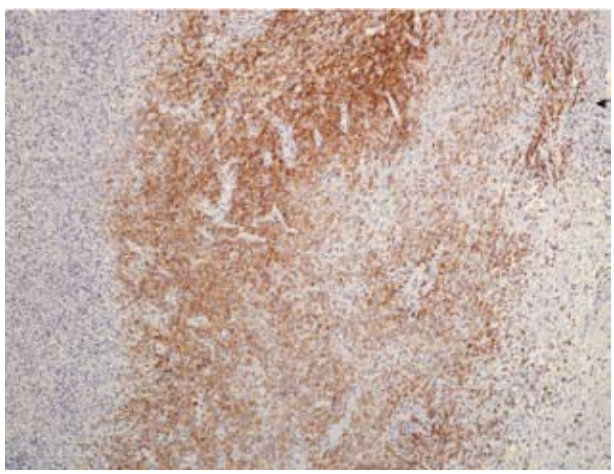

Fig. 8. CD2 positivity (original magnification X100).

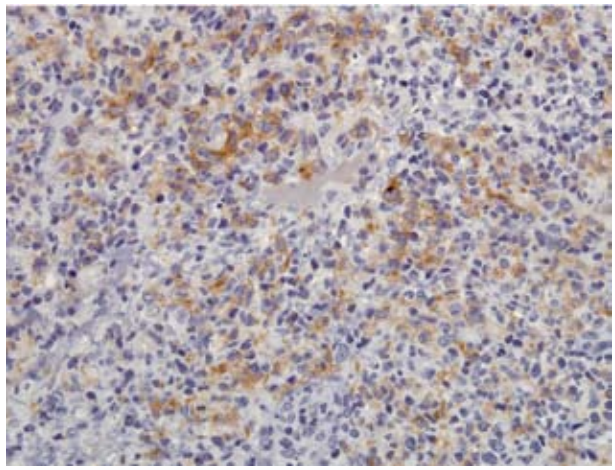

Fig. 9. Scattered membrane and perinuclear dot-like positivity for CD30 (original magnification X400).

eosinophils and neutrophils, primarily in the area of necrosis. Atypical lymphocytes expressed CD30 in a membrane and Golgi pattern, CD2, CD3, CD45RO, granzyme B and EMA antigens. The cells were ALK, CD15, BCL6, CD56, CD21, CD10 and CD20 negative, with partial loss of CD8, CD7, CD5 and CD4 antigens. Proliferative antigen Ki67 was positive in 40%-50% of described atypical lymphocytes (Figs. 5-10).

Histologic examination of the skin showed large, atypical lymphatic cells, which were immunohistochemically positive for CD30, EMA, CD8, granzyme B, and negative for CD56 TIA, CD4, Cd20

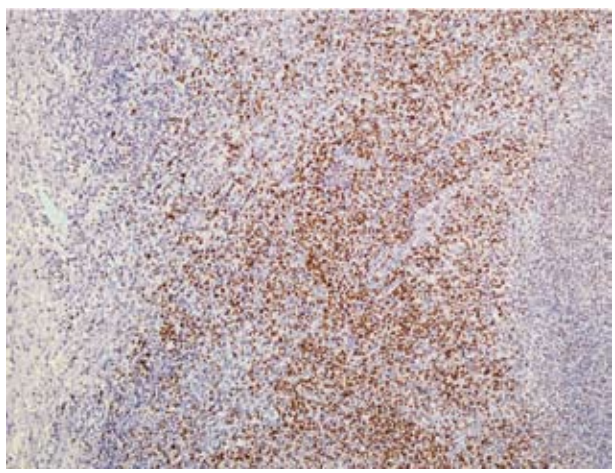

Fig. 10. Nuclear positivity for proliferation antigen Ki67 (original magnification X100).

and ALK1.

Routine blood tests were normal except for erythrocyte sedimentation rate, which was slightly elevated. Viral markers to HIV, HCV and HCB were negative. Scintigraphy of the whole body and SPECT/low dose computed tomography of the head showed only pathologic activity in the mandible, however, the rest of the body showed no pathologic changes. Bone marrow biopsy specimen revealed no signs of tumor process within it.

The patient was referred to hematology oncologist and was treated with cyclophosphamide, oncovin (vincristine), etoposide, prednisone (COEP regimen), which consists of cyclophosphamide 750 mg/2 i.v., etoposide 100 mg/m^2 on the first day, vincristine 1.4 mg/m^2 on the first, second and third day and prednisone 60 mg/m^2 orally from the first to fifth day. Therapeutic cycles were repeated every three weeks[3]. The patient's staging was T3b, N0, M1 according to the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC) proposal on Tumor, Lymph Nodes and Metastases (TNM) classification of cutaneous lymphoma other than mycosis fungoides (MF) and Sézary syndrome (SS)[4].

As mandibular bone beneath the bridge 35-38 became very necrotic, the bridge was taken out and sequestrectomy of the adjacent mandible was performed. Mandibular necrosis started before chemotherapy.

After three cycles of chemotherapy, complete regression of the symptoms in the oral cavity occurred, however, some skin lesions subsided while other developed.

Discussion

Matsumoto *et al*.[5] report that the mean age of patients with oral NHL was 54.6 (range 12-77) years and that the gender distribution was equal. One half of the cases occurred in the gingiva (44.4%), followed by the lip (22.2%), palate (11.1%) and tongue (11.1%), and 44% were not accompanied with lymphadenopathies. Furthermore, all of the reported patients complained of swelling occasionally, combined with ulceration and pain as the first symptom. Oral lesions may appear as painless enlargement, often with surface ulceration secondary to trauma. If bone is the primary site, tooth and alveolar bone loss is often seen. Pain, swelling, numbness of the lip and pathologic fractures may be associated with bone lesions[6]. Anaplastic large cell lymphoma (ALCL) accounts for 2%-7% of all NHLs. ALCL has also been reported in immunosuppressed individuals (HIV+ and iatrogenically immunosuppressed). Clinical presentation of ALCL is variable, extranodal presentation is common, especially in the skin. May *et al*.[7] report on two cases of oral-cutaneous CD4 positive T-cell lymphoma having manifestations as tongue and skin nodules. Matsumoto *et al*.[5] report on an ALCL characterized by CD30+positive findings and large epitheloid cell proliferation with a highly anaplastic T-cell phenotype, which also expresses CD45RO, granzyme B, TIA-1 (T-cell intracytoplasmic antigen 1), perforin and p80$^{NPM/ALK}$.

Immunocytochemical analysis is an imperative in the diagnosis of CD30-positive or Ki-1 positive ALCL. The cells are also positive for CD30, others may be such as LCA, EMA, pan T-cell markers such as UCHL-1 and pan-B-cell markers such as L26, although almost 25% of cases will not stain for B-cell or T-cell markers at all[8,9]. Rarely, NHL can be diagnosed solely on the basis of cytologic examination[10]; biopsy finding is almost always needed. Differential diagnosis when encountering oral ulcerations might be mechanical trauma, histiocytosis, vesiculobullous disease, mycosis fungoides, extranodal NK/T-cell lymphoma, CD8+ epidermotropic cytotoxic primary cutaneous T-cell lymphoma, benign lymphoid hyperplasia, lymphomatoid papulosis, CD30 positive T-cell lymphoproliferative disorder, poorly differentiated carcinoma, adult T-cell leukemia/lymphoma, low grade MALT lymphoma, HL, amelanotic melanoma, malignant melanoma, leukemic infiltrates, sarcoidosis, chronic bacterial infections (tuberculosis, syphilis), chronic fungal infections, traumatic eosinophilic granuloma and vasculitis[11,12].

Unfortunately, the patient died, so follow up biopsy and PET/CT scans were not performed.

So far, only around twenty cases of oral ALCL have been reported in the literature. Currently, WHO considers two ALCL types, ALK-negative and ALK-positive, and those who are ALK-negative show an inaccurate behavior with a relatively unfavorable

prognosis, as was also seen in our case[13]. Based on the review of the existing literature, Rozza-de-Menezes *et al.*[14] report that there is a slight male predilection for ALCL, which could not be confirmed in our case report. However, in accordance with these authors[14], gingiva was the most frequent site of ALCL appearance together with bone resorption, as also seen in our patient.

Conclusion

Dentists should be aware that differential diagnosis when dealing with oral ulcerations and/or isolated gingival/periodontal lesions might be the result of certain malignant blood diseases, especially when bone necrosis underneath is seen.

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Sažetak

SIMULTANA POJAVA ORALNOG I KOŽNOG ANAPLASTIČNOG LIMFOMA VELIKIH T STANICA

A. Milenović, V. Vučićević Boras, I. Ilić, S. Dotlić, I. Aurer, S. Bašić Kinda, M. Mayer, M. Mikulić, Č. Tomasović-Lončarić i *I. Škrinjar*

U radu se prikazuje slučaj oralnog i kožnog anaplastičnog limfoma velikih T stanica u 68-godišnje osobe. U bolesnice su na prvom pregledu uočene opsežne ulceracije i nekrotično tkivo u području gingive na mandibuli lijeve strane lica. Na ortopantomogramu su se vidjele opsežne nekrolitične lezije na kosti mandibule toga dijela. Patohistološki nalaz sluznice usne šupljine, a poslije i kože potvrdio je dijagnozu anaplastičnog limfoma velikih T stanica. Most na zubima 35-37 je izvađen. Nakon tri ciklusa kemoterapije oralne lezije su se povukle, za razliku od kožnih lezija. Stomatolozi pri diferencijalnoj dijagnostici oralnih ulceracija moraju imati na umu i moguću povezanost tih lezija s malignim hematološkim bolestima.

Ključne riječi: *Limfom, T stanični, kožni; Oralni ulkus; Prikaz slučaja*