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Case Report

Peripheral T-Cell Lymphoma not otherwise specified with oral manifestation: A Case Report.

Linfoma Periférico de Células T no especificado con manifestación oral: Reporte de caso.

Alvaro Vigouroux.[1]
Felipe Lillo.[2]
Francisca Donoso.[3]

Affiliations:
[1]Hospital San Juan de Dios, Santiago, Chile.
[2]Servicio de Anatomía patológica, Hospital San Juan de Dios, Santiago, Chile.
[3]Servicio de Cirugía Maxilofacial, Hospital San Juan de Dios, Santiago, Chile.

Corresponding author: Alvaro Vigouroux. Hospital San Juan de Dios, Avenida Portales 3239, Santiago Centro, Chile.
E-mail: a.vigouroux@hotmail.com

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Abstract: Peripheral T-Cell Lymphoma Not Otherwise Specified it is a rare type of Non-Hodgkin t-cells malignant tumor whose oral manifestations are difficult to diagnose. A case of a 48-year-old male with a hemi-maxillary lesion histological and immunohistochemically compatible with Peripheral T-Cell Lymphoma not otherwise specified is presented. A case of a 48-year-old male with a hemi-maxillary lesion histological and immunohistochemically compatible with Peripheral T-Cell Lymphoma not otherwise specified is presented. The patient treatment consisted of chemotherapy, but after the second cycle, died from immunosuppressive complications. Early stage diagnosis of oral lesions is imperative to avoid aggressive treatment and low overall survival rate of such pathologies.

Keywords: Non-Hodgkin lymphoma; Lymphoma, T-cell, Peripheral; Mouth neoplasms; neoplasms; middle aged.

Resumen: Introducción: El linfoma periférico de células T no especificado es un tipo raro de tumor maligno no Hodgkin de células T cuyas manifestaciones orales son difíciles de diagnosticar. Se presenta el caso de un varón de 48 años con lesión hemimaxilar histológica e inmunohistoquímicamente compatible con linfoma periférico de células T no especificado. El tratamiento del paciente consistió en quimioterapia, pero después del segundo ciclo, falleció por complicaciones inmunosupresoras. El diagnóstico temprano de las lesiones orales es imperativo para evitar un tratamiento agresivo y la baja tasa de supervivencia.

Palabra Clave: *Linfoma no Hodgkin; Linfoma de células T; Neoplasias de la boca; Neoplasias; Persona de mediana edad.*

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INTRODUCTION.

Oral lymphomas represent 3% of all lymphomas in the general population and are the third most common oral cavity malignancies after squamous cell carcinoma (SCC) and malignant neoplasms of the salivary glands. Since their oral manifestations are rare and can emulate various clinical lesions, they are very hard to diagnose, which can lead to delayed treatment thus lowering overall survival rate.[1]

Non-Hodgkin lymphomas (NHL) involves a diverse type of lymphomas with varied clinical and histological presentation; within this category there is peripheral T-cell lymphoma-not otherwise specified (PTCL–NOS), defined as a group of lymphomas with undefined characteristics including diverse cell origin, morphological patterns, and phenotypes.[2]

PTCL-NOS represents 10% of all NHL, gender distribution is 2:1, affecting more males than females, with a mean age of 60 years.[3]

The PTCL-NOS etiology is unknown, but some risk factors include AIDS, autoimmune diseases, infections caused by human T-cell lymphotropic virus, Epstein-Barr virus, and human herpesvirus.[8]

Diagnosis is based on tissue biopsy, clinical behavior, and gene expression. Oral cavity presentation and imaging studies may mimic most head and neck tumors. Radiological findings appear as radiolucent uni- or multilocular intraosseous areas with diffuse edges, mostly aggressive to near anatomical structures. Clinically, patients present general lymphadenopathy with or without extra-nodal disease, including involvement of skin, gastrointestinal tract, liver, spleen, and bone marrow.

Differential diagnosis on the oral cavity must be made mostly against SCC and neoplasms of salivary glands, although any maxillofacial tumor may fit the criteria for differential diagnosis.[4,5]

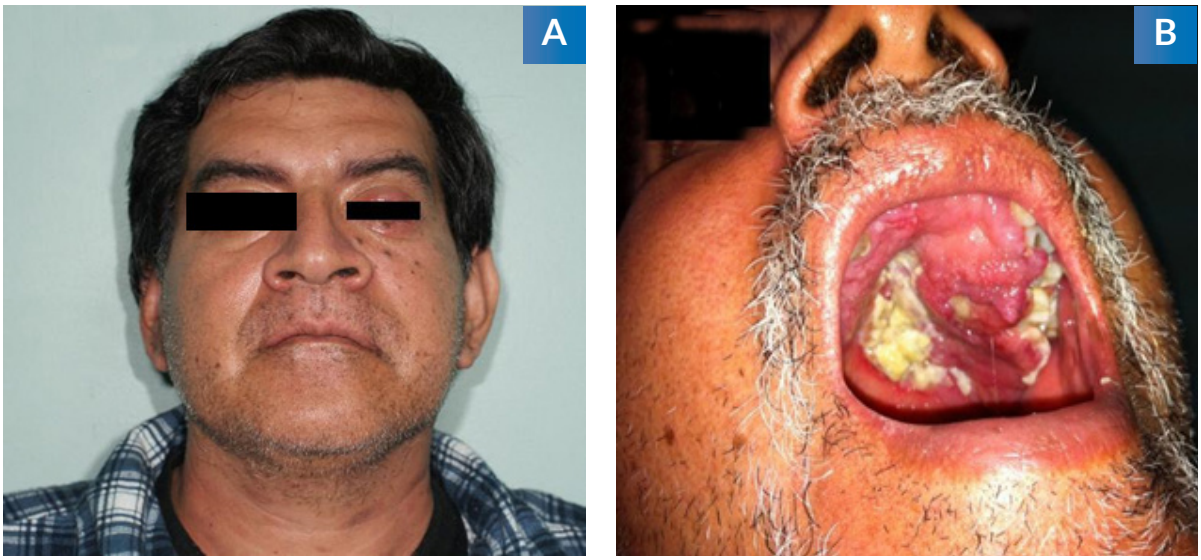
Is extremely aggressive, with a 20-32% overall survival rate in 5 years. Its incidence varies from 0.5-2 per 100.000 people per year, with a wide epidemiological distribution. Upon diagnosis, most patients (69%) had an advanced disease stage (III/IV), the most common treatment on 74% of cases it is CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy that may include radiotherapy or not.[6,7]

CASE REPORT.

A 48-year-old male patient with no morbid background was admitted to the Maxillofacial Surgery Service with a chief complaint of seven days of facial asymmetry induced by left periorbital cellulitis.

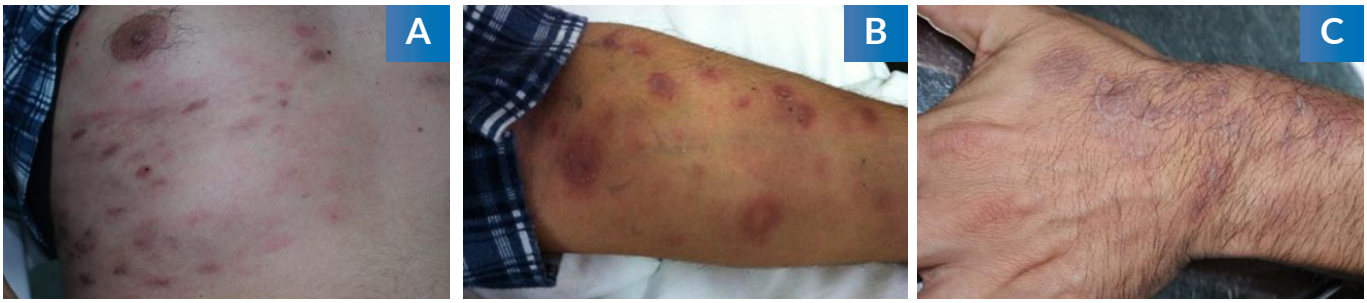
Clinical evaluation showed edema and erythema on the left eye conjunctiva, ipsilateral palpebral edema with visual acuity, with reflexes preserved. (Figure 1A) Intraoral examination was conducted finding a large

Figure 1. **Clinical examination.**



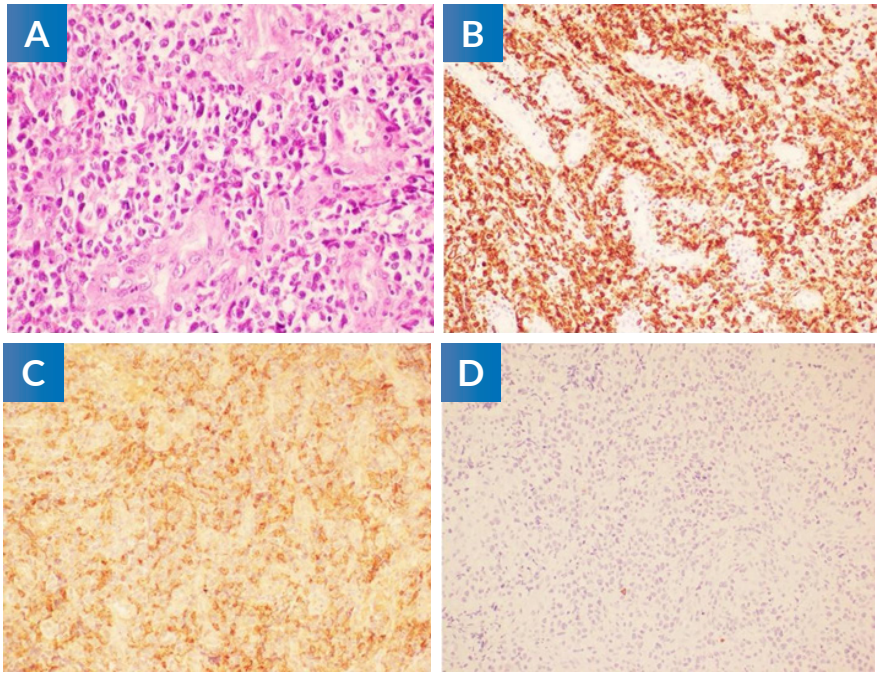
A. Left eye inflammation, palpebral edema. **B.** Hemi-maxillary tumor.

Figure 2. Patient skin Lesions.



A. Thorax. **B.** Forearm. **C.** Hand.

Figure 3. Representative examples of immunohistochemical analysis of lesion biopsy.



A. T-cell Lymphocytes infiltrate. **B.** Positive CD3 C. **C.** Positive CD4. **D.** Negative CD20.

Figure 4. Hemimaxilla tumor after 1 cycle of chemotherapy.

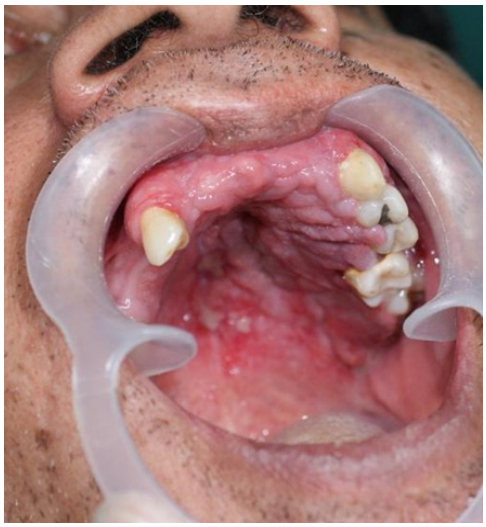


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Tabla 1. Immunohistological findings of the lesion.

Marker	Reactivity
CD3	+++
CD4	+++
CD5	+
CD8	-
CD10	-
CD20	-
CD30	-
CD79a	-

ǂ: Wilcoxon signed rank test. ***p*-value<0.05:** Is considered statistically significt. ****p*-value<0.01:** Significant. *****p*-value<0.01:** Highly significant.

mass tumor on the left hemi-maxilla compromising from the palatal midline to the buccal mucosa. Its surface was irregular, erythematous with a soft consistency and ill-demarcated white macules. Lesion was partially covering molars and premolars of the left side, with no associated dental mobility or pain . (Figure 1B)

During physical examination, skin lesions were found on the thorax, forearm, and hands in the form of macules and papules eczema plaques, in different stages of evolution. No lesions were found on mucosa, palms and soles. (Figure 2)

Complete blood count was within normal parameters, HIV test was negative, and early biopsy discarded squamous cell carcinoma and drug induced dermatomyositis. The histopathological study presented diffuse and atypical lymphoid proliferation of medium to large cells, clear cytoplasm, irregular and pleomorphic nuclei with a high proliferation rate.

Immunohistochemical analysis for CD3 and CD4 antigen was positive in 100% of neoplastic cells, CD5 antigen was positive in a moderate proportion, and negative for CD8, CD10, CD20, and CD79a antigens, (Table 1) compatible with diagnosis of peripheral T-cell lymphoma not otherwise specified. (Figure 3)

The patient went under CHOP treatment and antibiotics, resulting in a substantial reduction of tumor size within the first chemotherapy cycle. (Figure 4) After the second cycle, the patient had multiple organ system failure and died.

Surgical resection was considered, but the extent of the tumor and posterior facial deformity were factors to ponder. Success of the first cycle of CHOP treatment discarded surgery.

DISCUSSION.

PTCL-NOS is an overly aggressive subtype of T-cell non-Hodgkin lymphoma and represents a heterogeneous group of lymphoid disorders that cannot be categorized into other peripheral T-cell lymphoma groups, thus making them an exclusion diagnosis. Its clinical presentation is heterogeneous with extremely variable signs and symptoms. Oral manifestations are rare and differential diagnosis has to be made primary against SCC and neoplasms of salivary glands, although any maxillofacial tumor may fit the clinical presentation and imaging characteristics. In this particular case, skin lesions were secondary to oral cavity and fitted the PTCL-NOS diagnosis.[8] The literature clearly mentions that T-Cell etiology occurs more frequently in patients with immunosuppression, AIDS, celiac disease, rheumatoid arthritis, congenital immunodeficiency and Sjogren's syndrome.[9]

Only 24% of non-Hodgkin's lymphoma (NHL) tumors present on extra nodal sites, most frequently on the gastrointestinal tract. Less than 25% of extra nodal involvement affects the head and neck region, mostly B-cell types; T-cell types, such as in this case, are rare. The case presented is atypical due to its intraoral rare manifestations compromising the hemi-maxilla and periorbital region and also the presence of cutaneous macular and papular lesions. Patient immunosuppression was discarded with clinical and complementary exams which is also uncommon.[9-10]

PTCL-NOS histology expression is positive for most T-cell antigens, including CD2, CD3, CD4, CD5, CD7 and CD8. The cytology is often pleomorphic with a mix of small and large cells with a high proliferation rate.[11] Some authors describe that immunohistochemical

CD3 is correlated to high staining percentage and low overall patient survival.

Gene expression of GATA-3 has been observed in 45% of PTCL-NOS, in association of MYC and MTOR proliferation signals studies with a worse outcome in those cases.[12]

There are multiple combinations and different approaches to treat PTCL-NOS. Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) is considered to be first line therapy, although novel agents are being tested in patients. The information available of clinical outcomes is insufficient to understand the role of molecular features, hence CHOP therapy plus its combinations are the main treatment therapy. Maxillofacial surgery might have been an option in this particular case, but several factors had to be taken into consideration, including extent and tumor infiltration, facial deformation, psychological alterations, and and the success of chemo- or radiotherapy.[13]

The patient underwent CHOP therapy after the first biopsy diagnosis. Despite the efforts to start treatment quickly, the advanced stage of the pathology prevented him from surviving after the second cycle due to kidney failure and neoplasm induced fever.

The proposed Prognosis Index for PTCL-NOS (PIT) uses the following survival predictive factors: Age >60 years, impaired performance status, elevated LDH, bone marrow involvement. Five years survival rate ranges from 20 to 35%, hence the importance of early diagnosis and treatment.[14]

CONCLUSION.

This case report shows how aggressive and rare NHL can be. It is important to highlight the importance of differential diagnosis, with SCC and salivary glands tumors the most common, although any oral tumor may emulate its clinical characteristics, sometimes underlying malignant diseases like PTCL-NOS.

The clinical characteristics, imaging and histopathological studies lead to timely diagnosis and therefore early treatment is essential to increase the rate of survival.

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