Extranodal NK/T cell Lymphoma, nasal type: clinical, radiological, histological features for early diagnosis

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Primary nasal type natural killer (NK)/T cell (NKTC) lymphoma, a specific form of malignant lymphoma, has a higher geographic incidence in Oriental, Mexican, and South American populations than the Western population. In Koreans, it comprises 9-12% of all cases of non-Hodgkin’s lymphoma. This type of lymphoma has also been named as angiocentric lymphoma and lethal midline granuloma because the most common site is the upper airway area and its clinical aggressiveness presents with a necrotic and destructive pattern. NKTC lymphoma can also be detected in different organs (testis, spleen, parotid gland, skin, gastrointestinal tract, central nervous system, lungs, bone marrow, etc.) other than the upper airway including the oral cavity. The lymphoma detected in the oral cavity shows various destructive and inflammatory changes, similar to the signs of inflammation and infection from periodontitis and pulpal disease, making a diagnosis difficult with just the clinical signs. For early detection, clinical, radiological, and pathological examinations are required. This report describes the clinical, radiological and histological characteristics with a case report for the early detection of NKTC lymphoma in the oral cavity.

Key words: Extranodal NK/T cell lymphoma nasal type, Early diagnosis, Clinical, Radiological, Histological


I. Introduction

Extranodal nasal type natural killer (NK)/T cell (NKTC) lymphoma is classified as a subtype of peripheral T-cell lymphoma, according to the new World Health Organization (WHO) classification system for lymphoid neoplasms established in 19991-4. NKTC lymphoma has a higher geographic incidence in Orientals, Mexicans, and South Americans compared to the Western population1. In Korea, the rate of occurrence of NKTC lymphoma is 9-12% of all non-Hodgkin’s lymphomas4. Its poor prognosis is caused by the prompt progression of the lesion into distinct organs6. Therefore, early diagnosis can be a valuable factor for improving survival rate and treatment outcome. The most prevalent area of NKTC lymphoma is the midface including the nasal cavity, oropharynx, and nasopharynx6. It presents as a progressive ulceration and necrotic granulomatous change when found in the midfacial area4-6. Although NKTC lymphoma rarely arises as a primary tumor intraorally, tumors of the nasal cavity may extend into the oral cavity, affecting the hard and soft palate6.

Initial oral manifestations of NKTC lymphomas are similar to the non-specific inflammatory process which may be easily misjudged with bacterial, viral or fungal infections or other inflammatory disease, such as cellulitis, abscess, periodontitis and recurrent aphthous ulcer (RAU). Therefore, it is common for NKTC lymphoma to be post-operatively diagnosed. The following cases are patients who came to the Yonsei University Dental Hospital complaining of inflammatory signs in the oral cavity and were ultimately diagnosed with NKTC lymphoma. In this article, we report these cases along with review of literature.

II. Case report

1. Case 1

A 34 year old woman visited the Yonsei University Dental Hospital outpatient clinic, complaining of an unhealed ulceration on her lower right posterior gingival area that has first appeared 1 month ago. During the first examination, a whitish necrotic ulceration was observed on the buccal gingival of #46, 47. (Fig. 1) #46 and 47 presented no mobility or percussion. Also paresthesia of the left chin and lower lip was noticed. The
panoramic view showed a periodontal ligament space widening of #46 and 47 along with mucosal thickening and haziness of both the maxillary sinus. (Fig. 2) Due to the clinical characteristics of the lesion, it was misjudged with RAU. After computed tomography (CT) image analysis, destructive changes of the nasal cavity, paranasal area, and right preseptal orbit were observed. (Fig. 3) It was decided to confirm the differential diagnosis of NKTC lymphoma through a biopsy of the right posterior gingiva. The initial biopsy showed a polymorphic infiltration of inflammatory cells, macrophage, B and T lymphocytes. A second biopsy and immunohistochemical study was performed a week later. The final diagnosis was NKTC lymphoma and she was treated with chemotherapy for 6 months. However, the patient died of gastrointestinal bleeding related to NKTC lymphoma involvement.

**Fig. 1.** A: First examination: whitish ulceration was seen on right posterior gingival, B: After 1 week: progressed necrotic ulceration was seen after biopsy, C: After 2 weeks – more progressed fetid, grey to brown, necrotic, painful ulceration with malodour after re-biopsy.

**Fig. 2.** The initial panoramic view showed a PDL space widening of #46 and 47, haziness and mucosal thickening in the maxillary sinus, both. (PDL: periodontal ligament)

**Fig. 3.** A: Disappearance of the left Rosenmüller fossa (arrows) due to infiltrative tumor along the mucosa of the nasopharynx on axial CT scan, B: Note the involvement of NKTC lymphoma into ethmoidal sinus, nasal cavity and bilateral maxillary sinus. (CT: computed tomography, NKTC: natural killer T cell)
2. Case 2

A 68 year old male was referred to the Yonsei University Dental Hospital outpatient clinic, for an unresolved midfacial swelling. At our hospital the patient was treated for left canine space abscess with incision and drainage and antibiotic therapy for 1 week, followed by extraction of the canine. Treatment was not effective and facial palsy of the left side arised after coming to our hospital. The panoramic view showed periapical radiolucency on #23 similar to an apical abscess and haziness of both the maxillary sinuses. (Fig. 4) CT images showed mucosal thickening on the left maxillary and ethmoidal sinus, and an infiltration close to the left orbit. (Figs. 5. A, B) The patient was referred to the department of ear, nose and throat (ENT), where a middle meatal antrostomy was preformed for biopsy purpose under general anesthesia. (Fig. 5. C) He was finally diagnosed with NKTC lymphoma. And he was treated successfully with concurrent chemotherapy and radiotherapy and is still alive with periodic follow up.

Fig. 4. A: The initial panoramic view showed a periapical radiolucency on #23 and haziness in maxillary sinus, both. B: A late facial palsy of the left side arised with previous midfacial and left orbital swelling.

Fig. 5. A, B: CT showing mucosal thickening of Lt. maxillary and ethmoidal sinus, C: Surgical specimen. (CT: computed tomography)
Ⅲ. Discussion

At the time of diagnosis, the most commonly observed symptoms of NKTC lymphoma suggesting involvement of nasal cavity are: nasal bleeding, congestion, and rhinorrhea. Oral cavity manifestations are extremely rare, especially involving the mandible as the primary tumor, and may easily be misjudged with other conditions. Such is the case of our first patient case, which presented an ulcerative lesion on the mandibular posterior gingival area and was misdiagnosed with RAU.

NKTC lymphoma involving the maxillary area usually shows necrotic granulation tissue formation, midfacial swelling, with or without oroantral fistula formation on involved area. It can be easily misdiagnosed with other dental related conditions, without considering clinical and radiologic findings simultaneously for a deferential diagnosis as in the case of our second patient, who presented an unresolved midfacial swelling and was misjudged with canine space abscess.

Clinical findings of lymphoma in the oral cavity are characterized by progressive ulceration and necrotic granulomatous changes with malodour[^65]. The uvula, posterior wall of phar...
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III. Histological findings showed lymphomatous infiltration with irregular nuclei involving the surface epithelium and subepithelial connective tissue, called polymorphic reticulosis. In addition, angiocentric, angiodestructive growths pattern were also shown with widespread ischemic necrosis\(^4,6,10\). However, due to its histological variations and confusion with other non-specific inflammation, the search for a diagnostic marker is needed for warrantee.\(^5,6,7\) (Figs. 6, 7)

Usually NKTC lymphomas express CD2, CD3, and CD56\(^4,6,11\). Also expression of perforin, T cell intracellular antigen (TIA-1), granzyme B, and Fas ligand suggests a high cytotoxic activity, and Epstein-Barr virus (EBV) status suggests a more aggressive and necrotic malignancy, which makes as a poor prognostic factor\(^7,10,12\). (Figs. 8, 9)

IV. Conclusion

In the field of oral and maxillofacial surgery and other dental disciplines, initial manifestations similar to those of NKTC lymphoma, is not common. Therefore, unhealed intraoral ulcerations, facial swellings, necrotic tissue formation caused by NKTC lymphoma may be misjudged with other conditions related to dental origin, causing a delay in diagnosis.

Due to prompt progression of the lesion into distinct organs, NKTC lymphomas have a poor prognosis with the cumulative probability of survival at 5 years ranging from 37.9% to 45.3%\(^6\). Its prognosis is influenced by stage of disease, histological grade of malignancy and the presence of EBV infection. Therefore, early diagnosis and staging with appropriate treatment are essential to achieve optimal treatment results. For an early diagnosis, clinicians must pay close attention to not only a patient’s clinical manifestations, but also to findings that may resemble radiographic characteristics of NKTC lymphoma and perform a tissue biopsy for an early diagnosis of NKTC lymphoma that may improve treatment outcome.

References