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CASE REPORT

# A Rare Case of Severe Facial Disfiguration Due to Extranodal NK/T-Cell Lymphoma

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**Background:** Extranodal NK/T-cell lymphoma, nasal type (ENKTCL-NT) is a rare, highly invasive Epstein-Barr virus associated hematological malignant tumor with an unfavorable prognosis. Although ENKTCL-NT has been previously reported, no relevant article has provided an intuitive, progressive series of schematic illustrations of the rapid progression of facial ulcers.

**Objective:** This article reports a serious case of ENKTCL-NT that involved the entire process from onset to death.

**Case Summary:** A 67-year-old man suffered a facial lesion started at the right ala nasi. The wound continued to spread uncontrollably to the nasion and the nasolabial groove. Subsequently, he used an unauthorized external application of herbal medicine, which unfortunately resulted in further expansion of the wound, encompassing the area from the right eyelid to the left inner canthus, extending up to the eyebrow arch, down to the right ala nasi, and deep into the nasal bone over six months. Histopathological analysis of the two biopsies revealed inflammatory necrotic granulation tissue.

**Conclusion:** Nasal extranodal NK/T-cell lymphoma presenting with non-specific symptoms could easily lead to misdiagnosis. It progresses quickly, while adequate, repeated, and multiple spot biopsies for histopathologic examination help confirm the diagnosis.

**Keywords:** ENKTCL-NT, misdiagnose, biopsy, pathology

## Introduction

ENKTCL-NT is an aggressive hematological malignancy and the third most common malignancy of the nasal cavity and paranasal sinuses, accounting for approximately 10% of non-Hodgkin lymphoma (NHL) and 30% of extranodal lymphomas in Asia and Latin America, making it the most common T-cell and NK-cell tumor.[1,2] In contrast, this disease is rare in the United States, Canada, and European countries, constituting less than 1.5% of NHL. Patients are mostly adults, with a median age ranging from 46 to 60 years.[3] ENKTCL-NT is more prevalent in males, representing 55% to 78% of the total number of cases in most studies.

The most common initial symptoms are similar to those of otolaryngological diseases, presenting non-specific symptoms followed by edema and necrotic ulceration and leading to frequent misdiagnoses when patients first present to otolaryngologists. There, early diagnosis of ENKTCL-NT is challenging. Here we present a rare case of severe facial disfiguration due to extranodal NK/T-cell lymphoma through an intuitive and progressive series of schematic illustrations so as to better understand the rapid progression of the disease.

## Case Presentation

A 67-year-old man presented to the ENT clinic with ragged wounds and facial swelling. Over the course of six months, the lesion gradually spread from the right ala nasi to encompass the entire face (Figure 1). At the beginning of the disease, the main manifestation was an ulcer on the right wing of the nose with little secretion on the surface, a local brown crust, and congestion and edema of the surrounding skin (Figure 1A). One month after onset, after anti-infection, local debridement, and dressing changes, the nasal skin ulcer gradually improved. Histopathological analysis of the two

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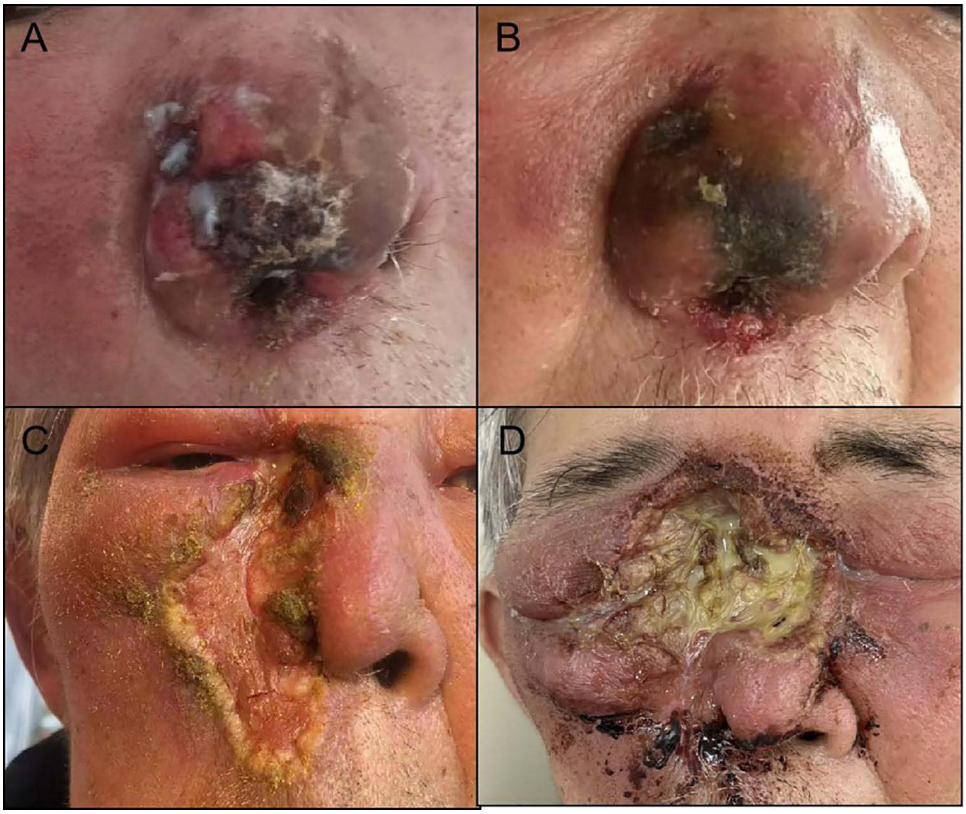


**Figure 1** The development process of facial lesions within 4 months. (**A**) Initially, there is an ulcer on the right wing of the nose, congestion, and edema of the surrounding skin. (**B**) The ulcer gradually improves after anti-infection treatment. (**C**) The lesion quickly spreads to the right inner canthus, nasal root, right cheek, and nasolabial groove. (**D**) The image depicts a man with an atypical presentation characterized by midfacial edema, necrotizing and destructive mass, bilateral periorbital involvement, and contracture atresia of the right nostril.

biopsies revealed that the hyperplastic inflammatory granulation tissue is accompanied by pseudotumor-like hyperplasia of some epithelia (Figure 1B). Two months later, the skin on the right side of the nose became red, swollen, and festered. After external application with traditional Chinese medicine, the lesion quickly spread to the right inner canthus, nasal root, right cheek, and nasolabial groove (Figure 1C). Four months later, the facial ulcer developed further, with large soft tissue defects on the right eyelid and nasal root reaching the bone, covering a large amount of purulent secretions and right anterior nostril contracture and atresia. The wound was covered with a significant amount of yellow-green pus mixed with cotton wool from gauze (Figure 1D). He experienced fever.

Since the lesion involved the eyes, he underwent ophthalmology specialist examination. The conjunctiva of the right eye was congested and edematous; secretions could be seen in the conjunctival sac, both of which were still transparent; the front was middle and deep, no pus iwas found, and the pupils were equicircular. The direct and subsequent reactions were sensitive. His blood test results indicated very high WBC counts ($41.5\times10^9$/L) and NEUT% (81.90%), with low LYMPH% (73.0%) and hemoglobin (HGB,94 g/L) levels. The Epstein-Barr virus-DNA copy numbers, serum anti-neutrophilic cytoplasmic antibodies, and ENA spectra are negative. Examination for lupus and rheumatism was negative. CT (Figure 2A) and MRI (Figure 2B) of the head and paranasal sinuses showed swelling and thickening of the soft tissues near the forehead and bilateral eyelids, absence of local skin and subcutaneous soft tissues in the maxillofacial region, and local defects of the nasal bone. Bacterial culture of his wound secretion was positive for *Escherichia coli*. Antibiotic sensitivity tests reveal that Cefoperazone Sodium and Sulbactam Sodium are the most sensitive. Considering the previous biopsy results suggesting inflammation, a biopsy was performed under general anesthesia, and large pieces of tissue from multiple sites, including the lesional and perilesional tissues, were used for pathological examination. Ulcer formation iwas observed, with a large amount of moderate to large lymphocyte-like cell infiltration in the subepithelial and dermal layers. Tumor cell invasion and destruction of blood vessel walls were also evident

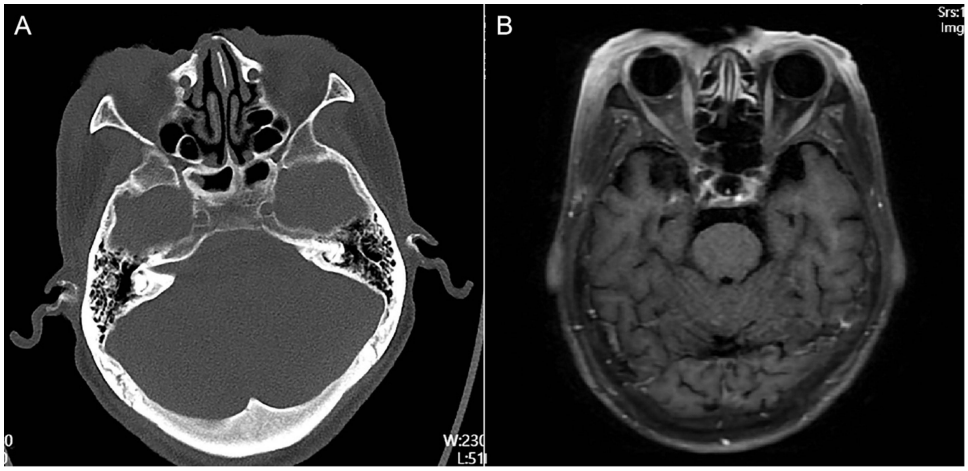


**Figure 2** The axial CT (**A**) and MRI (**B**) scan reveals a substantial area of tissue loss in the midfacial region, involving the nasal bone and resulting in markedly asymmetrical facial contours.

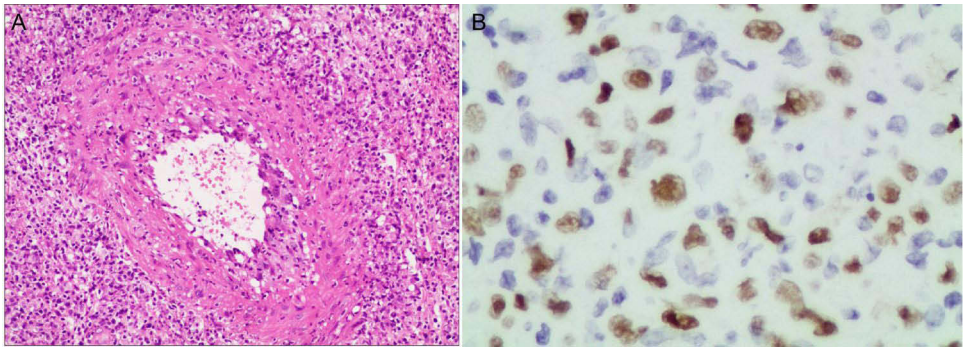


**Figure 3** Microscopic hematoxylin and eosin, and in situ hybridization features. (**A**) The image shows a lymphoid infiltrate comprising moderate to large cells with an angiocentric and angiodestructive growth pattern (H-E,×200). (**B**) The positivity of Epstein Barr virus by in situ hybridization is essential for confirming the diagnosis (ISH-EBV,×400).

(Figure 3A). Lastly, the diagnosis of nasal type extranodal NK/T-cell lymphoma is aided by the positivity of Epstein-Barr virus by in situ hybridization (EBER+) (Figure 3B).

## Discussion

Extranodal NK/T-cell lymphoma, nasal type (ENKTCL-NT) predominantly manifests in the midline facial areas, such as the nasal and paranasal areas, and accounts for 12.0–17.1% of non-Hodgkin lymphoma (NHL) in China.[4] Patients may experience non-specific symptoms such as nasal obstruction, discharge, nosebleeds, and headaches, which can persist for months to years before progressing to edema and necrotic ulceration. These ulcers can affect the middle face and upper aerodigestive tract, particularly the skin and mucosa of the nose, nasal septum, sinuses, and the nasopharynx. In addition, lesions can extend to the cheeks, orbits, upper lip, palate, and oropharynx as the disease advances.[5,6] Early diagnosis of ENKTCL-NT is challenging because it is often misdiagnosed as other conditions and treated with antibiotics and antifungals. Histopathological examination is crucial for early diagnosis; however, obtaining representative specimens from extensive necrotic tissues can be difficult. Therefore, multiple and deeper biopsies of the lesional and perilesional tissues may be necessary to establish a correct diagnosis.[7] Even if the initial pathology is negative, the possibility of ENKTCL-NT cannot be completely ruled out, and further biopsies should be performed if necessary. Microscopically, ENKTCL-NTs often exhibit remarkable lymphocytic infiltration and angiodestructive features, leading to areas of geographic necrosis. Surface atrophy or ulceration with secondary superimposed subacute inflammation is common. Immunohistochemical staining is often positive for EBER, cytotoxic molecules (TIA1, perforin, and granzyme B), CD2,


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cCD3, and CD56, as the disease is more often of NK cell origin with neoplastic elements. Positivity for ISH-EBV is essential for diagnosis.

In most cases, antibiotics or antifungal agents are initially effective because of the inflammation associated with necrosis, which can sometimes overshadow the neoplastic component. In this case, the wound is dressed and washed daily with diluted anerdians. Prior to pathogen analysis, Cefoperazone Sodium and Sulbactam Sodium are administered every 12 hours. The bacterial culture indicated the presence of *Escherichia coli*, and the use of Cefoperazone Sodium and Sulbactam Sodium was deemed appropriate based on the antibiotic sensitivity test. A biopsy is performed under general anesthesia, and the typical pathological features confirmed the diagnosis of extranodal NK/T-cell lymphoma, nasal type (EBER+) (Figure 3).

We recommend a combination of chemotherapy and radiotherapy; however, the treatment is delayed because of its high cost. Subsequently, the patient was discharged and returned to the local hospital for regular dressing, without medication. Sadly, the patient died three months later.

In this case, an accurate diagnosis of ENKTL-NT is ultimately achieved after more than six months and three biopsies. At the beginning, when the lesion is only localized to the right ala of the nose, it was misdiagnosed as a common inflammation and not taken seriously, only receiving routine anti-infective treatment. Subsequently, there was a temporary control of the disease, which led to a sense of complacency, and the patient's condition was not monitored and the treatment plan not adjusted timely. As a result, the disease progressed rapidly, involving the right inner canthus, nasal root, right cheek, and nasolabial groove. Four months later, because of external application of Traditional Chinese Medicine herbs leading to the growth of anaerobic bacteria, aggravating the progression of tumor and tissue necrosis, the facial ulcer further developed, with significant soft tissue defects and bone involvement in the right eyelid and the radix of the nose, covered with a large amount of purulent secretions. The right anterior nostril contracted. This serves as a reminder that missed and incorrect diagnoses of ENKTCL-NT can lead to rapid disease progression and hasten mortality.

Currently, there is no consensus among specialists regarding optimal treatment strategies, although L-asparaginase-based chemotherapy combined with radiotherapy appears to be the most suitable option.[8] Owing to the side effects of L-asparaginase, the authors recommended sequential P-GEMOX and radiotherapy for early stage ENKTCL-NT.[9] In advanced or relapsed cases, immunotherapy (PD-1/PD-L1 inhibitors) and autologous or allogeneic hematopoietic stem cell transplantation should be considered.[10] Reported survival rates range from 33–61%, with higher rates observed in patients treated with a combination of chemotherapy and radiotherapy, especially pediatric patients.[5]

## Conclusion

ENKTL-NT presents non-specific symptoms so it is easily misdiagnosed. Adequate representative specimens obtained through repeated biopsies are crucial for histopathological examination. Chemotherapy combined with radiotherapy is the most appropriate treatment option. Surgery is used only for biopsy and tissue repair.

## Ethics Approval and Informed Consent

This study is approved the Ethics Committee for Human Study at the Third Affiliated Hospital of Sun Yat-sen University (China). The patient's son is informed of the purposes and procedures of the study and provided written informed consent for the case details and images to be published.

## Author Contributions

All authors make a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; give final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

We declare no competing financial interests.

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