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Case Report

Extranodal nasal-type NK/T-cell lymphoma with facial swelling as the initial symptom

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Abstract: Extranodal natural killer (NK)/T-cell lymphoma (ENKTL), nasal type, is an uncommon subtype of non-Hodgkin lymphoma that frequently involves the nasal cavity and nasopharynx. Initially, it can be confused with non-nasal areas, including the skin, gastrointestinal tract, lungs, liver, salivary gland, and testes. The median age at diagnosis of patients with ENKTL is about 50-55 years. This article describes a patient with a single lesion of facial swelling as the first symptom. In cases of ENKTL without a typical clinical course, early histological testing and biopsy could help correct diagnosis.

Keywords: Extranodal NK/T-cell lymphoma, facial swelling, nasal type

Introduction

Extranodal NK/T-cell lymphoma (ENKL), nasal type, is a distinct subtype of lymphoma that predominantly occurs in extra-nodal sites, including nasal/paranasal area, skin, gastrointestinal (GI) tract, or other organs [1]. Nodal onset is rarely observed, but secondary nodal involvement is often recognized. The 2016 World Health Organization classification includes both nasal and extra-nasal categories of ENKL [2, 3]. The tumor more commonly affects male than female adults in the ratio of 3:1 in the fifth decade of life and mainly involves the nasal cavity and paranasal sinuses. Symptoms are nonspecific in the majority of cases, and the clinical picture reveals rhinorrhea, nasal obstruction, and epistaxis, mimicking an upper airway infection [4, 5]. As the disease progresses, extensive necrotic areas develop, and prognosis becomes poor with low survival [6]. The hemophagocytic syndrome, characterized by the activation of the mononuclear phagocyte system, can overlap, leading to even more unfavorable outcomes.

Clinical presentation

A woman aged 45 presented with a two-year history of progressive left facial swelling and pain. She gradually developed eyelid swelling, which prompted her to visit the hospital. She was diagnosed with facial cellulitis by computed tomography and received an anti-infective treatment (cefoxitin sodium and levofloxacin) in a primary hospital. The patient felt the symptoms improve significantly and was discharged after treatment for 1 week. The swelling and pain on the left face were gradually aggravated after several days, as reported by the patient. CT scan showed thickening of the left maxillary sinus mucosa and swelling of the left maxillofacial soft tissue (**Figure 1**). Nasal endoscopy examination revealed that purulent secretions and abscesses in large amounts filled the left nasal cavity. The left inferior turbinate and lateral nasal wall were enlarged, and the anterior mucosa of the inferior turbinate was broken and hunched slightly (**Figure 2**). The left inferior turbinate showed the lymphocytes in the mucosa exhibited extensive coagulative necrosis (**Figure 3**). In addition, immunohistochemistry was conducted to further explore the pathophysiology in this case, which showed small cell dysplasia expressing CD2(+), CD7(+), CD56(+), TIA-1(+) (**Figure 4**). After definitive diagnosis, the patient refused treatment and died 8 months later.

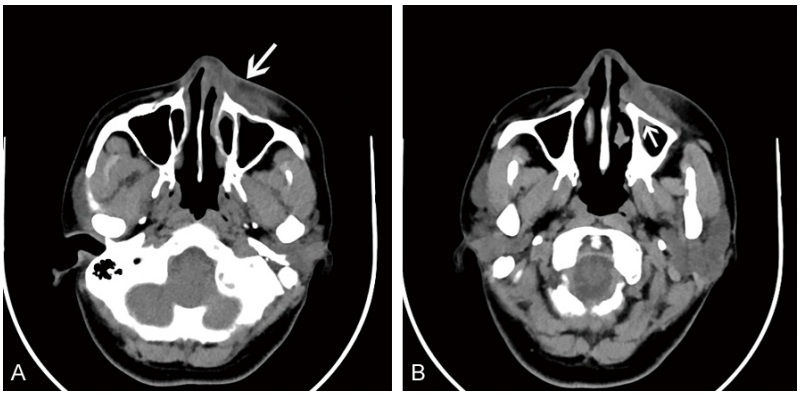

Figure 1. Sinus CT, left maxillofacial soft tissue swelling (A, arrow), Left maxillary sinus mucosa thickened (B, arrow) (axial position).

Discussion

ENKTL is a rare but aggressive type of non-Hodgkin lymphoma, which is etiologically related to the EB virus [7]. Generally, ENKTL (nasal type) easily invades the skin, digestive tract, respiratory tract, and testes. Only 3% of the cases involve the central nervous system. The nasal type, which is the main subtype, is observed in roughly 80% of cases, and its prognosis is related to the clinical stage [8, 9]. A limited disease, as observed in stage I/II cancers without invasiveness, is markedly better than an extensive disease, such as stage I/II with local invasiveness, stage III/IV, and extra-nasal NK/T-cell lymphomas [10]. ENKTL (nasal type) that involves the CNS or primary ENKTL is regarded as an extensive disease and has a worse outcome than that of a limited disease.

Nasal NK/T-cell lymphoma often presents nasal congestion, runny nose, and other symptoms and is at times accompanied by nasal bleeding, tinnitus, hoarse and sore throat, swallowing discomfort, and mucosal ulcers [11]. It can subsequently invade the sinuses, as well as the orbital, cheek, and frontal bones. If the center line is affected, septal perforation, palate perforation, bridge penetration, and even facial skin involvement may occur. Histopathological manifestations include tumor cell diffusion, invasion and destruction of blood vessel walls, and onion-skin lesions of the affected skin, leading to massive tissue necrosis [12]. Tumor cells vary in size and are mainly mixed with small and medium-sized lymphocytes. Immunophenotyping mainly shows CD2+, CD56+, and cytoplasmic CD3+ positive/CD3+ negative, most of which express cytotoxic granule-related proteins, such as granzyme B, TIA-1, and perforin. CD43, CD45, and Fas are also frequently expressed, whereas CD30 positive is occasionally expressed. In *in situ* hybridization, most of them are positive [13-15].

Imaging is an important diagnostic method for nasal NK/T-cell lymphoma and bears clinical significance for the diagnosis and staging of lesions. Early imaging changes are often atypical and may exhibit only nasal mucosa incrassation in the anterior inferior turbinate or septum of the nasal cavity, spreading through the mucosa or natural space [16]. Its characteristic was bottom of the turbinate or septum swelling and thickening, with a soft-tissue shadow in the nasal cavity. In the progressive stage, it would infiltrate in the ipsilateral sinus mucosa, the most common of which is the maxillary sinus, followed by the ethmoid sinus, which appears as the sinus mucosa or the soft tissue of the sinus hyperplasia. Tumor tissues can spread to the lumen along the lateral wall of the maxillary sinus. It can even enter the inferior temporal fossa to infiltrate the postmaxillary fat or erode the anterior maxillary sinus wall to infiltrate the subcutaneous tissue of the face. Tumors invading the ethmoid sinus can also enter the anterior cranial fossa through the screen plate or damage the orbital bone to enter the orbital. CT generally showed moderate tumor density, uniform distribution, and rarely liquefied necrosis. MRI revealed that T1-weighted image presented equal or a slightly lower signal, which was similar or slightly lower than that of the muscle, T2-weighted image showed an equal or slightly higher signal than that of the muscle but lower than that of the nasal mucosa [17, 18]. The tumor at times exhibited mild to moderate enhancement, which could be related to the t-cell type of nasal cavity. Nasal NK/T-cell lymphoma is mainly treated by radiotherapy and chemotherapy [19]. Clinical application of autologous or allogeneic hematopoietic stem cell transplantation has increased in recent years. However, this type of lymphoma has a relatively poor pro-

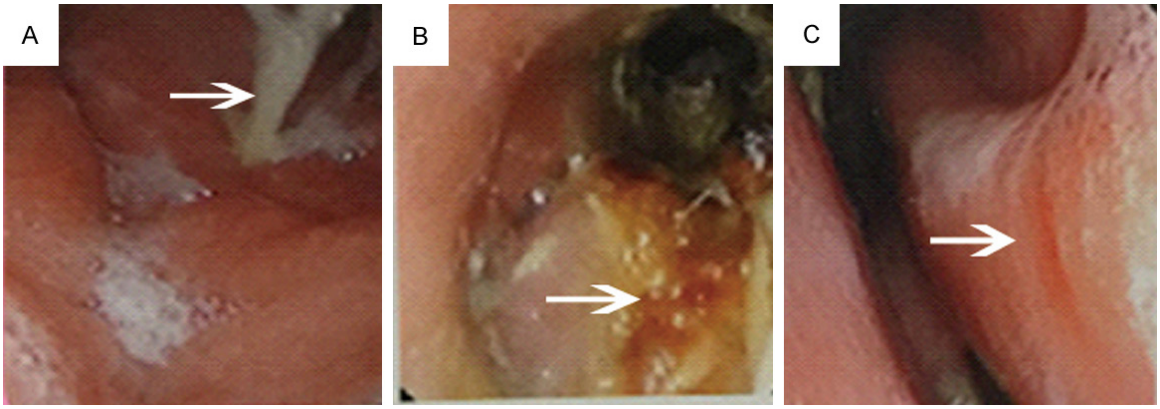

Figure 2. Findings of nasal endoscopy. A large amount of purulent secretion and scab sticking to the left nasal cavity (A, B, arrow). The mucosa of the anterior part of the inferior turbinate was broken and slightly bulge (C, arrow). Left inferior turbinate and nasal lateral wall were swollen (C, arrow).

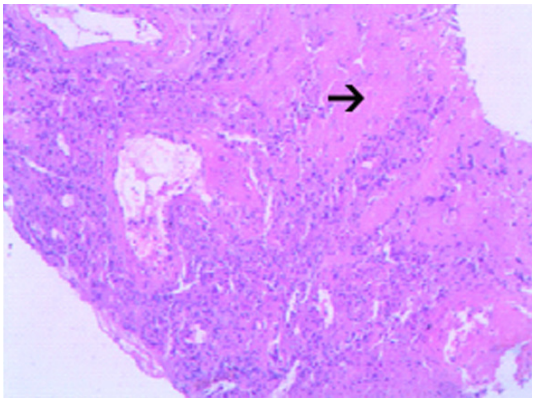

Figure 3. Pathological examination shows the polymorphous lymphocyte, accompanying with mass solidification necrosis.

gnosis, with a 5-year survival rate of only 20%-56%.

In this case, the first symptom was face swelling, which was difficult to differentiate from cellulitis. This difficulty could be attributed to the lack of features in the early imaging findings. Short-term antibiotics and hormone therapy may conceal the real condition. Patients received no specialized examination such as nasal endoscopy in the early stages. Facial swelling was the only clinical manifestation in the absence of typical clinical symptoms and could be easily misdiagnosed as facial cellulitis. Therefore, the clinical manifestations of facial cellulitis, particularly in those whose symptoms were gradually aggravated after conventional anti-infection treatment, should be highly suspected of tumors. Relevant examinations should be completed as soon as possible.

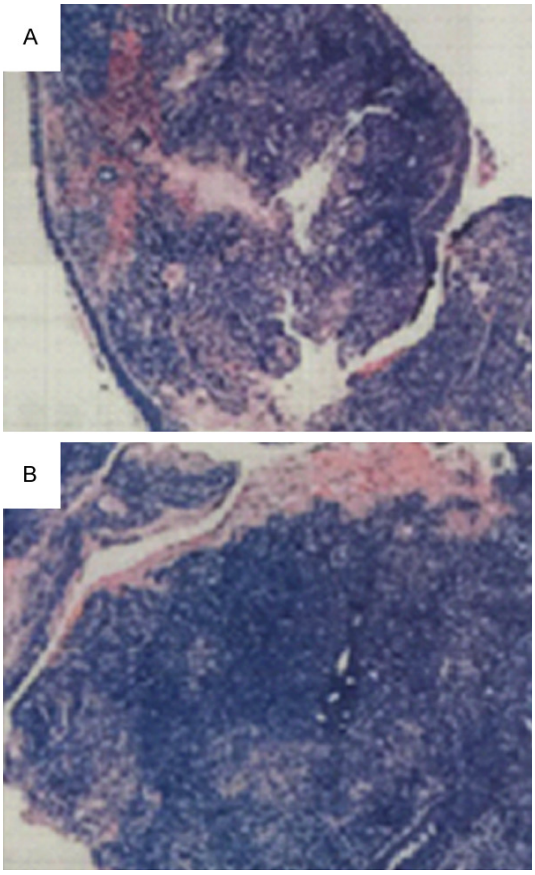

Figure 4. Immunohistochemical staining shows small dysplastic cells expressing CD2(+), CD7(+), CD56(+), TIA-1(+).

However, pathological examination should be conducted for the diagnosis.

In summary, nasal NK/T-cell lymphoma is often difficult to diagnose because of its complex

clinical manifestations and early nonspecific changes, thereby delaying its treatment. Clinicians need to master relevant knowledge and auxiliary examination of the disease, particularly imaging performance, which can help reduce the rate of misdiagnosis and missed diagnosis, avoid delay, and provide standardized diagnosis and treatment for patients in a timely manner.

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