

Extranodal natural killer/T cell lymphoma, nasal type in the middle cranial fossa

A case report

Han Wang, MD^a, Xiaolong Xia, MD^b, Cong Qian, MD^{c,*}

Abstract

Introduction: Extranodal natural killer (NK)/T cell lymphomas, nasal type, are aggressive, non-Hodgkin lymphomas. Extranodal NK/T cell lymphomas, nasal type, involving the central nervous system (CNS) are rare; therefore, delayed diagnosis easily occurs and is associated with a poor prognosis. Early diagnosis and patented systemic chemotherapy are necessary.

Case presentation: We present a case of 34-year-old male with facial numbness and diplopia. He was diagnosed with extranodal NK/T cell lymphoma, nasal type, involving the CNS. The tumor, located in the right middle fossa, was subtotally removed, and 3 cycles of systemic chemotherapy were given. He later died of severe neutropenia and infection.

Conclusion: NK/T cell lymphomas should be considered to be a potential cause of facial numbness and diplopia. A L-asparaginase-based regimen resulted in reasonable tumor suppression, but adverse effects, including fatal neutropenia, should be carefully considered.

Abbreviations: APTT = activated partial thromboplastin time, CBC = count of blood cell, CNS = central nervous system, CPA = cerebellopontine angle, CR = complete response, CSF = cerebrospinal fluid, EB = Epstein-Barr, EBER = EB virus encoded early small RNA, FPS = free progression survival, GI = gastrointestinal, H&E = hematoxylin and eosin, HBV = hepatitis B virus, MRI = magnetic resonance imaging, MTX = Methotrexate, NK = natural killer, OS = overall survival, PT = prothrombin time, SPECT = single photon emission computed tomography, TIA-1 = T cell-restricted intracellular antigen 1.

Keywords: central nervous system, chemotherapy, natural killer/T cell lymphoma, pathology

1. Introduction

Extranodal natural killer (NK)/T cell lymphomas, nasal type, are highly aggressive non-Hodgkin lymphomas; pathologically, they present as significant vascular damage and destruction, with apparent tissue necrosis and cytotoxicity.^[1,2] Extranodal NK/T

cell lymphomas are commonly located in the upper respiratory and digestive tracts, such as the nasal cavity, and sometimes occur in the skin or gastrointestinal (GI) tract, but rarely invade the central nervous system (CNS).^[3] Only a few cases of a NK/T cell lymphoma invading the CNS have been reported;^[4-6] here, we reported a case of an extranodal NK/T cell lymphoma in the right middle cranial fossa, with diplopia and facial numbness as the initial presenting symptoms.

This study was approved by the Ethics Committee of Zhejiang University School of Medicine Second Affiliated Hospital, and the informed consent form was signed by patient.

2. Case report

A 34-year-old man was admitted to our hospital on June 12, 2017, due to right facial numbness with diplopia, which had been present for 1 month. He progressively felt right facial numbness develop for no reason, and several days later, diplopia was present; no hearing loss, blurry vision, epistaxis, or fever occurred. He had a history of hepatitis B (HBV) infection, but no history of any other diseases. Upon neurological examination, right trigeminal, and abducens nerve paralysis was found; all other cranial nerves were intact. The general examination was normal. Other than the presence of a HBV infection, the results of the initial laboratory examination were normal, including the blood cell counts (CBC), routine urinalysis, activated partial thromboplastin time (APTT), prothrombin time (PT), and tumor markers. Enhanced magnetic resonance imaging (MRI) demonstrated a right middle fossa mass with obvious and uniform

Editor: N/A.

The data were curated by HW and CQ. Formal analysis was done by CQ. The methodology and resources were provided by CQ. This study was supervised by CQ and originally drafted by HW and XX. This paper was reviewed and edited by HW and CQ.

DW and XX contributed equally to this work.

This work was supported by National Natural Science Foundation of China, No. 81701152.

The authors report no conflicts of interest.

^a Department of Geriatrics, Tongde Hospital of Zhejiang Province, Hangzhou,

^b Department of Neurosurgery, Lanxi People's Hospital, Lanxi, ^c Department of Neurological Surgery, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China.

* Correspondence: Cong Qian, Department of Neurosurgery, the Second Affiliated Hospital, Zhejiang University School of Medicine, Jiefang Road 88th, Hangzhou, Zhejiang Province 310009, China (e-mail: congqian@zju.edu.cn).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2018) 97:34(e12028)

Received: 26 April 2018 / Accepted: 31 July 2018

<http://dx.doi.org/10.1097/MD.00000000000012028>

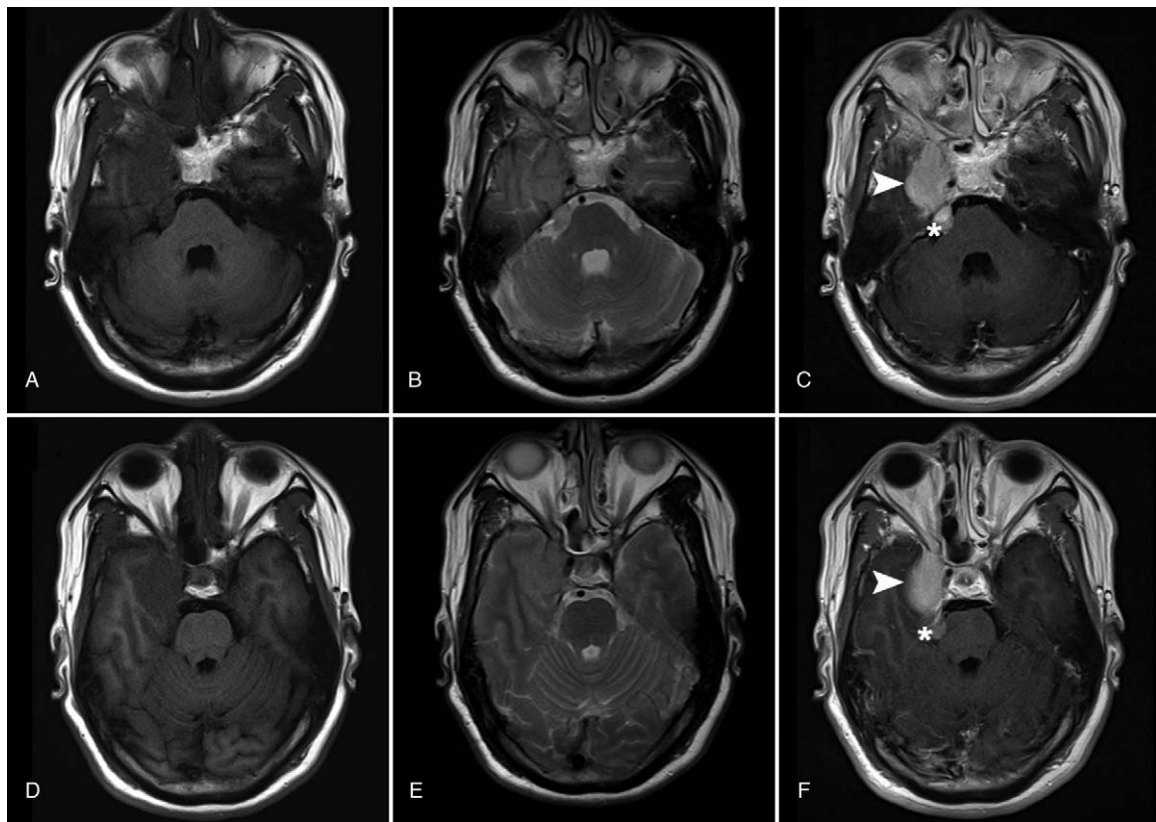


Figure 1. Preoperative cranial magnetic resonance imaging (MRI) demonstrated a right middle fossa mass with a low signal in T1WI, isodensity in T2WI and obvious enhancement after contrast agent injection in T1WI (white arrow). The tumor had invaded into the subarachnoid space at the right cerebellopontine angle (CPA) (white asterisk); no obvious brain edema was found. CPA=cerebellopontine angle, MRI=magnetic resonance imaging.

enhancement; no cysts or calcifications were found, and no obvious brain edema was present (Fig. 1). The patient was diagnosed with a right middle fossa neoplasm; schwannomas and meningiomas were considered.

He received a right craniotomy with neoplasm resection via an infratemporal approach. The bulk of the tumor was ashen, with ill-defined borders; the tumor was subtotally removed. He developed fever after surgery, and his symptoms did not improve until methylprednisolone was given. Malignant NK/T cell lymphoma was diagnosed via a pathological examination, but his situation deteriorated with fever, bilateral hearing loss and impaired kidney function. Upon hematoxylin and eosin (H&E) staining, diffuse pleomorphic tumor cells were observed infiltrating the vessels and ganglia, along with a large number of necrotic cells. Immunohistochemical staining demonstrated that NK/T cell markers, including CD3 ϵ , CD56, granzyme B, and T cell-restricted intracellular antigen 1 (TIA-1), were positive, but B cell markers, such as CD20, were negative (Fig. 2).

The patient was transferred to the hematology department for further assessment and treatment, his Epstein-Barr (EB) virus test was positive, and single photon emission computed tomography (SPECT) demonstrated a malignant lymphoma involving multiple extranodal organs, including the head, lung, pericardium, kidney, and bone (Fig. 3). According to the Ann Arbor system, he was stage III/IV; he received 3 cycles of chemotherapy with dexamethasone, methotrexate (MTX), L-asparaginase, gemcitabine, and oxaliplatin. Although tumor invasion was temporarily

blocked, severe neutropenia and infection made a 4th chemotherapy treatment impossible and resulted in his death after 6 months of illness.

3. Discussion

Extranodal NK/T cell lymphomas are rare but aggressive non-Hodgkin lymphomas and are closely related with EB virus infection, etiologically.^[7] Generally, extranodal NK/T cell lymphomas, nasal type, easily invade the skin, digestive tract, respiratory tract, and testis; only 3% cases involve the CNS.^[3]

The nasal type is the main subtype and is observed in roughly 80% of cases, and its prognosis is related to the clinical stage.^[8] Limited disease, as observed in stage I/II cancers without invasiveness, is markedly better than extensive disease, such as stage I/II with local invasiveness, stage III/IV, and extranasal extranodal NK/T cell lymphomas. Extranodal NK/T cell lymphomas, nasal type, that affect the CNS or primary extranodal NK/T cell lymphomas are considered to be extensive disease and have a worse outcome.

Currently, diagnosis of NK/T cell lymphoma is dependent on a pathological examination; a large amount of pleomorphic tumor cell infiltration with vascular damage is a typical characteristic observed on H&E staining. The tumor usually presents as a typical NK cell phenotype, in addition to being CD2 positive; its cytoplasmic CD3 ϵ is commonly positive, surface CD3 is negative, and CD56 is positive in most cases. Cytotoxic molecules,

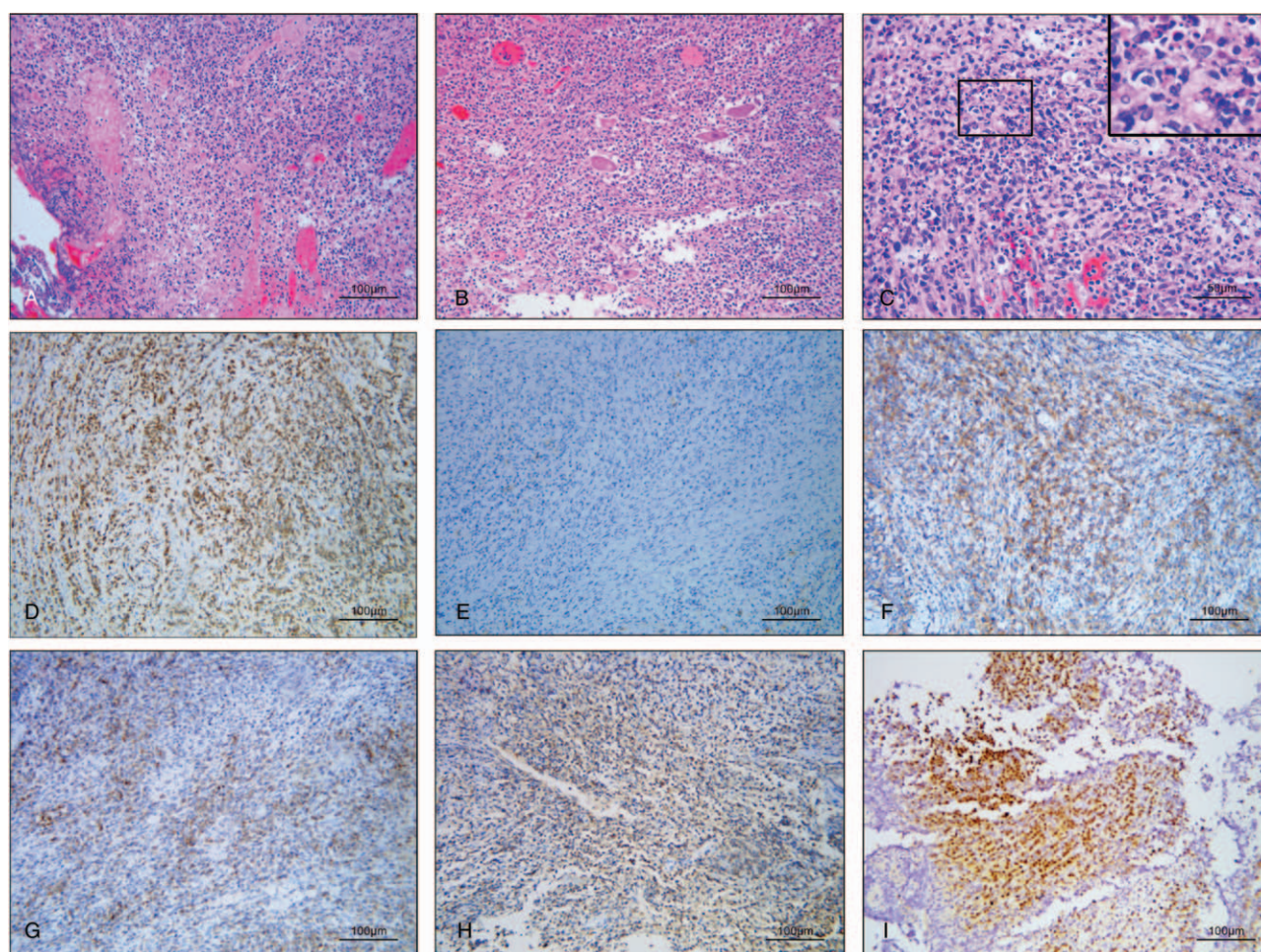


Figure 2. Histological examination of extranodal natural killer (NK)/T cell lymphoma, nasal type. A, B & C diffuse tumor cell infiltrated ganglia with obvious angiocentric growth patterns and a large number of necrotic cells on hematoxylin and eosin (H&E) staining. D - I Immunohistochemical staining. CD3 ϵ (D), CD56 (F), granzyme B (G), T cell-restricted intracellular antigen 1 (TIA-1) (H) and EB virus encoded early small RNA (EBER) (I) were positive, CD20 (E) was negative, which indicated extranodal NK/T cell lymphoma. H&E = hematoxylin and eosin.

including granzyme B, perforin, and TIA-1 are usually positive. In addition, EB virus encoded early small RNA (EBER) is also positive due to widespread EB virus infection.^[1,2] In our case, the features on H&E staining, such as diffuse pleomorphic tumor cell infiltrated vessels, along with a large number of necrotic cells, were typical and the characteristics of immunohistochemical staining presenting with positive CD3 ϵ , CD56, granzyme B, and TIA-1 were consistent with the diagnostic standards. Although a delayed diagnosis is difficult to avoid due to its rarity, NK/T cell lymphoma must be included in the differential diagnosis.

Generally, a L-asparaginase-based regimen, such as SMILE, including dexamethasone, MTX, ifosfamide, L-asparaginase, and etoposide, is recommended to treat extranodal NK/T cell lymphomas,^[2,9,10] but no extranodal NK/T cell lymphoma involving the CNS has previously been treated by a L-asparaginase-based regimen. Several articles on extranodal NK/T cell lymphomas involving the CNS or primary CNS NK/T cell lymphomas reported treatment strategies, including MTX-based chemotherapy and radiotherapy.^[3,6] However, this treatment strategy is the standard treatment regimen for B cell lymphomas; the curative effect on extranodal NK/T cell lymphoma remains unknown.

Based on the published literature, the overall survival (OS) of extranodal NK/T cell lymphoma involving the CNS, treated with

MTX-based chemotherapy, was 2 to 29 months (median: 8.5 months), which is significantly shorter than the OS of cases not involving the CNS. In our case, the patient was treated with an L-asparaginase-based regimen (dexamethasone, methotrexate, L-asparaginase, gemcitabine, and oxaliplatin), the invasiveness of tumor was blocked by chemotherapy, but the patient developed severe neutropenia and infection and died before the 4th chemotherapy treatment. Severe side effects, such as neutropenia and infection, may prove to be a significant problems when using an L-asparaginase-based regimen.^[2]

There are several limitations in our case report: individual differences made this case report lack universality; confounding factors, such as age and gender, were not corrected.

4. Conclusion

NK/T cell lymphoma should be considered to be a potential cause of facial numbness and diplopia. An L-asparaginase-based regimen induced reasonable tumor suppression, but adverse effects, such as fatal neutropenia, should be taken into consideration. Alternative potent and safe systemic chemotherapy regimens are needed immediately.

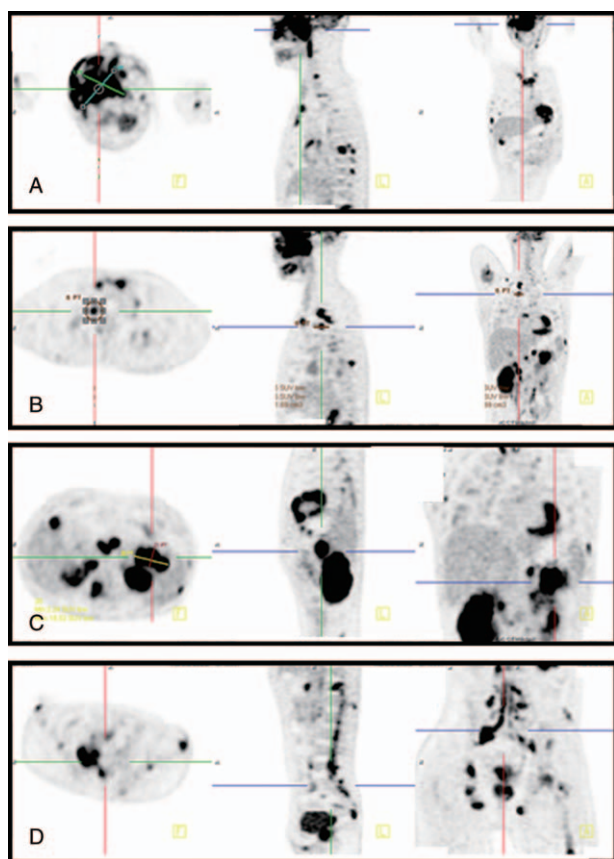


Figure 3. Single photon emission computed tomography (SPECT) image of extranodal natural killer (NK)/T cell lymphoma. A, Lesions of the NK/T cell lymphoma at the right cranial base. B, Extranodal NK/T cell lymphomas of the right lung. C, bilateral kidneys were invaded by NK/T cell lymphomas. D, Multiple lesions were found in the bones. NK=natural killer, SPECT=Single photon emission computed tomography.

Author contributions

Data curation: Han Wang, Cong Qian.

Formal analysis: Cong Qian.

Methodology: Cong Qian.

Resources: Cong Qian.

Supervision: Cong Qian.

Writing – original draft: Han Wang, Xiaolong Xia.

Writing – review & editing: Han Wang, Cong Qian.

References

- [1] Liang R. Advances in the management and monitoring of extranodal NK/T-cell lymphoma, nasal type. *Br J Haematol* 2009;147:13–21.
- [2] Chaudhary RK, Bhatt VR, Vose JM. Management of extranodal natural killer/t-cell lymphoma, nasal type. *Clin Lymphoma Myeloma Leuk* 2015;15:245–52.
- [3] Luther N, Greenfield JP, Chadburn A, et al. Intracranial nasal natural killer/T-cell lymphoma: immunopathologically-confirmed case and review of literature. *J Neurooncol* 2005;75:185–8.
- [4] Jiang X, Yin W, Song J, et al. Primary central nervous system extranodal NK/T cell lymphoma, nasal type, with antecedent hemophagocytic syndrome in a child. *Pediatr Dev Pathol* 2014;17:482–6.
- [5] Mai HC, Chen DX, Lu D, et al. Extranodal natural killer/T-cell lymphoma presenting as cavernous sinus syndrome. *Mol Clin Oncol* 2017;6:543–6.
- [6] Miyata-Takata T, Takata K, Kato S, et al. Clinicopathological analysis of primary central nervous system NK/T cell lymphoma: rare and localized aggressive tumour among extranasal NK/T cell tumours. *Histopathology* 2017;71:287–95.
- [7] Jaffe ES. Nasal and nasal-type T/NK cell lymphoma: a unique form of lymphoma associated with the Epstein-Barr virus. *Histopathology* 1995;27:581–3.
- [8] Kim TM, Heo DS. Extranodal NK /T-cell lymphoma, nasal type: new staging system and treatment strategies. *Cancer Sci* 2009;100:2242–8.
- [9] Lee J, Suh C, Park YH, et al. Extranodal natural killer T-cell lymphoma, nasal-type: a prognostic model from a retrospective multicenter study. *J Clin Oncol* 2006;24:612–8.
- [10] Tse E, Kwong YL. How I treat NK/T-cell lymphomas. *Blood* 2013;121:4997–5005.