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Brain Abscess as a Rare Complication of Primary Extranodal Nasal-type Natural Killer/T-cell Lymphoma

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ABSTRACT

We present the case of a 58-year-old Japanese woman with a natural killer T (NK/T)-cell lymphoma complicated by brain abscess. NK/T-cell lymphomas represent a rare type of lymphoma derived from either activated NK cells or, rarely, cytotoxic T cells. They are aggressive Epstein-Barr virus (EBV)-associated lymphomas that involve mainly the nasal cavity. Brain abscess associated with primary extranodal nasal-type NK/T-cell lymphoma is extremely uncommon: to our knowledge, this is the first reported case of this lymphoma with brain abscess as the initial clinical manifestation. Endoscopic surgery was performed for definitive diagnosis under intraoperative navigation system. Chemotherapy followed by radiotherapy was performed and was effective: 72 months later the tumor has not recurred. Recommendations of endoscopic management for diagnosis and treatment of this rare neoplasm are discussed.

Key words brain abscess; natural killer/T-cell lymphoma

Extranodal natural killer (NK/T)-cell lymphoma, nasal type, is an aggressive lymphoma that was originally described to involve the midline facial area, mainly the nasal cavity. The nasal cavity is, by far, the most common and prototypic site of involvement, but other primary sites have been reported, including the paranasal sinuses, pharynx, skin, gastrointestinal tract, and testis. Although there have been isolated cases involving the brain, none of these reports has been convincing for brain abscess involvement as initial clinical manifestation. Here we report a case of extranodal NK/T lymphoma with brain abscess.

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Abbreviations: CSF, cerebrospinal leakage; CT, computed tomography; EBV, Epstein-Barr virus; EBER, EBV-encoded small RNA; MDR, multi-drug resistance; MRI, magnetic resonance imaging; NK/T-cell lymphoma, Natural Killer/T-cell Lymphoma; SMILE, steroid, methotrexate, ifosfamide, L-asparaginase, and etoposide; WHO, World Health Organization

PATIENT REPORT

A 58-year-old Japanese woman was admitted to our hospital with the chief complaint of frontal headache and nasal obstruction for a period of approximately 1 month. Repeated biopsies from a right-side nasal mass had been performed at another hospital but had revealed only necrotic tissue, with no neoplastic cells. Endoscopy showed a white-coated necrotic mass in the right nasal cavity (Fig. 1). Coronal and axial computed tomography showed a soft-tissue-density mass in the right frontal, maxillary, sphenoid, and ethmoid sinuses and the right nasal cavity. The orbital medial wall, the nasal septum, and the frontal skull base had been destroyed by the tumor (Fig. 2). Axial T1-weighted and Gd-enhanced magnetic resonance imaging (MRI) revealed a well-circumscribed, low-signal-intensity mass situated in the right frontal, ethmoid, and sphenoid sinuses. Coronal T2-weighted MRI showed a low- to high-signal-density mass extending from the right frontal, ethmoid, and sphenoid sinuses to the intracranial frontal lobe; the mass had the appearance of a brain abscess (Fig. 3). Laboratory tests showed the following: leukocyte count, 4660/μL; hemoglobin, 12.8 g/dL; C-reactive protein, 0.17 mg/dL; LDH, 309 IU/L; soluble IL-2 receptor, 394 U/mL; serum creatine, 1.31 mg/dL; anti-neutrophil cytoplasmic antibodies, negative; and Epstein-Barr virus (EBV)-DNA, below the detectable level. Endoscopic sinus surgery and biopsy of the tissue from the nasal

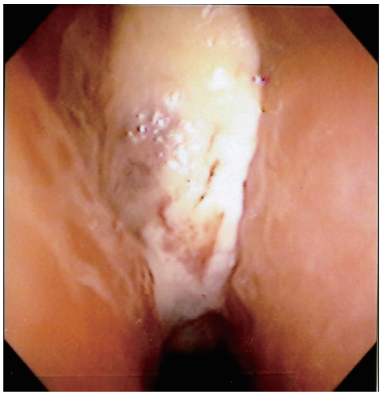

Fig. 1. This endoscopic view shows the white-coated mass in the right nasal cavity.

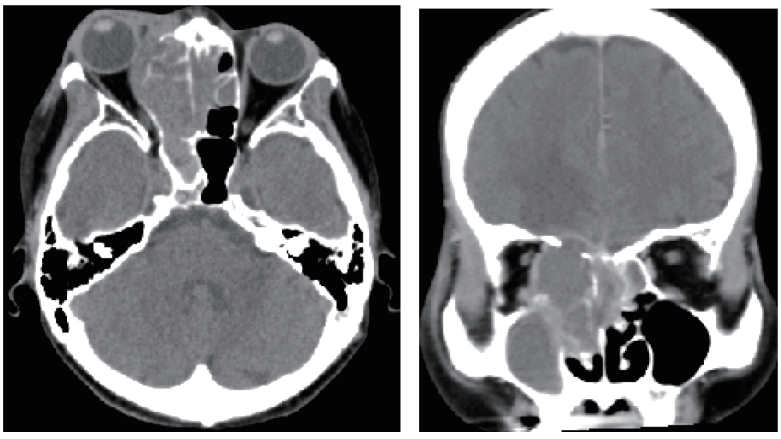

Fig. 2. Coronal and axial computed tomography shows a soft-tissue-density mass in the right frontal, maxillary, sphenoid, and ethmoid sinuses and the right nasal cavity. The orbital medial wall, nasal septum, and frontal skull base have been destroyed by the tumor.

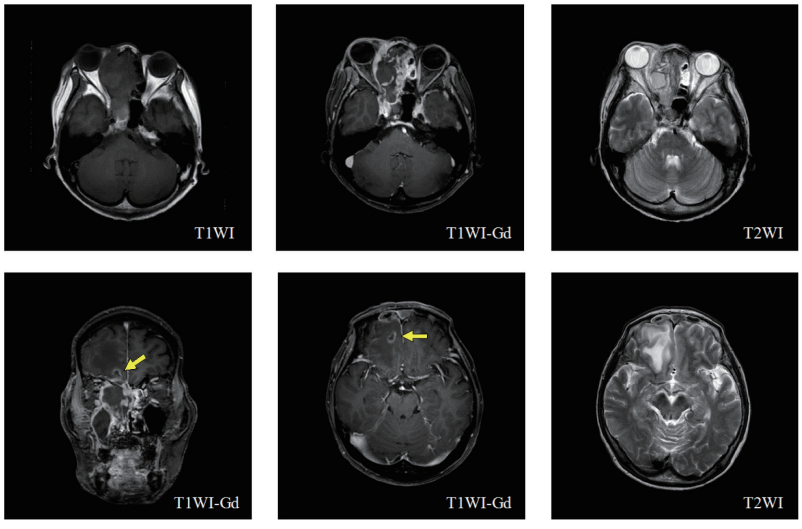

Fig. 3. Axial T1-weighted and Gd-enhanced magnetic resonance images show a well-circumscribed, low-signal-intensity mass situated in the right frontal, ethmoid, and sphenoid sinuses. Coronal T2-weighted magnetic resonance images show a low- to high signal-density mass extending from the right frontal, ethmoid, and sphenoid sinuses to the intracranial frontal lobe.

mass were performed under general anesthesia for a definitive diagnosis. A soft, easily bleeding, white-coated mass occupied the area between the middle and inferior turbinates. To avoid cerebrospinal leakage (CSF), the occupied lesion was removed with piece by piece under intraoperative navigation system and admitted to pathological examination. Pulsative purulent discharge in the frontal sinus was observed. The wall of the frontal sinus was partially damaged and the location of this area was confirmed at the lower portion of the brain abscess with intraoperative navigation system. Brain abscess was drained through the frontal sinus. CSF was not observed and bacterial culture of drained purulent discharge was negative, however, high dose systemic chemotherapy (Cefotax: 1.5g/day) was performed for 10 days to prevent meningitis after surgical manipulation. The surgical specimen contained a dense polymorphic cell infiltrate consisting of histiocytes and a great number of atypical lymphoid cells. These atypical cells had large nuclei and were hyperchromatic; some of them had abnormal mitotic figures. Immunohistochemically, the tumor cells were positive for CD3, CD56, and EBV-encoded small RNA (EBER), but negative for CD20 (Fig. 4). The clinical and histological features were consistent with a diagnosis of primary extranodal nasal-type NK/T-cell lymphoma, stage IE. The patient received intensity-modulated radiotherapy to the nasofrontal area and part of the intracranial region (50 Gy) over 5 weeks.

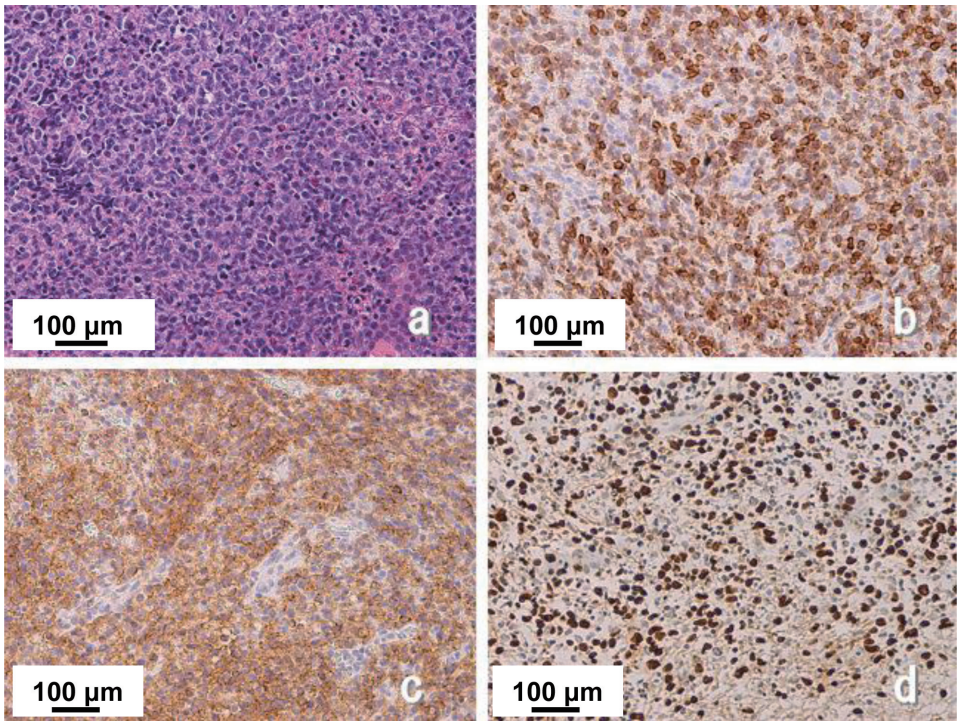

Fig. 4. Histologic sections showing a dense polymorphic cell infiltrate consisting of histiocytes and a large number of atypical lymphoid cells. The atypical lymphoid cells have large nuclei and are hyperchromatic; some of them have abnormal mitotic figures. Immunohistologically, the tumor cells were positive for CD3, CD56, and EBER (**a**, HE; **b**, CD3; **c**, CD56; **d**, EBER). Bar = 100 μm.

After radiotherapy, the patient received three courses of DeVIC chemotherapy (carboplatin 200 mg/m^2, etoposide 67 mg/m^2, ifosfamide 1 g/m^2, and dexamethasone 40 mg). The clinical course was satisfactory, and 72 months after the initial treatment the patient is well, with no evidence of tumor.

DISCUSSION

To our knowledge, this is the first report of a primary extranodal nasal-type NK/T-cell lymphoma with brain abscess as the initial clinical manifestation. The mechanism underlying the brain abscess in this case was blockage of the frontal rescess by the tumor expanding from the nasal cavity over a long period of time. In spite of repeated biopsy out-patient basis, definitive diagnosis could not be obtained, and endoscopic surgery was performed under general anesthesia with intraoperative navigation system. For making diagnosis precisely, enough volume of surgical specimen was mandatory, however, endoscopic surgery for this case was still challenging because of the narrow working space, the angled, anatomically variable frontal recess, and the proximity to the orbital tissue, olfactory fossa, and anterior skull base. Intraoperative navigation system was useful tool to identify the location. To prevent meningitis, high dose systemic chemotherapy was performed, and the cefotax was selected for this case because of pharmacodynamics of this agent with high delivery rate to brain tissues. The current World Health Organization (WHO) classification includes two types of NK/T-cell lymphoma: extranodal nasal-type NK/T-cell lymphoma and aggressive NK-cell leukemia.[1, 2] These diseases are mostly endemic to Latin America and East Asian countries. EBV is usually detected in the tumor cells, suggesting that it plays an important role in lymphomagenesis.[1–5] In terms of site of origin, extranodal NK/T-cell lymphoma can be divided into two major subtypes: nasal and extra-nasal.[3, 4] In advanced cases of both subtypes a highly aggressive clinical course and poor prognosis have been reported.[1, 2, 6] Extranodal nasal-type NK/T-cell lymphoma is rare, and P-glycoprotein, which is a product of the multi-drug resistance (MDR1) gene, is expressed on neoplastic cells of extranodal NK/T-cell lymphoma or aggressive NK-cell leukemia.[2, 6–8] This expression is a major cause of the refractoriness of NK/T-cell lymphoma to conventional chemotherapeutic regimens containing anthracycline. Although several case series indicate that the disease has an aggressive pattern and overall poor prognosis, DeVIC or a new chemotherapeutic regimen called SMILE (steroid, methotrexate, ifosfamide, L-asparaginase,

and etoposide) has recently showed promising results for extranodal nasal-type NK/T-cell lymphoma.[1, 2, 6–8] The amount of EBV-DNA in whole blood was useful for predicting tumor response, toxicity, and prognosis, and for monitoring during follow-up after DeVIC or SMILE chemotherapy.[1, 2, 6–8] For patients with primary extranodal nasal-type NK/T-cell lymphoma of stage IE or contiguous stage IIE with cervical lymph node involvement, concurrent chemotherapy with radiation and DeVIC chemotherapy has recently been recommended as a first-line treatment.[2, 6–8] Recent studies have also found that SMILE is effective for extranodal nasal-type NK/T-cell lymphoma, but considering the strong myelotoxicity of this modality its use in treating primary extranodal nasal-type NK/T-cell lymphoma needs some modification.[6, 7] In our patient, radiotherapy was performed as an induction therapy before DeVIC chemotherapy from the general conditions of patient and risk of side effects of combined therapy. The result supports the effectiveness of DeVIC for primary extranodal nasal-type NK/T-cell lymphoma. The highly aggressive course, with poor response and short survival with standard therapies, has led some investigators to recommend consolidation with bone- marrow or peripheral-stem-cell transplantation to prevent various chemotherapy-related complications.[1, 2] Clearly, new and better treatment modalities are needed for primary extranodal nasal-type NK/T-cell lymphomas; these will likely incorporate radiation therapy.

In conclusion, we have presented an extremely rare case of primary extranodal nasal-type NK/T-cell lymphoma complicated by brain abscess. Primary extranodal nasal-type NK/T-cell lymphoma should be kept in mind in the work-up of brain abscess, which itself can give rise to various life-threatening complications.

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The authors declare no conflict of interest.

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