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Atypical cauda equina presentation of an extranodal nasal type NK/T cell lymphoma: A case report

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ABSTRACT

Background: Extranodal NK/T-cell nasal type lymphoma, is an uncommon subtype of non-Hodgkin's lymphoma. It is mostly located in the nasal cavity, but in some cases can be found outside of it. The central nervous system (CNS) is a rare site of primary or progression of this lymphoma. Only one similar case of cauda equina syndrome had been reported previously in a postmortem patient. Patients with this type of lymphoma have a poor prognosis and some authors have described a median overall survival of 8.5 months from diagnosis (range 3.8–24 months from CNS involvement).

Case report: We report a case of a 38-year-old female with diagnosis of extranodal NK/T-cell nasal lymphoma. After radiotherapy and chemotherapy, she was admitted to the emergency room presenting neurologic impairment in the limbs (2/5 in MRC grading scale). Brain neuroimaging did not show any abnormality and lumbar puncture was not possible despite multiple attempts. Thoracolumbar imaging showed an involvement of the cauda equina and intraoperative findings revealed thickening and swelling of the nerve roots confirming an infiltration by lymphoma in the pathology. To date, our patient has an overall survival of 18 months from diagnosis of lymphoma and 7 months from peripheral nervous system involvement (actually 5/5 in MRC grading scale).

Conclusions: In this particular case, the surgery goal was to obtain a diagnosis to guide treatment but not to relieve symptoms. We considered its diffusion and knowledge as imperative for all practitioners involved in the care of this patient.

1. Introduction

Lymphomas are divided into 2 groups, Hodgkin's and non-Hodgkin's lymphomas (NH). These can arise from B-cell or T-cell with a prevalence of 85% and 15%, respectively (1). Among subtypes of NH T-cell lymphomas, the extranodal NK/T-cell lymphoma nasal type (ENKTL) accounts for around 10% of all NH T-cell lymphomas [1]. This type of lymphoma has been associated with Epstein-Barr virus (EBV) infection [2,3] and is located mainly in the upper aerodigestive tract. Therefore, it is named as ENKTL nasal type [1,4]. Other locations such as skin, soft tissue, gastrointestinal tract and testis are less common [1,2,4]. On the other hand, 0 to 11% of patients with diagnosis of ENKTL [2–4] have extension by proximity to the central nervous system (CNS).

To guide the diagnosis is necessary imaging of the nasal sinuses by magnetic resonance imaging or computed tomography and biopsy of the lesion. Because this is a rare type of lymphoma, ENKTL final diagnosis is based on molecular findings, especially in extranasal locations. ENKTL cells commonly express cytoplasmic CD3, CD56 and cytotoxic proteins

Abbreviations: ENKTL, extranodal NK/T-cell lymphoma; EBER, in situ hybridization for EBV encoded RNA; CNS, central nervous system; 18F-FDG, fluorine-18-fluorodeoxyglucose; PET/CT, positron emission tomography/computed tomography; MRI, magnetic resonance image; LP, lumbar puncture; CSF, cerebrospinal fluid; EBV, Epstein Barr Virus; OS, overall survival; PFS, progression-free survival.

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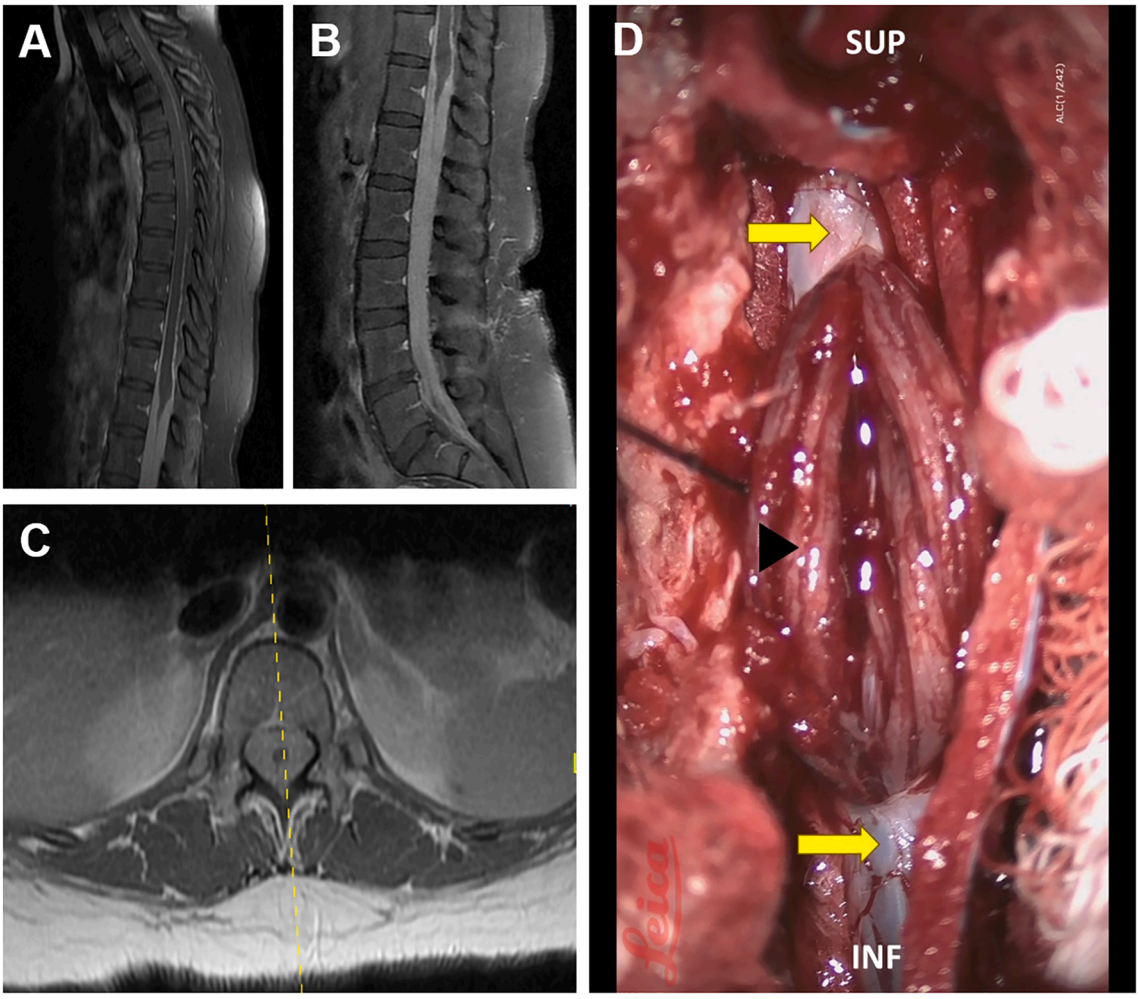

Fig. 1. Thoracolumbar MRI shows no passage of cerebrospinal fluid toward the cauda equine, mimicking a solid tumor. (A) Thoracic MRI T1 sequence, (B) Lumbar MRI T1 sequence (C) Axial MRI T1 sequence at lumbar level. (D) Intraoperative photo showing nerve roots of cauda equina protruding by severe swelling (black arrowhead) after dural opening (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

as perforin, granzyme B, and TIA1 [5–7]. Differential diagnosis includes other types of hematolymphoid neoplasms like aggressive NK cell leukemia, angioimmunoblastic T-cell lymphoma, and others [5–7].

We present the case report of a young patient with diagnosis of ENKTL nasal type with a rare distal extranasal location in the cauda equina, which provides insight into this rare condition for neurosurgeons.

2. Case report

We present a 38-year-old Hispanic female patient with a past history of an ENKTL nasal type, located in right nasal fossae diagnosed 12 months ago, without bone marrow or other organ involvement. She underwent concurrent chemoradiation therapy with DeVIC + radiotherapy regime (radiation 50 Gy and 3 courses of dexamethasone, etoposide, ifosfamide and carboplatin) after initial diagnosis. Three months after finishing the treatment, the patient evaluation with fluorine-18-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) did not show progression of the disease but showed an increased physiological uptake of 18F-FDG in the nasal and paranasal tissue, not distinguishable between residual infiltration or of inflammatory origin. Treatment-related complications were 2 episodes of neutropenia, 1 episode of sinusitis, and right ethmoidal mucocele.

She was admitted to our emergency room with a 2-week history of severe headache 7/10 in the Visual Analog Scale for pain, photophobia, diplopia, weakness and numbness in lower limbs (2/5 in MRC grading scale), and small urine volume during urination. She did not have a fever.

Physical examination revealed neurologic impairment of oculomotor (non-complete) and hypoglossal left cranial nerves, gait instability and paresthesia with loss of strength in the lower limbs.

Laboratory tests were normal. The cranial CT scan and cerebral magnetic resonance image (MRI) showed right ethmoidal mucocele and pansinusitis; the brain and other structures were normal. Because of the pansinusitis findings, an antibiotic regime ampicillin-sulbactam was started. Renal/Urinary tract ultrasound evidenced urinary retention. Analgesic treatment with acetaminophen and hydromorphone was started, with adequate control of headache grading 0/10 in the Visual Analog Scale for pain.

On suspicion of paraneoplastic inflammatory neuropathy Dexamethasone was administered from the sixth day of admission. Also, an electromyography and nerve conduction of all extremities were developed reporting damage in the conus medullaris and lumbar nerve roots.

A lumbar puncture (LP) was not possible despite multiple attempts by several doctors, including an anesthesiologist. Thus, a complete spinal cord MRI was made, where a mass occupying the entire dural sac from T11 to L5 and cerebrospinal fluid (CSF) without flow downwards

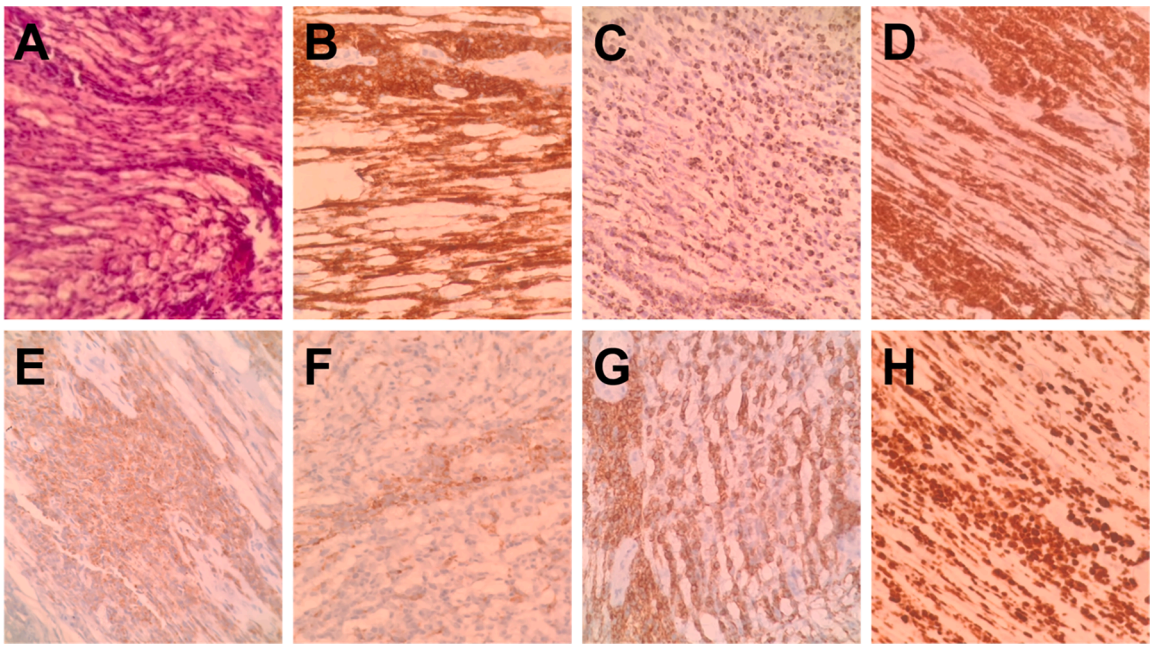

Fig. 2. (A) Peripheral nerve bundles infiltrated by lymphoma. The neoplastic cells are medium-sized with slightly irregular nuclear contours and inconspicuous nucleoli. H&E 40x. At low magnification (40x), the composite picture shows that the neoplastic cells clearly express CD56 (B), TIA1 (C), CD3 (D), CD2 (E), CD4 (F), CD8 (G). Ki67 index was >95% (H).

was evident (Fig. 1).

For all these reasons, the patient underwent a surgical open biopsy. During the surgical procedure, a dural opening was performed under microscopic view. No CSF flow through the duramater opening. No mass was evident either. Otherwise, swelling of the cauda equina nerve roots was observed. It was thickened and reddened, protruding with high pressure after dura opening (Fig. 1). A dorsal rhizotomy was made and sent to pathology study.

The microscopic study showed a tumor characterized by a proliferation of monotonous lymphoid infiltrate with focal vascular invasion (Fig. 2). The lymphocytes were of medium size, folded nuclei, indistinct nucleoli and moderate amount of cytoplasm. Frequent mitoses and extensive coagulative necrosis was observed. Immunohistochemical studies were performed (Fig. 2) and the atypical cells were positive for CD45 (LCA), CD2, CD8, CD56 and TIA1. Ki67 proliferation index was 95–100%. They were negative for granzyme B, Perforin, CD30 and AE1AE3 cyotokeratin. In situ hybridization for EBV encoded RNA (EBER) shows reactivity in most tumor cells. The pathology diagnosis was consistent with an ENKTL nasal type.

A new PET/CT showed progression of the disease. A second surgery performed by otorhinolaryngology staff confirmed a mucocele in the right ethmoidal lesion.

The patient was referred to another institution for administration of new treatment regime proposed by Hematology and Oncology staff: MeAD (methotrexate, asparaginase and dexamethasone) accompanied by radiation therapy, and bone marrow transplant.

Follow-up of the patient was 18 months from diagnosis. To date, after last treatment, the gait instability, paresthesia and loss of strength in the lower limbs is relieved (5/5 in the MRC grading scale).

3. Discussion

ENKTL nasal type is a rare aggressive subtype of lymphoma which accounts about of 0.2% of all non-Hodgkin's lymphomas and 1–2% of all NK/T cell lymphomas. Aggressive and predominantly extranodal lymphoma of NK/T cell origin is characterized by angiotropism and angiodestruction, necrosis and association with EBV infection [1,7–10]. It is mostly located in nasal cavity but a little percentage can be found in extranasal locations [1,3]. The extranasal sites classically described are skin, soft tissue, gastrointestinal tract and testis [1]. CNS is a rare location for the primary tumor progression of the disease. Although ENKTL in the CNS is infrequent, some authors have reported a range of involvement from 16 to 21% [1,4], being leptomeningeal mostly involved, and in rare cases, parenchymal metastasis which seems like an abscess-like appearance on neuroimaging leading to misdiagnosis [3,4]. CSF flow cytometry could be useful in the context of a patient with clinical suspicious and normal imaging. In our case, LP was not possible because of swelling in the nerve root of the cauda equina, which did not allow CSF flow downward (Fig. 1).

Molecular studies include JAK/STAT activation (JAK3 mutation in 33% of cases, JAK3 inhibition leads to decrease in the invasiveness of cell lines), STAT3 and STAT5B mutations (STAT3 mutations in exon 20 and 21 in 33% of patients), mutations of DDX3X in 20% of cases, upregulation of miR-155 and miR-21 and Genomic hybridization (Common gains: 1q21-q44, 2q13-q14, 2q31-q32, 6p25-p11, 7q11-q34, 7q35-36, 17q21, 20q11; Common losses: 6q16-q25, 11q23, 11q24-q25, 13q14, 17p13) [11,12].

The differential diagnosis includes: Aggressive NK cell leukemia, Angioimmunoblastic T cell lymphoma, Peripheral T cell lymphoma NOS, EBV positive diffuse large B cell lymphoma and T cell large granular lymphocytic leukemia [5,6].

The prognosis is considered very poor and could be determined by localized/disseminated disease [1,3,4]. To date, our patient has an overall survival (OS) from ENKTL diagnosis of 18 months. Akbal et al., have reported a median OS of 24 months (range 4–31 months) in patients with CNS primary involvement, although locations were not mentioned [1]. On the other hand, Nevel et al. reported a median OS of 3.8 months from CNS diagnosis and 8.5 months from ENKTL diagnosis [4]. In addition, our patient had an interval of 12 months of progression-free survival (PFS) from ENKTL diagnosis to CNS involvement. This is in accordance with that reported by Nevel et al. with a range of 0–12.5 months PFS [4]. To date, our patient has a OS of 6 months from CNS involvement.

Multiple treatment regimens have been recommended for this type of lymphoma. However, optimal treatment remains controversial. Among recommended chemoradiotherapy regimens for localized ENKTL are:

RT-DeVIC (dexamethasone, etoposide, ifosfamide, and carboplatin), RT-VIDL (etoposide, ifosfamide, dexamethasone, and L-asparaginase), and RT-SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide). In case of advanced, relapsing, or refractory stages of ENKTL, L-asparaginase-based regimens is considered the key drug of the treatment [13,14], this include: SMILE, MeAD/AspaMetDex (modified SMILE regime; asparaginase, methotrexate, and dexamethasone) and P-GemOx (peg-asparaginase, gemcitabine, oxaliplatin). In our patient, the initial treatment was based on RT-DEVIC regime, because it was a localized ENKTL. This regime is recommended like standard of care for localized ENKL in some countries, for example in Japan [7,14]. For advance-stage disease chemotherapy alone is the standard, but it is possible to consider radiotherapy or autologous stem-cell transplantation for consolidation. In the case of our patient, this last option was considered by the Hematology and Oncology staff. She underwent chemotherapy with MeAD regime and subsequent autologous stem-cell transplantation.

A similar case reported by Shimatani et al., described a patient with a clinical rapidly progressive dementia in whom autopsy revealed severe involvement of the cauda equina by lymphoma cells [2]. No other similar cases were found in the literature (Search date in Scopus and Pubmed: 22/12/2020).

4. Conclusions

This case represents a diagnostic challenge for all physicians involved in the care of these patients, especially for neurosurgeons. Surgery in this case, may be useful to get a definitive diagnosis, but it does not provide a therapeutic relief of the symptoms. Targeted treatment should include radiation therapy and chemotherapy. Communication and discussion of this case provides knowledge for this rare disease.

5. Authorship statement

P.A.-R.H. wrote original draft., P.A.-R.H., and M.-G.D. wrote the manuscript., P.A.-R.H., M.-G.D., and L.M.-R.L. performed research, collected patient information, and helped to analyze data; Y.-M.A. performed bioinformatics and biostatistical analysis; A.E.-R.R. analyze the biopsy; ALL AUTHORS. review and editing. and S.-T.B. designed the research, directed the work, analyzed data, provided funding and was the main surgeon.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] M. Akbar, E. Clasen-Linde, L. Specht, Extranodal NK/T-cell lymphoma, nasal type, with extranasal presentation – a case report and a review of the literature, Acta Oncol. 59 (12) (2020) 1480–1487, https://doi.org/10.1080/0284186X.2020.1795250.

[2] Y. Shimatani, Y. Nakano, N. Tsuyama, S. Murayama, R. Oki, R. Miyamoto, N. Murakami, K. Fujita, S. Watanabe, H. Uehara, T. Abe, H. Nodera, T. Kawarai, Y. Izumi, R. Kaji, Extranodal NK/T-cell lymphoma, nasal type, manifesting as rapidly progressive dementia without any mass or enhancing brain lesion, Neuropathology 36 (5) (2016) 456–463, https://doi.org/10.1111/neup.2016.36.issue-510.1111/neup.12285.

[3] Y. Yang, Z. Li, C. Zhiyang, H. Liang, Extranodal natural killer/T-cell lymphoma nasal type with central nervous system involvement mimicked tuberculous meningitis: a case report, Medicine (Baltimore) 98 (34) (2019), e16747, https://doi.org/10.1097/MD.0000000000016747.

[4] K.S. Nevel, E. Pentsova, M. Daras, Clinical presentation, treatment, and outcomes of patients with central nervous system involvement in extranodal natural killer/T-cell lymphoma, Leuk Lymphoma 60 (7) (2019) 1677–1684, https://doi.org/10.1080/10428194.2018.1551541.

[5] S. El Hussein, K.P. Patel, H. Fang, et al. Genomic and immunophenotypic landscape of aggressive NK-cell leukemia. Am J Surg Pathol. 2020;44(9):1235-1243. doi: 10.1097/PAS.0000000000001518.

[6] M.L. Marques-Piubelli, Y.I. Salas, C. Pachas, R. Becker-Hecker, F. Vega, R. N. Miranda, Epstein-Barr virus-associated B-cell lymphoproliferative disorders and lymphomas: a review, Pathology 52 (1) (2020) 40–52, https://doi.org/10.1016/j.pathol.2019.09.006.

[7] M.M. Cheung, J.K. Chan, W.H. Lau, W. Foo, P.T. Chan, C.S. Ng, R.K. Ngan, Primary non-Hodgkin's lymphoma of the nose and nasopharynx: clinical features, tumor immunophenotype, and treatment outcome in 113 patients, J Clin Oncol 16 (1) (1998) 70–77, https://doi.org/10.1200/JCO.1998.16.1.70.

[8] Y.K. Jeon, J.H. Kim, J.Y. Sung, J.H. Han, Y.H. Ko, Hematopathology Study Group of the Korean Society of Pathologists, Epstein-Barr virus-positive nodal T/NK-cell lymphoma: an analysis of 15 cases with distinct clinicopathological features, Hum Pathol. 46 (7) (2015) 981–990, https://doi.org/10.1016/j.humpath.2015.03.002.

[9] Y.L. Kwong, A.C. Chan, R. Liang, et al. CD56+ NK lymphomas: clinicopathological features and prognosis. Br. J. Haematol. 1997;97(4):821-829. doi: 10.1046/j.1365-2141.1997.1462962.x.

[10] S. Li, X. Feng, T. Li, et al. Extranodal NK/T-cell lymphoma, nasal type: a report of 73 cases at MD Anderson Cancer Center. Am. J. Surg. Pathol. 2013;37(1):14-23. doi: 10.1097/PAS.0b013e31826731b5.

[11] S. de Mel, S.S. Hue, A.D. Jeyasekharan, W.J. Chng, S.B. Ng, Molecular pathogenic pathways in extranodal NK/T cell lymphoma, J Hematol Oncol 12 (1) (2019) 33, https://doi.org/10.1186/s13045-019-0716-7.

[12] J. Liu, L.i. Liang, D. Li, L. Nong, Y. Zheng, S. Huang, B.o. Zhang, T. Li, JAK3/STAT3 oncogenic pathway and PRDM1 expression stratify clinicopathologic features of extranodal NK/T-cell lymphoma, nasal type, Oncol Rep. (2019), https://doi.org/10.3892/or10.3892/or.2019.7112.

[13] P.B. Allen, M.J. Lechowicz, Management of NK/T-cell lymphoma, nasal type, J Oncol Pract 15 (10) (2019) 513–520, https://doi.org/10.1200/JOP.18.00719.

[14] M. Yamaguchi, M. Oguchi, R. Suzuki, Extranodal NK/T-cell lymphoma: Updates in biology and management strategies, Best Pract. Res. Clin. Haematol. 31 (3) (2018) 315–321, https://doi.org/10.1016/j.beha.2018.07.002.