

DESTRUCTIVE SINONASAL DISEASE AS A PRESENTATION OF NASAL-TYPE EXTRANODAL NK/T-CELL LYMPHOMA: A FOUR-CASE SERIES

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ABSTRACT

Background: Extranodal natural killer/T-cell lymphoma, nasal type (ENKTL) is a rare, but highly aggressive non-Hodgkin lymphoma. Clinical presentation are often nonspecific and May mimic inflammatory disease such as Granulomatosis with Polyangiitis (GPA), resulting in delayed diagnosis. Extensive tumor necrosis makes histopathological findings difficult.

Objective: To present an evidence-based case series of extranodal NK/T-cell lymphoma, nasal type (ENKTL), initially misdiagnosed as GPA, focused on its clinical manifestations and diagnostic workup, with the aim of improving early detection, reducing misdiagnosis, and facilitating appropriate management.

Methods: An evidence-based case series was conducted involving patients with destructive sinonasal disease at Dr. Hasan Sadikin General Hospital, initially diagnosed as granulomatous diseases. All patients underwent diagnostic workup including detailed history, otorhinolaryngological examination, nasal endoscopy, laboratory tests, chest radiography, and abdominal ultrasonography, followed by biopsy of the sinonasal mass as the gold standard and immunohistochemical analysis for definitive diagnosis. A structured literature search was performed in PubMed, Scopus, and DynaMedex, and eligible studies were qualitatively analyzed using a PICO framework.

Results: Four patients presented with progressive destructive sinonasal disease and were initially misdiagnosed as inflammatory or granulomatous conditions, including GPA and midline granuloma. Common findings included blackish crusting, septal destruction, nasal obstruction, foul-smelling discharge, facial swelling, and orbital or systemic involvement. All patients underwent biopsy of the sinonasal mucosa followed by immunohistochemical examination, confirming ENKTL within the spectrum of high-grade T/NK-cell lymphoma. Initially, all were managed as suspected granulomatous disease while awaiting biopsy results. The literature review identified four studies showing similar patterns, including nonspecific early symptoms, diagnostic delays, and challenges due to extensive necrosis requiring repeated biopsies. Key features included angiocentric destruction, rapid progression, and poor response to conventional therapy.

Conclusion: ENKTL should be suspected in patients with progressive destructive sinonasal disease unresponsive to conventional therapy. Diagnosis relies on adequate biopsy from the interface between the lesion and viable mucosa, rather than necrotic tissue, demonstrating angiocentric destruction, followed by immunohistochemical evaluation. Early recognition and appropriate diagnostic approach are essential to reduce delay and improve clinical outcomes.

Keywords: *Extranodal NK/T-cell lymphoma; Sinonasal destructive disease; Diagnostic challenge*

How to cite this article: 1 Roshida Fitri Riphath 2 Lina Lasminingrum 3 Sally Mahdiani 4 Sinta Sari Ratunanda. DESTRUCTIVE SINONASAL DISEASE AS A PRESENTATION OF NASAL-TYPE EXTRANODAL NK/T-CELL LYMPHOMA: A FOUR-CASE SERIES. Int J Drug Deliv Technol. 2026;16(85s):503-509. DOI: 10.25258/ijddt.16.85s.47.

INTRODUCTION

Extranodal natural killer/T-cell lymphoma, nasal type (ENKTL), is a rare but highly aggressive subtype of non-Hodgkin lymphoma that predominantly involves the nasal cavity and upper aerodigestive tract.^{1,2} The disease shows a strong association with Epstein-Barr virus (EBV) infection and is histopathologically characterized by angiocentric and angiodestructive infiltration, frequently leading to extensive tissue necrosis.^{2,3}

Early clinical manifestations are often nonspecific, including nasal obstruction, rhinorrhea, crusting, and epistaxis.⁴ These symptoms can closely resemble benign inflammatory or infectious conditions such as chronic rhinosinusitis or granulomatosis with polyangiitis, frequently resulting in delayed or missed diagnosis.^{4,5} Furthermore, the presence of widespread necrosis may compromise biopsy adequacy, rendering initial histopathological evaluation inconclusive and necessitating repeated tissue sampling along with comprehensive immunohistochemical and EBV-related studies.^{3,6}

Given its aggressive clinical course and poor prognosis when untreated, early recognition and prompt diagnosis are crucial.^{2,7} However, in routine otorhinolaryngology practice, ENKTL remains a diagnostic challenge due to its overlapping presentation with more common sinonasal diseases.

In this case series, we present four patients with destructive sinonasal lesions suspicious for ENKTL. Through these cases, we aim to highlight key clinical features, radiological and pathological findings, as well as common diagnostic pitfalls, emphasizing the importance of maintaining a high index of suspicion to facilitate timely diagnosis and appropriate management.

CASE PRESENTATION

Case 1.

A middle-aged man, A 53-year-old man presented with recurrent epistaxis following a severe coughing episode, accompanied by hematemesis of approximately 1 liter of dark-red blood. The symptoms were intermittent over 12 hours prior to admission. He also reported generalized weakness, unintentional weight loss of 3 kg over two months. The patient had previously been scheduled for a nasal biopsy due to suspected granulomatosis with polyangiitis. On examination, he was hemodynamically stable and afebrile. Nasal endoscopic examination revealed extensive necrotic tissue and crusting within the nasal cavity. The mucosa appeared largely destroyed, foul-smelling, and extremely friable, with a tendency to bleed easily upon contact. A whitish plaque measuring approximately 4 × 3 cm was noted involving both the soft and hard palate (figure 1), suggestive of a destructive midline process.

Laboratory evaluation demonstrated significant anemia and mild thrombocytopenia, while chest radiography was unremarkable. The patient was managed with anterior nasal packing, antifibrinolytic therapy, and blood transfusion. Subsequently, an endoscopic sinonasal biopsy was performed under general anesthesia. Histopathological examination of the biopsy specimen favored malignant lymphoma of the nasal cavity. Immunohistochemical analysis demonstrated CD3 positivity, CD20 negativity, and a high Ki-67 proliferation index. These findings were consistent with extranodal NK/T-cell lymphoma, nasal type, involving the nasal cavity.

Case 2.

A 40-year-old man presented with a 3-month history of progressive left-sided nasal obstruction, worsening over the past 2 months, accompanied by greenish foul-smelling nasal discharge, left facial swelling extending to the periorbital region, facial pain, and intermittent fever. He denied weight loss and visual symptoms. Prior treatment with saline nasal irrigation and intranasal corticosteroids provided no improvement. On examination, the patient was hemodynamically stable. Facial asymmetry with left-sided swelling and a fixed cervical mass (10 × 10 × 5 cm) at levels II–III were noted. Intranasal examination revealed purulent secretions, crusting, and septal perforation bilaterally, while oropharyngeal findings were unremarkable. (Figure 2) Nasal endoscopy showed mucopurulent secretions, crusting, and septal perforation with inflamed mucosa. Laboratory evaluation demonstrated mild anemia, thrombocytopenia, and hyponatremia. Imaging revealed left frontal and maxillary sinusitis without thoracic involvement. Given the progressive destructive features and cervical mass, a malignant process was suspected. Endoscopic excision and biopsy were performed. Histopathology suggested non-Hodgkin lymphoma, and immunohistochemistry demonstrated CD3 positivity, CD56 and granzyme expression, a high Ki-67 index, and negative CD20, consistent with extranodal NK/T-cell lymphoma, nasal type.

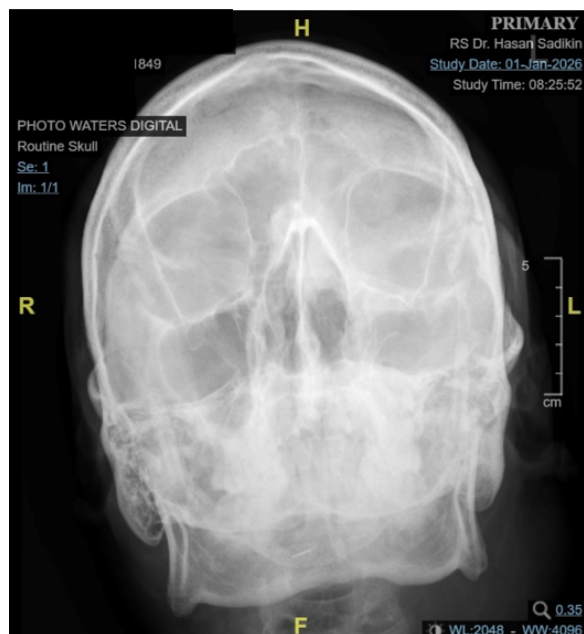


Figure 1. Waters photograph demonstrating marked left-sided facial swelling with asymmetry and periorbital involvement, suggestive of locally invasive sinonasal disease with soft tissue extension.

Case 3.

A 30-year-old woman presented with a 2-month history of right-sided nasal obstruction and a progressively enlarging nasal lesion, initially appearing as a small wound. Over the preceding 3 weeks, she developed greenish foul-smelling purulent nasal discharge, black crusting over the right nasal ala, and progressive facial swelling extending to the periorbital region, accompanied by anosmia. She had previously been hospitalized and referred with a suspected diagnosis of granulomatosis with polyangiitis. On examination, she was hemodynamically stable. Facial asymmetry with periorbital edema and black crusting over the right nasal ala was noted. Intranasal examination revealed purulent secretions in both nasal cavities without cervical lymphadenopathy or cranial nerve deficits. (Figure 3) Nasal endoscopy showed extensive purulent secretions limiting evaluation. Computed tomography demonstrated an aggressive sinonasal mass with bony destruction and extension toward the medial orbital wall. Given the destructive features, a malignant process was suspected. The patient underwent surgical excision and biopsy. Histopathology suggested non-Hodgkin lymphoma, and immunohistochemistry demonstrated CD3 positivity, CD56 and granzyme expression, focal CD30 positivity, CD20 negativity, and a high Ki-67 index (>60%), consistent with extranodal NK/T-cell lymphoma, nasal type, with extensive necrosis clinically correlating with angioinvasive disease.

Figure 2. Axial (left), and Sagittal (right) CT images of the paranasal sinuses demonstrate an ill-defined, heterogeneous soft tissue mass centered in the nasal cavity with extension into the ipsilateral maxillary sinus. The lesion shows areas suggestive of necrosis and causes destruction of the lateral nasal wall and maxillary sinus walls. There is extension to the medial orbital wall with erosion of the lamina papyracea, indicating early orbital involvement. Associated infiltration of adjacent facial soft tissues is also observed, consistent with an aggressive, locally invasive sinonasal process.

Case 4.

A 17-year-old female presented with a 2-month history of right-sided nasal obstruction, initially associated with a small lesion on the right nasal region that progressively enlarged over one month. Over the preceding 3 weeks, she developed profuse foul-smelling purulent nasal discharge, black discoloration over the nasal bridge, fever, and progressive swelling of the right periorbital region extending to the contralateral side. On examination, the patient was hemodynamically stable. Facial examination revealed right preseptal orbital cellulitis with inflammatory changes over the nasal region. Intranasal examination demonstrated mucopurulent secretions, while no significant cervical lymphadenopathy was noted. (Figure 4) Laboratory investigations showed anemia, hypoalbuminemia, hypokalemia, and elevated inflammatory markers, while chest radiography excluded thoracic pathology. Given the progressive destructive sinonasal features with orbital involvement, a malignant process was suspected. The patient underwent surgical extirpation of a right sinonasal mass. Histopathological evaluation suggested malignant lymphoma involving the inferior turbinate and nasal septum. Immunohistochemical analysis demonstrated CD45 positivity with negative CD3 and CD20 expression, and a high Ki-67 proliferation index (>70%), consistent with a high-grade lymphoma of probable T-cell lineage.

DISCUSSION

This case series highlights the significant diagnostic challenges posed by extranodal natural killer/T-cell lymphoma, nasal type (ENKTL), in routine otorhinolaryngology practice. Across all four cases, patients presented with progressive destructive sinonasal disease characterized by nasal obstruction, foul-smelling discharge, crusting, and extensive tissue necrosis. Advanced manifestations, including septal perforation, palatal involvement, facial swelling, cervical lymphadenopathy, and orbital extension, were observed, underscoring the aggressive and locally invasive nature of ENKTL.^{1,2}

ENKTL should be considered within the spectrum of midline destructive lesions (MDL), a group of

disorders characterized by progressive destruction of nasal and midfacial structures. This spectrum includes granulomatosis with polyangiitis (GPA), invasive fungal infections, chronic bacterial infections, cocaine-induced midline destruction, and malignancies such as lymphoma. Differentiating ENKTL from other MDL entities is crucial, as management strategies and prognosis differ substantially.^{3,4} In our series, at least two patients were initially suspected to have GPA, illustrating the substantial clinical overlap and the potential for misdiagnosis.^{2,5,10}

The distinction from GPA is particularly nuanced. Both conditions can present with nasal crusting, epistaxis, septal perforation, and progressive tissue destruction. However, ENKTL typically follows a more rapidly progressive course, with prominent necrosis and a foul odor due to tumor-associated angioinvasion and ischemia. In contrast, GPA is a systemic vasculitis often associated with pulmonary and renal involvement, with positive antineutrophil cytoplasmic antibody (ANCA) serology. The absence of systemic vasculitic features and a lack of response to immunosuppressive therapy should strongly raise suspicion for ENKTL.

Similarly, distinguishing ENKTL from invasive fungal sinusitis (IFS) is critical, as both can present with the "black turbinate sign" on imaging—a finding historically considered classic for IFS but now recognized as a nonspecific sign of tissue necrosis from any cause, including ENKTL. A case report by Kawaji-Kanayama et al. (2020) highlighted a patient initially suspected of having ENKTL based on clinical and imaging findings, who was ultimately diagnosed with chronic IFS, demonstrating the complex two-way diagnostic dilemma. Key differentiating factors include the lack of response to antifungal therapy, the absence of immunocompromising conditions (though not absolute), and the specific immunohistochemical findings of lymphoma.

The distinction between ENKTL and GPA is particularly challenging. Both conditions may present with nasal crusting, epistaxis, septal perforation, and progressive tissue destruction. However, ENKTL typically demonstrates a more aggressive and rapidly progressive course, with prominent necrosis and foul odor due to tumor-associated tissue ischemia. In contrast, GPA is a systemic vasculitis often associated with pulmonary and renal involvement, along with positive antineutrophil cytoplasmic antibody (ANCA) serology. The absence of systemic vasculitic features and lack of response to immunosuppressive or conventional therapies should raise suspicion for an alternative diagnosis such as ENKTL.

Infectious etiologies further complicate the diagnostic landscape. Several patients in this series presented

with purulent discharge, fever, and facial swelling—features commonly attributed to bacterial or fungal infections. The presence of black crusting or necrotic tissue may also mimic invasive fungal sinusitis, particularly in immunocompromised individuals. Consequently, patients are frequently treated with repeated courses of antibiotics or antifungal agents without clinical improvement, contributing to delayed diagnosis.^{4,6} A key distinguishing feature of ENKTL is the persistence and progression of destructive lesions despite appropriate antimicrobial therapy.⁶

A major diagnostic pitfall in ENKTL is the high likelihood of nondiagnostic biopsy results. The angiocentric and angiodestructive growth pattern of ENKTL leads to vascular occlusion, ischemia, and extensive tissue necrosis. As a result, biopsy specimens obtained from central necrotic areas may contain only inflammatory debris and fail to demonstrate malignant cells.^{2,5} This challenge was evident in our cases, where definitive diagnosis required adequate sampling and, in some instances, repeated biopsies. Targeting viable tissue at the periphery of necrotic lesions is essential to improve diagnostic yield.^{5,7}

Targeting viable tissue at the periphery of necrotic lesions is essential to improve diagnostic yield. In cases where surgical biopsy is inconclusive, repeated sampling or fine-needle aspiration from accessible sites like cervical lymph nodes, as highlighted by Kaur et al., should be considered

Histopathological and immunohistochemical evaluation remains the cornerstone of diagnosis. ENKTL typically demonstrates positivity for cytoplasmic CD3, CD56, and cytotoxic molecules such as granzyme B, along with a high proliferative index (Ki-67). Negative CD20 staining helps exclude B-cell lymphoma. Importantly, Epstein-Barr virus (EBV) plays a central role in the pathogenesis of ENKTL, and tumor cells characteristically show EBV-encoded RNA (EBER) positivity on in situ hybridization. Detection of EBV is not only diagnostically supportive but may also carry prognostic significance. In our series, although not all cases had complete immunophenotypic or EBV evaluation due to practical limitations, the overall findings were consistent with ENKTL or high-grade T/NK-cell lymphoma.^{2,7}

Radiological imaging provides valuable information regarding disease extent and local invasion. In our patients, computed tomography revealed aggressive sinonasal masses with bony destruction and extension to adjacent structures, including the orbit. These findings reflect the infiltrative nature of ENKTL and are important for staging and treatment planning. However, imaging alone is insufficient for definitive

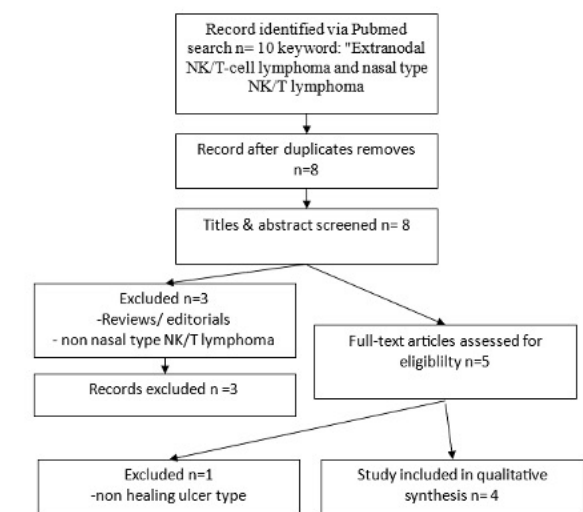
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diagnosis, as similar features may be seen in other malignant or infectious conditions.⁹

From a clinical standpoint, several “red flag” features should prompt suspicion for ENKTL. These include persistent or progressive nasal obstruction unresponsive to standard therapy, foul-smelling discharge, black crusting, recurrent epistaxis, and evidence of midline tissue destruction. The presence of facial swelling, orbital involvement, or cervical lymphadenopathy further suggests advanced disease. Constitutional symptoms such as weight loss, as observed in one of our patients, should heighten concern for malignancy.^{1,3}

The clinical photographs in our series (Figures 1–5) illustrate the spectrum of midfacial destruction, necrosis, and soft tissue involvement characteristic of ENKTL. These visual findings are important, as early-stage disease may initially appear subtle and be easily misinterpreted as benign inflammatory conditions.

Early recognition is critical, as ENKTL is an aggressive malignancy with poor prognosis if diagnosis and treatment are delayed.^{1,2,8} Current management strategies typically involve combined chemoradiotherapy, often incorporating L-asparaginase-based regimens, which have demonstrated improved outcomes compared to conventional chemotherapy. Therefore, timely diagnosis directly impacts therapeutic options and survival outcomes.



Author & Years	Patient	Diagnosis	Report	Follow-up
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Han et al. (2022)	48 year-old woman	Extranodal Nasal NK/Tcell type non-hodgkins lymphoma	highly aggressive and prone to recurrence and metastasis.	
Stefanescu et.al (2017)	47 year old Woman	Extranodal NK/T-cell lymphoma, nasal type with cutaneous involvement	extranodal NK/T-cell lymphoma, nasal type with secondary cutaneous involvement. The patient was in Ann Arbor stage was IVA.	
Kanizai et.al (2025)	32 year-old Male	Extranodal NK/T-Cell Lymphoma, Nasal Type,	Extranodal NK/T-Cell Lymphoma, Nasal Type, with Epstein-Barr involvement	The patient died approximately 11 months after initial presentation due to progressive

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				disseminated disease
Guedes (2017) ⁷	46 year-old male	Nasal-type extranodal T-cell/NK lymphoma in association with hemophagocytic syndrome	revealed an infiltrate with atypical small and medium lymphoid cells in the deep dermis and some large pleomorphic lymphocytes	treatment protocols for NK/T-cell lymphoma are yet not well established, but combinations of radiotherapy and chemotherapy are routinely used, and bone marrow transplant has been investigated

The findings in this case series are in line with several previously reported cases that emphasize the aggressive nature and diagnostic complexity of extranodal NK/T-cell lymphoma, nasal type. A case reported by Han et al. (2022) described a middle-aged woman with ENKTL who initially presented with nonspecific sinonasal symptoms but rapidly progressed to advanced disease with a high risk of recurrence and metastasis. This parallels our cases, in which early symptoms were deceptively mild yet evolved into destructive lesions with local invasion, reinforcing the importance of early clinical suspicion.

Similarly, Stefanescu et al. (2017) reported a case of ENKTL with secondary cutaneous involvement at an advanced stage (Ann Arbor stage IVA), highlighting the potential for systemic dissemination. Although cutaneous involvement was not observed in our series, the presence of cervical lymphadenopathy in one patient and orbital extension in others reflects a comparable pattern of aggressive local and regional spread. These findings suggest that ENKTL should not be regarded as a purely localized disease, even when initial presentation appears confined to the sinonasal region.

A more concerning clinical course was illustrated in the report by Kanizai et al. (2025), where a patient with EBV-associated ENKTL experienced rapid disease progression and succumbed within 11 months of diagnosis. This underscores the well-established association between EBV and ENKTL pathogenesis, as well as the disease's poor prognosis when diagnosis and treatment are delayed. In our series, although EBV status was not available in all cases, the clinical behavior—marked by rapid progression, necrosis, and tissue destruction—strongly supports the typical biological aggressiveness described in EBV-driven disease.

Furthermore, Guedes et al. (2017) described a case of ENKTL associated with hemophagocytic syndrome, illustrating the potential for severe systemic complications. While none of our patients developed hemophagocytic syndrome, one case demonstrated significant hematologic abnormalities, including anemia and thrombocytopenia, which may reflect early systemic involvement or disease burden. This highlights the need for comprehensive systemic evaluation in patients with suspected ENKTL, even when initial symptoms appear localized.

Taken together, these reports consistently demonstrate that ENKTL often presents with nonspecific sinonasal complaints but rapidly progresses to a destructive and potentially disseminated disease. The overlap with inflammatory, infectious, and autoimmune conditions frequently leads to misdiagnosis and delayed treatment, as also observed in our cases. Importantly, across both our series and the reviewed literature, several recurring clinical “red flags” emerge: persistent nasal obstruction unresponsive to therapy, foul-smelling discharge, black necrotic crusting, midline tissue destruction, and early extension to adjacent structures.

In this context, our case series reinforces the critical role of early biopsy and adequate tissue sampling. As highlighted both in our experience and in prior studies, superficial or necrotic tissue samples may yield nondiagnostic results, necessitating repeated biopsies targeting viable tissue. This principle is consistently

emphasized in the literature as a key factor in reducing diagnostic delay.

CONCLUSION

In conclusion, ENKTL remains a challenging diagnosis due to its nonspecific presentation and significant overlap with inflammatory, infectious, and autoimmune conditions. A high index of suspicion is essential in patients presenting with refractory sinonasal symptoms accompanied by tissue necrosis, black crusting, or progressive midfacial destruction. Early and adequate biopsy, with careful targeting of viable tissue and repeated sampling when necessary, is critical to avoid false-negative results. Comprehensive immunohistochemical analysis, supported by EBV evaluation, plays a pivotal role in confirming the diagnosis.

REFERENCES

1. Tse E, Kwong YL. The diagnosis and management of NK/T-cell lymphomas. *Best Pract Res Clin Haematol*. 2017;30(1–2):34–43.
2. Au WY, Weisenburger DD, Intragumtornchai T, et al. Clinical differences between nasal and extranasal NK/T-cell lymphoma: a study of 136 cases. *Blood*. 2009;113(17):3931–3937.
3. Suzuki R. NK/T-cell lymphoma: updates in biology and management. *Hematology Am Soc Hematol Educ Program*. 2018;2018(1):513–521.
4. Kim SJ, Kim K, Kim BS, et al. Clinical characteristics of extranodal NK/T-cell lymphoma. *Ann Oncol*. 2009;20(6):1032–1039.
5. Chan JKC, Quintanilla-Martinez L, Ferry JA, et al. Extranodal NK/T-cell lymphoma, nasal type. In: Swerdlow SH, Campo E, Harris NL, et al., editors. *WHO Classification of Tumours of Haematopoietic and Lymphoid*

As a case series, this study has inherent limitations, including a small sample size and lack of a control group. Furthermore, long-term follow-up and complete EBV data were not available for all patients. However, the strength of this report lies in its detailed clinical phenotyping and its practical relevance to clinicians facing this diagnostic challenge.

This case series underscores the importance of recognizing key clinical “red flags” and considering ENKTL within the spectrum of midline destructive lesions. Prompt diagnosis is crucial, as delayed recognition may lead to advanced disease with poorer prognosis. Early multidisciplinary involvement and timely initiation of appropriate oncologic management are essential to improve patient outcomes

- Tissues. Revised 4th ed. Lyon: IARC; 2017. p. 368–371.
6. Jaffe ES. Pathobiology of NK/T-cell lymphomas. *Blood*. 2016;127(20):2376–2384.
7. Yamaguchi M, Suzuki R, Oguchi M. Advances in treatment of extranodal NK/T-cell lymphoma. *Cancer Sci*. 2018;109(6):1509–1515.
8. Li YX, Yao B, Jin J, et al. Radiotherapy as primary treatment for stage I/II nasal NK/T-cell lymphoma. *J Clin Oncol*. 2006;24(1):181–189.
9. King AD, Lei KI, Ahuja AT, et al. MR imaging of nasal T-cell/natural killer cell lymphoma. *AJNR Am J Neuroradiol*. 2000;21(7):1336–1342.
10. Young LS, Rickinson AB. Epstein–Barr virus: 40 years on. *Nat Rev Cancer*. 2004;4(10):757–768.
11. Kawaji-Kanayama Y, et al. Chronic Invasive Fungal Rhinosinusitis with Atypical Clinical Presentation in an Immunocompromised Patient. *Infect Drug Resist*. 2020;13:3225–3232