Bikash Gurung,[1] Urmila Gurung,[2] Nar Maya Thapa,[2] Bibhu Pradhan,[2] Anjan Shrestha,[3] Shreya Shrivastav,[4]

[1]Department of ENT Head & Neck Studies, Pokhara Academy of Health Sciences, Pokhara, Nepal

[2]Department of ENT Head & Neck Studies, Tribhuvan University Teaching Hospital, Institute of Medicine, Maharajgunj, Kathmandu, Nepal.

[3]Department of Medicine, Tribhuvan University Teaching Hospital, Institute of Medicine, Maharajgunj, Kathmandu, Nepal

[4]Department of Pathology, Tribhuvan University Teaching Hospital, Institute of Medicine, Maharajgunj, Kathmandu, Nepal

Corresponding author

Dr. Bikash Gurung, Department of ENT Head & Neck Studies , Pokhara Academy of Health Sciences, Pokhara, Nepal

Email:b4bkas@gmail.com
Phone: +977-9816136342

ORCID ID: 0000-0002-2850-0985

EXTRANODAL NATURAL KILLER / T-CELL LYMPHOMA PRESENTING WITH RECURRENT NASAL VESTIBULITIS: A CASE REPORT

ABSTRACT

Extranodal NK/T-cell lymphoma, nasal type is a rare lymphoid neoplasm, which is aggressive non-Hodgkin's type, grouped with a variety of granulomatous diseases in the past. It commonly involves the sinonasal tract leading to destruction of the midline structures of face. Its histological diagnosis can be difficult because of extensive tissue necrosis and has an ominous prognosis.This case report is of a middle-aged woman who presented with recurrent right nasal vestibulitis, mimicking as nasal granulomatosis. Immunohistochemistry confirmed that it was ENKL of nasal cavity. She attained complete remission with L-asparaginase, vincristine, prednisolone regimen with sandwiched radiotherapy. The vague presentation is one of the causes of delayed diagnosis for this type of condition. Radiological imaging along with histopathological examination with immunohistochemistry is essential for early diagnosis.

Keywords: Extra-nodal NK/T-cell lymphoma, Epstein-Barr virus, LVP regimen, recurrent nasal vestibulitis

INTRODUCTION

Extranodal NK/T-cell lymphoma (ENKL), nasal type mostly originates from NK cells but a small proportion originate from cytotoxic T cells. ENKL usually occurs in adult men and is more common in Asian and Latin American countries. [1]

The nasal cavity, oro-nasopharynx and other parts of upper aerodigestive tract are the most frequently affected sites. However, there have been reports of non-nasal involvement in skin, eyes, testes, gastrointestinal tract, salivary glands and muscles. It has poor prognosis and current treatment regimens combine chemotherapy with radiation for localized disease or chemotherapy alone for more advanced disease.[2]

This case report is of a middle-aged woman from Nepal with ENKL masquerading as recurrent right nasal vestibulitis.

CASE REPORT

A female aged 38 presented to our institute, with recurrent right nasal vestibulitis. She was conservatively managed five times with antibiotics and one time with incision and drainage within a span of 4 months elsewhere before presenting to our facility. In our center, she was admitted for intravenous antibiotics and underwent incision and drainage. She developed right nasal stenosis after discharge. The CT scan of nose and PNS showed soft tissue density in right nasal cavity causing right vestibular stenosis for which vestibuloplasty was done. Three months after vestibuloplasty, she had to be admitted again for fever with right nasal pain and received conservative treatment. She presented further again with recurrence of similar symptoms.

On examination, her general condition was fair without pallor and lymphadenopathy. Her vitals were stable and BMI was 19.11kg/m2. However, her right alar groove was obliterated, right-nares was swollen, erythematous and was narrow (Figure 1). Septum was deviated to left with tender and stenosed right nasal vestibule. Furthermore, a bulge from roof & lateral wall of nasal cavity extending to choana with exposed bone & crusts was visible in flexible Nasoendososcopic examination. Provisional diagnosis of right nasal cavity granulomatous disease was made.

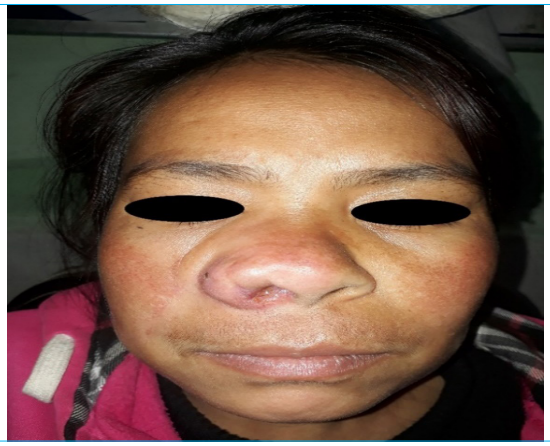

Figure 1: Erythematous, swollen right nostril with stenosis

On admission, the total leukocyte count and hemoglobin level were 3,480/µL and 11 g/dL, respectively, and remained persistently mildly reduced throughout the hospital stay. The erythrocyte sedimentation rate (ESR) was 26 mm/hour on admission and did not normalize during hospitalization, remaining around 24 mm/hour. Acid-fast bacilli (AFB), Gram, and fungal stains performed on the swab specimen were negative.

Peripheral blood smear, bone marrow study, liver function tests, uric acid level, ultrasonography of abdomen & pelvis and chest x-ray findings were normal.

Mantoux test, and tests for RA factor, ANA, dsDNA, HBsAg, HCV & HIV were all negative. Her serum LDH was 559 U/L which was high persistently.

MRI of the nose and paranasal sinuses revealed a contrast-enhancing lesion with intermediate signal intensity on T1-weighted images (Figure 2) and iso- to low-signal intensity on T2/STIR sequences, suggestive of a neoplastic pathology.

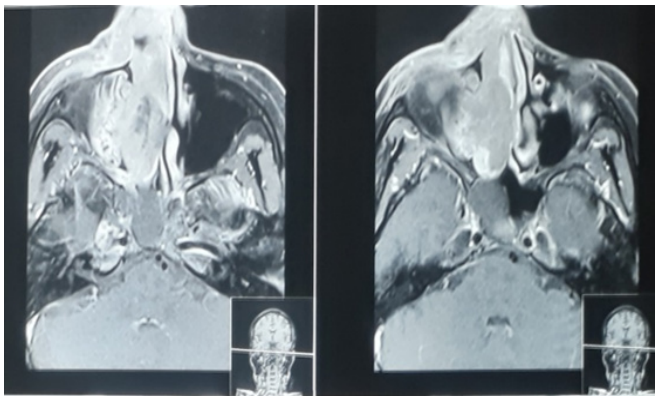

Figure 2: Post-contrast T1-weighted MRI of the nose and paranasal sinuses showing homogenously enhancing mucosal thickening in the right nasal cavity extending from the choana to the nares, with erosion of the turbinates and medial wall.

Histopathological examination of punch biopsy from right nasal vestibule revealed multiple fragments with predominant necrosis and few tiny fragments with sheets of atypical appearing cells & occasional mitoses. However, stains for AFB & PAS were negative.

Immunohistochemistry of the biopsy was suggestive of EBV associated ENKL (Figure 3)

CT scan neck, chest and abdomen showed no significant lymphadenopathy. Stage I ($T_1N_0M_0$) EBV associated Extranodal NK/Tcell lymphoma, nasal type was diagnosed. She underwent 6 cycles of LVP (L-Asparaginase, Vincristine, and Prednisolone) with sandwiched radiotherapy. She attained remission (Fig. 4) after the completion of chemoradiotherapy. Her repeat CT scan of Nose and PNS (Figure 5) done after 6th cycle of chemotherapy showed absence of residual disease.

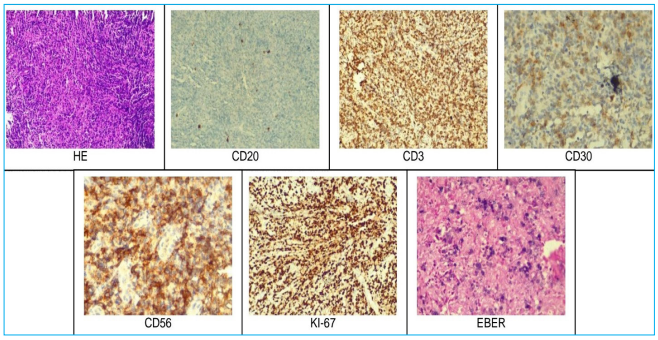

Figure 3. Immunohistochemisty showing immunoreactivity of the lesional cells; 76-100% cells for CD3, CD45RO & CD4, 70-80 % cells for KI-67, 51-75% cells for CD56, CD30 and EBER-ISH, 26-50% cells for CD8.

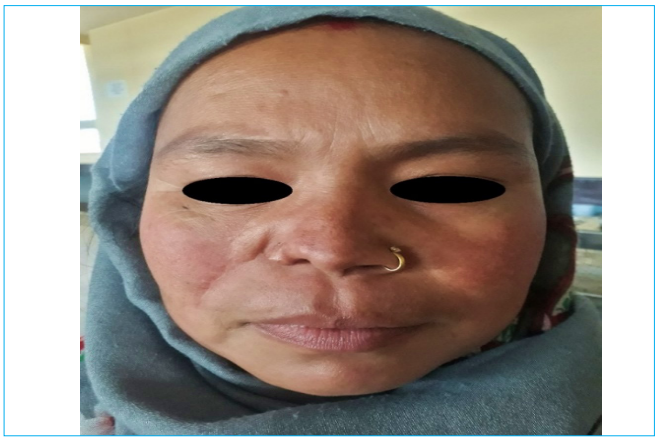

Figure 4: Improvement in right nasal vestibular swelling and stenosis after completion of chemoradiotherapy

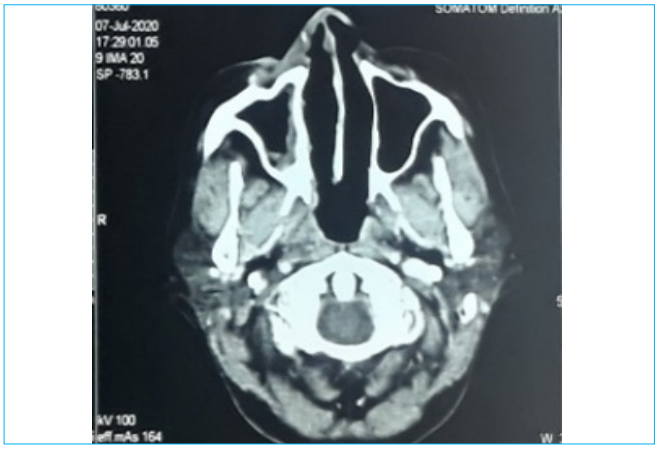

Figure 5: Contrast enhanced CT nose and PNS after completion of chemoradiotherapy

DISCUSSION

Extranodal natural killer (NK)/T-cell lymphoma, nasal type consists of 3-10% of non- Hodgkin lymphoma in Asia and South America, whereas its prevalence is less than 1% in western countries.[1] The male to female ratio of ENKL is 3:1 with a mean age of onset of 52 years.[3] The malignant lymphocytes in ENKL, the NK or cytotoxic T cells almost always harbor Epstein-Barr virus (EBV) which is believed to be the driver of malignant transformation.[4]

Initially found as progressive ulceration and necrotic granuloma in the nasal cavity, palate, and nasopharynx, the tumor frequently invades surrounding tissues and develops extensive destructive midline lesions. The most common symptoms are nasal obstruction and bloody rhinorrhea. Sometimes swelling of cheek or orbit, sore throat, hoarseness and type "B" symptoms may also be seen.[1] ENKL has overall 5 years survival rate of 40-50 %.[5] Non-nasal variant has presentations related to respective sites. It can be disseminated, rarely, with infiltrations in liver, spleen, skin, lymph nodes, and bone marrow leading to NK/T-cell lymphoma/leukemia. Such patients present with fever, lymphadenopathy, rashes, hepatosplenomegaly, hyperferritinaemia, pancytopenia and hemophagocytosis.[6]

Nasal endoscopic evaluation is an initial step of assessment. Large and adequate biopsies should be taken if there is any suspicion of a destructive pathology to distinguish ENKL from other destructive etiologies.[7] About 45% of patients present with elevated levels of serum lactate dehydrogenase.[8]

The CT and MRI appearances of ENKL are nonspecific and can be seen as diffuse mucosal thickening along the nasal turbinates or as a destructive midline mass difficult to distinguish from fungal infection, Wegener's granulomatosis, or other neoplasms.[9,10] It can be homogeneous in both CT and MRI with slight enhancement.[11]

Histologically, ENKL shows angiocentric pattern of growth with vascular destruction and necrosis. Tumor cells may be small to large and are dispersed among plasma cells, lymphocytes, eosinophils, and histiocytes. Immunohistochemistry stains demonstrate the presence of T and NK cell markers (CD2, CD56, CD3), along with cytotoxic molecules, such as granzyme B, TIA-1, and perforin. The case reported was positive for CD56, CD3, CD45RO & CD4, CD56, CD30 and CD8 with expression of EBV RNA by in situ hybridization.[7]

Combined chemoradiotherapy is standard of treatment of localized early stage ENKL. Traditional anthracycline-containing chemotherapies, such as cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP regimen) has shown insufficient therapeutic outcomes. Recently, L-asparaginase based regimen is developed in prospective clinical trials.[3]

A phase 2 study of 26 patients with stage I/II nasal lymphoma treated with LVP regimen (L-asparaginase, vincristine, and prednisolone) for 6 courses with sandwiched radiotherapy after 2 courses showed that the protocol was a safe and effective for treatment of localized ENKL.[12] We also used the same regimen to treat the patient.

CONCLUSION

To summarize, vague presentation like this i.e. recurrent nasal vestibulitis is one of the causes of delayed diagnosis. Radiological imaging strengthened with adequate histopathological examination of the tissue along with immunohistochemistry is essential to reach the diagnosis early. Combined chemotherapy-radiotherapy is effective at an early stage.

Conflict of interest: The authors declare no conflicts of interest.

REFERENCES

1. Harabuchi Y, Takahara M, Kishibe K, Nagato T, Kumai T. Extranodal natural killer/T-cell lymphoma, nasal type: basic science and clinical progress. Front Pediatr. 2019;7:141. Available from: https://www.frontiersin.org/articles/10.3389/fped.2019.00141/full
2. Tse E, Kwong YL. How I treat NK/T-cell lymphomas. Blood. 2013;121(25):4997-5005.
3. Liang R. Advances in the management and monitoring of extranodal NK/T-cell lymphoma, nasal type. Br J Haematol. 2009;147(1):13-21.
4. Shannon-Lowe C, Rickinson AB, Bell AI. Epstein-Barr virus-associated lymphoid proliferations, a 2018 update. Pathology. 2018;50(1):37-63.
5. Su YJ, Wang PN, Chang H, Shih LY, Lin TL, Kuo MC, et al. Extranodal NK/T-cell lymphoma, nasal type: clinical features, outcome, and prognostic factors in 101 cases. Eur J Haematol. 2018;101(3):379-88.
6. Tse E, Kwong YL. The diagnosis and management of NK/T-cell lymphomas. J Hematol Oncol. 2017;10(1):85.
7. Tuşaliu M, Zainea V, Mogoantă CA, Dragu AA, Goanță CM, Nițescu M, et al. Diagnostic and therapeutic aspects in malignant sinonasal lymphoma. Rom J Morphol Embryol. 2016;57(1):233-6.
8. Yamaguchi M, Miyazaki K. Current treatment approaches for NK/T-cell lymphoma. J Clin Exp Hematop. 2017;57(3):98-108.
9. Ou CH, Chen CCC, Ling JC, Chai JW, Wu CH, Chen WH, et al. Nasal NK/T-cell lymphoma: computed tomography and magnetic resonance imaging findings. J Chin Med Assoc. 2007;70(5):207-12.
10. Vasan S, Rajalakshmi P, Thulkar S. Imaging case: NK/T-cell lymphoma, nasal type. Iran J Otorhinolaryngol. 2015;27(83):481.
11. Guan P, Chen Z, Chu L, Zhen L, Zhang L, Pan L, et al. Extranodal NK/T-cell lymphoma in adolescents: imaging findings of a consecutive 7-year case series. J Int Med Res. 2019;47(3):1210-20.
12. Jiang M, Zhang H, Jiang Y, Yang Q, Xie L, Liu W, et al. Phase 2 trial of "sandwich" L-asparaginase, vincristine, and prednisone chemotherapy with radiotherapy in newly diagnosed, stage IE to IIE, nasal type, extranodal natural killer/T-cell lymphoma. Cancer. 2012;118(13):3294-301.