Case Report

NHL - Extranodal T-cell lymphoma

Seema Devi, Richi Sinha[1], Rakesh Kumar Singh[1], Gagan Mehta[2]

Departments of Radiation Oncology and [1]Otolaryngology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, [2]Department of Dental Sciences, King George's Medical University, Lucknow, Uttar Pradesh, India

Address for correspondence:
Dr. Seema Devi,
Department of Radiation Oncology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.
E-mail: doctorseema71@gmail.com

ABSTRACT

Extranodal NK/T-cell lymphoma, nasal type (ENKL) is a rare lymphoid neoplasm that in the past has been grouped with a variety of granulomatous diseases. ENKL occurs in all age groups. However, it seems to occur more often in people in their 50s and affects more men than women. It is strongly linked to the Epstein-Barr virus (EBV), especially in people of Asian countries. Because this type of lymphoma occurs in organs or tissues other than lymph nodes, it is called ENKL. This is a case report of a 25-year-old female patient who presented with a nonhealing ulcer at the right nasal ala involving the upper lip and cheek for the last 2 months, which had been treated with antitubercular treatment without success. After biopsy and immunohistochemical (IHC) analysis, the patient had been diagnosed a case of extranodal T-cell lymphoma.

Key words: Extranodal, lymphoma, nasal

Introduction

Lymphoma is the most common among blood cancers. The two main forms of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of a type of lymphocyte (the cells of the immune system are called lymphocytes) travel to many parts of the body, including the lymph nodes, spleen, and bone marrow, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).[1]

Lymphocytes account for 3-5% of all malignant tumors. NHLs account for 60% of all lymphomas; involvement of the nasal cavity and paranasal sinuses by these tumors is uncommon.[2]

Extranodal NK/T-cell lymphomas, nasal type (ENKLs) are aggressive, locally destructive, midfacial necrotizing lesions characterized by extranodal involvement, particularly the nasal/paranasal area, and represent about 75% of all nasal lymphomas, the rest being B-cell lymphomas.[3,4] The lesion typically causes local destruction of cartilage, bone, and soft tissues.[5] Incidence of ENKL varies considerably in different parts of the world, but it remains a rare disease since its first description in 1933. However, the number of new, diagnosed cases per year is on the increase, due to improved knowledge of this disease.[6]

ENKL is a rare type of NHL. This type of lymphoma was previously called angiocentric lymphoma. It is more common in Asian and Central and South American countries than it is in North America. ENKL can develop in either T cells or natural killer (NK) cells, which attack foreign cells. Sometimes it is difficult to tell which cells—T cells or NK cells—are present.[7]

ENKLs are subcategorized into nasal and nasal-type NK/T-cell lymphomas according to the major site of anatomic involvement. In limited cases, NK/T-cell lymphomas may predominantly occur in extranasal sites without involvement of the nasal cavity or nasopharynx.[6]

Advances in tumor cell biology have led to the ability to subclassify NHLs using the World Health Organization (WHO) classification of lymphoma.[6] The terminology becomes more precise as our ability to genetically characterize these tumors improves.[8]

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Controversy still exists regarding the normal counterpart of NK cell lymphoma: Whether NK cell lymphoma represents the presence of a true NK cell or merely the presence of a T cell with abnormal cell markers is under debate. In the absence of unequivocal proof of the exact lineage of NK cell lymphoma, many investigators prefer to use the term NK/T-cell lymphoma when classifying this condition. Further understanding of its development and the identification of more specific cell markers of NK and T cells will likely resolve this controversy in the future.[9]

The nasal and nasal-type NK/T-cell lymphomas have distinct presentations and prognoses, and they are believed to have different pathogeneses.

Compared with nodal lymphomas, sinonasal tract lymphomas are difficult to identify correctly because of the biopsy size. Nasal NK/T-cell lymphomas are typically seen in the nasal and paranasal sinus areas and are associated with Epstein-Barr virus (EBV) infection.[10] The patients often experience localized stage I/II disease but an aggressive clinical course. Radiotherapy alone has been used for the treatment of limited-stage extranodal T-cell lymphoma, but the 5-year overall survival rate is approximately 50%. Recently, several groups have treated patients with irradiation of more than 40-50 Gy followed by courses of chemotherapy, and the reported overall 5-year survival rate of this procedure reached 70%.[11]

Case Report

A 25-year old illiterate female patient presented at the Ear, Nose, and Throat (ENT) department of the Indira Gandhi Institute of Medical Science (IGIMS), Patna with a complaint of gradually progressive ulcerative lesion on the infra-alar region of the right side of the face over the last 2 months. She had consulted with a local doctor and received 9 months of antitubercular treatment as advised by him/her. The lesion was increasing in size, so she came to IGIMS for a second opinion. On examination, an ulcerative lesion was noted on the upper lip region toward the right side just below the nasal area, 4.5 × 3 cm^2 and edematous margins, with yellowish dry slough on the base of the ulcer. The periculer edema was noted to include the right ala of the nose and right side of the cheek, extending up to the infraorbital region and also involving the lower lid. There was induration in the base region. The nasal cavity and palate were normal. There was no other lesion or lump seen on ENT examination. No other lymph node was palpable in any other part of the body. The chest x-ray, ultrasonography (USG) abdomen, and routine blood investigation were normal.

The biopsy was performed by an ENT surgeon and the tissue was sent for histopathological examination. Microscopic examination showed the features of T-cell lymphoma, and the use of immunohistochemical (IHC) markers was advised. After IHC analysis, CD45 (leukocyte common antigen or LCA) was positive (3+) [Figure 1] and CD3 was positive (1+) [Figure 2]; the impression was of NHL T-cell immunophenotype on examination. Although NK marker studies could not be done, the biological behavior of NK-positive and T-positive nasal extranodal lymphomas is similar, hence they are collectively termed NK/T-cell lymphomas. Thus, based on the clinical picture, histopathology and IHC were used toward the diagnosis of ENKL.

After the histopathology and IHC marker reports, the patient was sent to the oncology department for further treatment. At our department, she received chemotherapy in the form of CHOP regimen [cyclophosphamide 750 mg/m^2, hydroxydaunorubicin or doxorubicin 50 mg/m^2, Oncovin (vincristine) 1.4 mg/m^2, and prednisone 40 mg/m^2] D1-D5, with all premedication cycles to be reported every 21-days regimen. She received six cycles of chemotherapy. She responded well to the chemotherapy and the ulcer has been healed completely, without any major side effects but with residual dry scar tissue.

Discussion

In 1982, Ishii *et al*. first recognized the presence of tumor cells expressing CD3 in this type of lesion and termed this disease "nasal T-cell lymphoma."[12] Diagnosis of these lymphomas is dependent on a series of laboratory studies, particularly cultures, but frequently a biopsy is required to establish a diagnosis.

It is essential that biopsy tissue be of sufficient size and adequate technical quality in order to allow the identification of atypical cells.[13] Even though an angiocentric T-cell lymphoma often does not have the classic histopathological features of a lymphoma microscopically, it behaves in a malignant fashion and responds to the same treatment to which a lymphoma responds.[14]

ENKL is rare in the USA, representing approximately 1.5% of all lymphomas. It is more prevalent among Asians, where it constitutes as much as 3% of NHLs, and among the indigenous peoples of Mexico, Central America, and South America. It occurs more often in adults and more commonly in men than in women.[15]

ENKL is typically observed in adults but may also be seen in children. Studies have shown a male:female

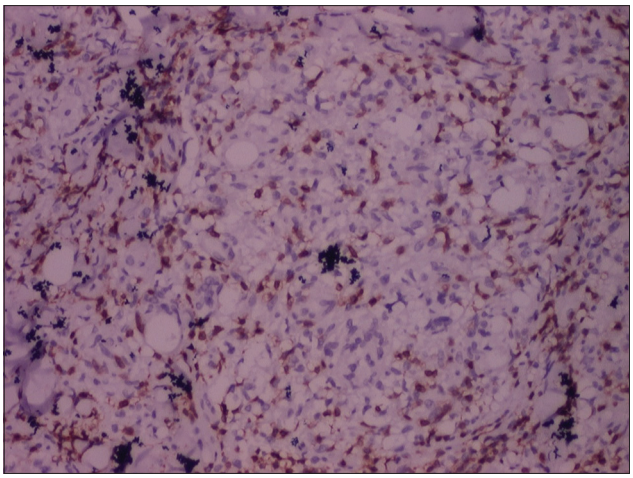

Figure 1: Immunohistochemistry CD45 positive (3+)

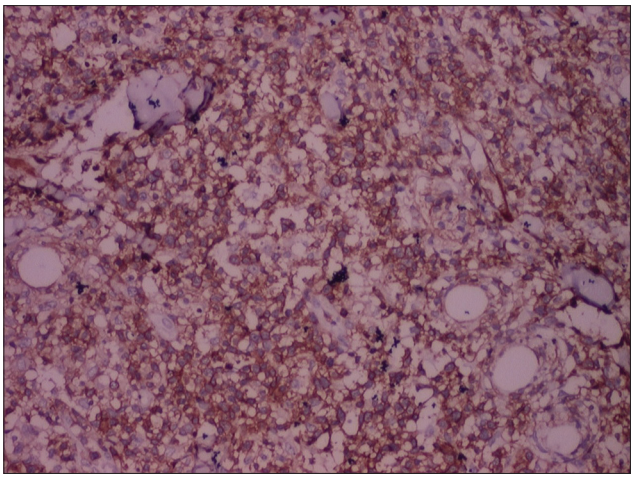

Figure 2: Immunohistochemistry CD3 positive (1+)

ratio of 2:3:1.[4] The clinical course of T-cell lymphoma varies with the clinical stage. Patients with early-stage lymphoma typically experience an indolent course of disease, the tumor being restricted to the original site, but others with the disease in advanced stages suffer rapid progression to systemic dissemination often accompanied by hemophagocytosis or disseminated intravascular coagulation. Extranodal nasal-type T-cell lymphomas demonstrate a predilection for the nasopharynx, palate, skin, soft tissues, orbit, gastrointestinal tract (GIT), and testes; lymphomas that manifest outside of the nose have a strong association with EBV in Asian patients, but this strong association is not present in white patients.[3]

Because this type of lymphoma occurs in organs or tissues other than the lymph nodes, it is called "extranodal." ENKL most commonly affects the nose or nasal passages and paranasal sinuses. It can cause swelling of the face, discharge from nose, nasal bleeding, and nasal blockage.[7]

It is now generally accepted that a large number of biopsies must be performed to confirm the diagnosis of ENKL.[16] The histological features of NK and T-cell lymphomas are similar regardless of the site of the lesion,[17,18] both consisting of sheets of atypical small, medium-sized, large, or giant Sternberg-like cells.

ENKL is often a fast-growing lymphoma. The prognosis for people with this type of lymphoma is often poor and the risk of relapse is high. People with ENKLs confined to the nose or nasal passages have better prognosis than those people with more widespread disease.[7]

Extranodal lymphomas can also affect other organs or tissues besides the nose and may be referred to as the extranasal type. It can affect the skin, testes, soft tissues, kidneys, brain, GIT, and respiratory system.[19]

This entity has also been referred to as lethal midline granuloma, polymorphic reticulosis, angiocentric immunoproliferative lesion, and angiocentric T-cell lymphoma. It is characterized by vascular damage and destruction, prominent necrosis, a cytotoxic phenotype, and an association with EBV.[20]

Nasal NK/T-cell lymphomas in Asians follow an aggressive course, with death occurring due to local relapse or systemic spread in 50% of the cases.[21] Multidrug chemotherapy (CHOP regimen) followed by involved-field radiotherapy appears to be the most effective treatment approach.[19] The delay in presentation and thus delay in diagnosis is possibly one of the reasons our patient appeared at an advanced stage and can be saved only with aggressive chemotherapy.

This case illustrates the unusual presentation of a rare lymphoma that has responded well to chemotherapy, and the patient has been on follow-up for the past 2 years.

Conclusion

Nonhealing ulcer at an unusual site often predates the appearance of mucosal involvement and tissue necrosis by 1 year or more. The ambiguous nature of these symptoms can cause delay in diagnosis. Representative biopsy material and good interaction with the pathologist is required. A diagnosis should be confirmed before commencing a treatment course. In conclusion, the clinician should consider extranodal lymphoma, which is a rare disease and can present with the difficulties of obtaining histological diagnosis, despite apparently adequate biopsies, because of illiteracy and ignorance about the disease, treatment, and prognosis. Usually, the patient presents at an advanced stage of disease and has worse prognosis. This patient presented at an advanced stage of disease.

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