

Extranodular nasal Natural Killer (NK) Cell/T-cell lymphoma: a diagnostic dilemma

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ABSTRACT

Diagnosis and treatment of the nasal type of Natural Killer (NK)/T-Cell Lymphoma can be challenging. NK/T-Cell lymphoma of the nasal type is very aggressive and invasive and may present with non-specific symptoms. This usually leads to delay in diagnosis and initiation of treatment. Lymphomatous lesions show areas of necrosis and hence multiple biopsies are usually needed for histopathological diagnosis with the aid of immunochemistry. We report the case of nasal type NK/T-Cell lymphoma in a middle aged lady who presented with unilateral nasal blockage, constitutional symptoms and soft palate perforating ulcer with delay in diagnosis.

Keywords: Natural Killer cell, T cell, lymphoma, soft palate, ulcer

INTRODUCTION

Nasal-type NK/T-Cell lymphoma also known as lethal midline granuloma is an aggressive type of extranodular lymphoma which causes a rapid destructive lesion in the midline structures of the head and neck region. It is called NK/T-Cell lymphoma as the cell lineage of T and NK cells has a wide range of cytological compositions and immunophenotypes. They share many antigens and their cytogenetic features are not defined. Non-specific clinical symptoms and challenging histopathological features are usually the cause of delay in diagnosis. We report here a case of nasal type of NK cell lymphoma in a middle aged lady.

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CASE REPORT

A 44-year-old female presented with a two-week history of nasal obstruction and blockage of her left ear. Initially, she was treated as sinusitis but her condition worsened over a period of three months. This was associated with intermittent fever, lethargy and bilateral epistaxis. There was also significant loss of appetite and loss of weight where she lost 8kg in a month. During the course of her illness she developed severe non-resolving sore throat and progressive ulcerative lesion over the soft palate. There was no chronic cough or any close contact with tuberculosis patients. There were also no cutaneous lesions or joint pain.

Clinically, she was pale and cachectic. She had multiple bilateral small painless

cervical lymph nodes with the largest measuring 1cm in diameter. Oropharyngeal examination revealed a large perforating ulcer (3 x 4cm) of the soft palate. The margin of the ulcer was necrotic. There were no palpable axillary or inguinal lymph nodes. The rest of the examination (neurological, pulmonary and abdominal) was unremarkable. Otoloscopic examination revealed a left middle ear effusion with normal right otoscopic findings.

Rigid nasoendoscopy revealed crusting at both inferior turbinates. The left lateral wall of the nasopharynx and the left Eustachian tube opening were noted to be covered with necrotic slough while the Fossae of Rosenmuller were not obliterated. Biopsies were taken twice from the left Torus Tubarius and soft palate ulcer. Histological examination only revealed necrotic and acute inflammatory tissue and was negative for fungus, tuberculosis and malignancy. Acid Fast Bacilli smear and culture were also negative. Hence, biopsy under general anaesthesia together with debriement of the soft palate and nasopharynx was done. Biopsies were taken from the nasopharynx and soft palate at the margin of the lesion and the pathologists were alerted regarding the possible diagnosis of lymphoma and the need for special staining.

Blood investigations showed she was anaemic with a haemoglobin level of 9.8 g/L. However, other haematological parameters and differential counts were normal. Blood urea, potassium, creatinine, calcium, lactate dehydrogenase, bilirubin, and transaminase levels were all within normal limits and showed no sign of tumour lysis. The serum EBV DNA was noted to be positive but HIV Antibody Screening (ELISA) was negative.

A computed tomography (CT) scan of the neck showed minimal mucosal changes over the left lateral wall of the nasopharynx and multiple bilateral small (< one cm) cervical lymph nodes at levels I and II. A CT scan of the abdomen and pelvis were normal but CT of the thorax showed three small nodules in the right lung base.

Histopathological examination revealed that the nasopharynx was heavily inflamed with fragments of tissue focally lined with squamous and pseudostratified ciliated columnar epithelium with surrounding necrotic tissue. The infiltrating cells included small lymphocytes, macrophages, plasma cells and polymorphs but there were no granuloma or organisms noted. Immunohistochemical studies revealed atypical small lymphocytes which were positive for CD3, CD56, perforin and TIA-1 but were negative for CD20. Based on these findings, a diagnosis of extranodal NK/T cell lymphoma nasal type was made.

A bone marrow aspiration showed no evidence of marrow infiltration. She was referred to the oncologists and was started on chemotherapy (SMILE protocol). She was given a total of five cycles of SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide) that was followed with two phases of radiotherapy over the nasopharynx and neck (40Gy was given during first phase and 45Gy on second phase). This was followed by an autologous stem cell transplant.

The clinical symptoms resolved and subsequent rigid nasoendoscopic findings revealed a normal looking nasopharyngeal mucosa. The soft palate perforation persisted but



Fig. 1: A perforating soft palate ulcer post debridement and biopsy under general anaesthesia showing clean margin (asterisk indicate nasotracheal tube) .

the margins were clean (Fig. 1) and there were no signs of recurrence. PET scan also showed no recurrence of the disease.

DISCUSSION

According to the World Health Organisation (WHO) classification, lymphomas can be divided into NK/T-Cell lymphomas, B-cell lymphomas and Hodgkin's lymphomas. NK/T-Cell and B cell lymphomas can be stratified into mature (peripheral) and precursor (lymphoblastic lymphoma) cells and then grouped further according to their major clinical presentations. These are predominantly disseminated (leukaemic), predominantly nodal or primarily extranodal neoplasm.¹

NK/T-Cell diseases show a wide variation in immunohistochemical studies and cytological composition. NK/T-Cell share many antigens and most of the antigen specific cytogenetic features are not well defined and definitive classification may not be possible.¹

It is an uncommon disease in the West but more frequently seen in Asia.² It accounted for 9% of all lymphomas in Korea

accounted for 9% of all lymphomas in reported in Korea and 6.2% in Hong Kong. It has a male predominance and the median age of presentation is 47 years old.^{3,4}

Clinically, systemic symptoms include fever, weight loss and loss of appetite. Local nasal symptoms include nasal blockage, rhinorrhoea and epistaxis. It might also involve the palate, orbit, nasopharynx, cutaneous, cervical lymph node and other systems such as the gastrointestinal tract, testis and kidney. Cutaneous lesions such as cutaneous eruptions of purplish and hard nodules may be seen. Orbital swelling, soft palate ulcer and testicular swelling are evidence of extranasal involvement. Diagnosis is difficult as the clinical features are not specific and repeated biopsies are usually necessary.⁵⁻⁷

Histopathologically, it is relatively challenging to diagnose mature NK/T-Cell lymphomas.³ In more than 45% of reported cases, the diagnoses were delayed as two or more biopsies were needed to reach the definite diagnosis.⁸ Even though the biopsies may show an angiocentric and angiodestructive growth pattern with area of zonal necrosis, immunochemistry staining is crucial to making a final diagnosis. NK/T-Cell lymphomas express CD56, CD3 ϵ^+ , CD3 $^-$, and variably CD16 and CD57.⁹ Epstein-Barr-encoded RNA is invariably detected¹⁰ and perforin¹¹ and TIA-1¹², which are specific markers for NK/T-Cells¹¹ may also be found in this disease. T-cell markers include CD2, CD3 and CD7, while NK-cells show negative surface CD3 but positive cytoplasmic CD3 ϵ and CD56.⁹

NK/T-Cell lymphoma of extranodal sites other than the nose has a worse progno-

sis compared to the other types. ⁴ Overall, the 5-year survival rates for NK/T-Cell lymphoma range from 14-87%. ¹⁰ The prognostic factors include the clinical stage at diagnosis, the initial treatment response, performance status, over-expression of Ki-67 (unfavourable) and over-expression of CD95 (favourable). ¹³

Due to the low incidence of this disease, there are currently no prospective studies looking at localised nasal NK/T-Cell lymphomas. Radiotherapy is recommended for localised nasal NK/T-Cell lymphomas and concurrent radiotherapy and chemotherapy in more aggressive lesions. ¹⁰

In conclusion, any ulcerative lesions over the midline structure of nose, nasopharynx and also oropharynx should raise the index of suspicion for malignancy. There should be a low threshold for biopsies under general anaesthesia in order to obtain adequate and representative biopsies. Finally good interactions with the pathologists are crucial as special staining is required to make a definitive diagnosis

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