

HHF Loong 龍浩鋒
CY Cheung 張志遠
YK Lam 林炎坤

A not-so-uncommon presentation of an uncommon disease: nasal natural killer/T-cell lymphoma

鼻的自然殺手細胞/T細胞淋巴瘤：不尋常病症的普通表徵

An otherwise well 70-year-old man presented with a non-specific complaint of epistaxis caused by an underlying necrotic natural killer-cell lymphoma complicated by a maggot infestation. He failed to attend for treatment after discharge but re-presented 3 weeks later with an acute exacerbation of his chronic pulmonary obstructive disease. During those 3 weeks his nasal condition had advanced rapidly with extensive tumour infiltration and necrosis affecting his nose and face. The natural clinical course, overall prognosis, and available treatment modalities are briefly discussed.

一名健康情況尚算良好的七十歲男性，因蛆蟲感染併發自然殺手細胞壞死淋巴瘤導致鼻出血。病人在出院後沒有再次求醫，三星期後其肺阻塞急性惡化。在這三個星期內其鼻病亦急劇惡化，出現腫瘤廣泛滲透及壞死，影響鼻部及面部。本文對此症的臨床原因、整體預後情況及可用的治療方式作廣泛討論。

Introduction

Previously known as polymorphic reticulosis or angiocentric T-cell lymphomas, natural killer (NK)-cell malignancies are uncommon. They are a distinct clinicopathological entity characterised by the presence of progressive necrotic lesions, the expression of an NK cell-associated marker—CD56—in the tumour cells, and a strong association with the Epstein-Barr virus (EBV). Although they are exceptionally rare in western countries, they remain prevalent in Asia. We report an elderly man with a not-so-uncommon presentation of this uncommon disease.

Case report

A 70-year-old single man presented to the Queen Elizabeth Hospital Accident and Emergency Department in February 2006 complaining of persistent epistaxis for 4 days. Although a chronic smoker and drinker with a known history of chronic obstructive pulmonary disease and treated pulmonary tuberculosis, he appeared to be in good health.

On examination, multiple insect larvae were found crawling out of both his nasal cavities. The patient was thus transferred to our unit for further management. He was fully conscious, alert, orientated, and of medium build. There were more than 50 maggot larvae crawling out of his nasal cavities. There was no associated cervical or peripheral lymphadenopathy and no hepatosplenomegaly.

We urgently consulted our otorhinolaryngologists. Bedside irrigation and douching failed to remove all the maggots. An emergency rhinoscopy was performed under anaesthesia the next day.

Intra-operatively, an extensive maggot infestation with submucosal infestation into the nose tip and the entire nasal septum up to the anterior wall of the sphenoid sinus was found. The upper lip and the anterior nasal floor were also involved, with penetration into the gingival surface of the upper lip (Fig 1). A septal perforation in the vestibule area of the anterior nasal septum was noted.

Key words:

Epistaxis;
Killer cells, natural;
Lymphoma

關鍵詞：

鼻出血；
殺手細胞，自然；
淋巴瘤

Hong Kong Med J 2006;12:470-2

Department of Clinical Oncology, Prince of Wales Hospital, Shatin, Hong Kong
HHF Loong, MB, BS, MRCP

Department of Medicine, Queen Elizabeth Hospital, Hong Kong
CY Cheung, FHKCP, FHKAM (Medicine)
YK Lam, MB, BS, MRCP (UK)

Correspondence to: Dr HHF Loong
(e-mail: h_loong@clo.cuhk.edu.hk)

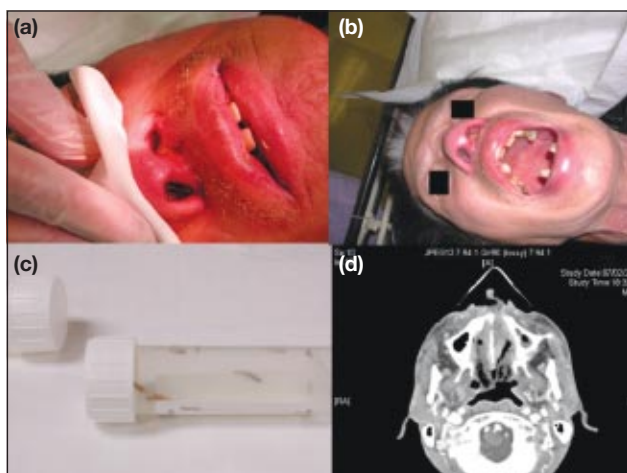


Fig 1. (a) and (b) Insect larvae are noted over the patient's nostrils; (c) multiple insect larvae obtained from the nostrils are sent to the microbiology lab for identification; (d) computed tomography of the head and neck with contrast showing mild increase in soft tissue irregularity within the nasopharynx

Submucosal elevation of the septal flaps on both sides exposed more maggots underneath. A nasal septal mucosa biopsy was sent for histological examination. More than 50 additional maggots were removed from the above locations. The incisions were sutured with Vicryl and haemostasis was achieved using packing and Merocel.

Postoperatively the patient's condition was complicated by septicaemic shock requiring inotropic support. A computed tomographic (CT) scan of the brain and nasopharynx with contrast performed the following day showed extensive soft tissue densities in both nasal cavities with small pockets of gas-filled densities suggestive of inflammation. There were also erosions in parts of the nasal septum and the turbinates. No focal mass lesion or abnormal attenuation was seen in the brain (Fig 1).

The biopsy of nasal septum mucosa was sent for histological section and staining. The section showed several pieces of necrotic nasal mucosal tissue containing necrotic tumour. The tumour cells had enlarged irregular to folded hyperchromatic nuclei and prominent nucleoli and infiltrate between the vessels and glands. Immunohistochemistry was positive for CD56 and CD2 but negative for CD20 and CD3, consistent with nasal NK/T-cell lymphoma.

In light of the histological findings, the patient was referred to the clinical oncology unit for further assessment and management and was discharged from our unit. He re-presented to our unit 3 weeks later with an acute exacerbation of his chronic pulmonary obstructive disease. He had opted not for treatment for his malignant nasal condition and did not attend for a staging whole body CT scan and a staging bone marrow examination. During the 3 weeks prior to admission the patient's nasal condition



Fig 2. The same patient admitted 3 weeks later for an exacerbation of his chronic obstructive pulmonary disease. Note the marked increase in destruction and tumour infiltration over his nose and face

rapidly deteriorated with extensive tumour infiltration and necrosis affecting his nose and face (Fig 2).

Discussion

Natural killer-cell lymphomas are classified into two histological categories by the World Health Organization: (1) NK/T-cell lymphoma, nasal type and (2) aggressive NK-cell leukaemia.¹ However, they are conventionally divided into three categories clinically: (1) nasal, (2) non-nasal, and (3) aggressive lymphoma/leukaemia subtypes. Each subtype has a different clinical manifestation and associated disease progression and prognosis.

Natural killer-cell lymphomas have a distinctive geographic distribution and are reported mainly in Asians and South Americans. In a local review, extranodal NK/T-cell lymphoma accounted for 6.27% (n=56) of all lymphomas diagnosed in the 10-year period from 1993 to 2002 at Queen Mary Hospital.² Most (n=40) were located nasally, with the rest being found in muscle, skin, gut, the testis, or disseminated at diagnosis.

Nasal NK-cell lymphoma is more common in males, with the median age being between 50 and 60 years.¹ The

histology usually shows variable neoplastic cell sizes associated with zonal necrosis and a polymorphic infiltrate of small lymphocytes, plasma cells, and eosinophils. Immunophenotypically, nasal NK-cell lymphomas are positive for CD2, cytoplasmic CD3e and CD56 but negative for surface CD3. These are extremely aggressive tumours, with a median survival of less than 12 months. Nasal obstruction, nasal discharge, and epistaxis are common presenting symptoms. The disease may present with facial swelling or midfacial/destructive disease formerly known as a lethal midline granuloma.

Staging of NK-cell lymphomas is traditionally based on the conventional Ann Arbor staging system derived from a contiguous lymphatic spread model initially intended for Hodgkin's lymphoma. However, as with other extranodal lymphomas, the Ann Arbor staging does not take into account the tumour size, an important determinant in locally invasive tumours. Other staging systems have also been tested, such as one devised originally for conventional sinonasal B-cell lymphomas as well as the International Prognostic Index which takes account of age, performance status, and the lactate dehydrogenase level.

The pathogenesis of NK-cell lymphomas remains controversial. There have been consistent reports of EBV infection in affected patients from Asia, Europe, and South America. A close correlation between plasma EBV DNA levels and the therapeutic response has been shown in a local study³ analysing a cohort of 18 patients. All patients who responded to treatment had a marked reduction in their plasma EBV DNA to low or undetectable levels. On the contrary, patients who failed treatment had a rapid increase in their plasma EBV DNA levels. It has been suggested that plasma EBV DNA levels measured on presentation are a strong predictor of clinical outcome: patients with ≥ 600 copies/mL of EBV DNA have significantly poorer overall survival. A similar effect has been observed in patients with nasopharyngeal carcinoma.⁴ Thus the test may be useful for deciding whether patients reaching remission should receive extra treatment. A patient in apparent clinical remission who has persistently high levels of circulating EBV DNA is likely to relapse; therefore additional therapy should be contemplated.

Radiotherapy is the treatment of choice in the stage I NK-cell lymphoma seen in our patient. According to the

literature, the overall response rate is between 60 and 80%, with complete remission rates of between 40 and 80%, and a 5-year overall survival rate of around 40%.^{5,6} Despite these relatively encouraging results, relapses are frequent (commonly reported as 50%), with most local failures occurring within the first year; recurrences after 2 years are very uncommon.⁷

Several studies have found that in patients with stage I disease who achieve clinical remission after radiotherapy, additional chemotherapy offers no survival advantage. However, the role of chemotherapy after radiotherapy in stage II patients remains controversial. It has been suggested that if chemotherapy is to be used as the initial treatment in early disease, supplementary radiotherapy should be initiated early.¹ 'Sandwich therapy' using a combination of chemotherapy with sandwiched Cisplatin-primed radiotherapy has also shown encouraging results.¹

Chemotherapy remains the mainstay of treatment in advanced disease (stage III/IV). Anthracycline-containing regimens have traditionally been used. The overall prognosis remains extremely guarded. The use of novel therapies such as monoclonal antibodies, immunoconjugates, and retinoids is now being studied with promising results.

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