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Extranodal NK/T-Cell Lymphoma, Nasal Type (ENKTL) Presenting with Odynophagia

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Abstract

Odynophagia is a common symptom in both otolaryngology and general practice. We report a case that presented with persistent odynophagia, diagnosed initially as inflammatory after examination and investigations including panendoscopy. Due to persistent symptoms despite medical management, further investigations in the form of scans and biopsies were undertaken. Eventually biopsies were reported as NK/T cell lymphoma, nasal type (ENKTL). We report this unusual case and discuss the literature of extranodal NK/T lymphoma (ENKTL) in head and neck. Clinical awareness of this condition and a high index of suspicion is the key to identifying this insidious but potentially serious disease.

Keywords: Odynophagia; Lymphoma; Haematology; Rhinosinusitis; Malignancy

Introduction

Extranodal NK/T-cell lymphoma, nasal type (ENKTL) is an aggressive, rare haematological condition that typically presents with the common features of rhinosinusitis and epistaxis. This presentation makes recognition and diagnosis notoriously difficult, combined with challenges in obtaining histological confirmation. The combined effect of this sadly often results in delayed treatment of this aggressive malignancy [1].

Our patient presented with an unusual clinical picture, with only one other case report similar reported in the literature. Furthermore, demographically she varied from the typical expectations of this disease in regard to gender, age and ethnicity. Through understanding her presentation and diagnostic journey, an opportunity is provided to facilitate more prompt diagnosis in a minority of affected patients. This allows a potential for quicker access to treatment and improved prognostic outcome in affected patients. Clinicians must be aware of this unusual presentation in order to facilitate this process.

Case Report

A 64-year-old Caucasian woman presented to the ENT outpatient clinic with progressively worsening odynophagia over 24 months and a more recent onset of mild dysphonia over the preceding few weeks. There were no further red flag symptoms reported, including referred otalgia, dysphagia, hemoptysis or weight loss. Her medical history included a panendoscopy 18 months prior to the current presentation for odynophagia, where no pathology but for laryngopharyngeal reflux was identified. At a similar time functional endoscopic sinus surgery (FESS) with polypectomy was performed for rhinitic symptoms with findings of a large polypoidal right middle turbinate. No biopsies were sent for histology due to lack of obvious pathology to the naked eye. Her remaining past medical history included hypertension and being an ex-smoker for six years.

Clinical examination demonstrated ulceration and irregularity of the soft palate and posterior pharyngeal wall. Examination of neck was normal but unfortunately she could not tolerate flexible nasoendoscopy (FNE). Due to persisting symptoms and an inability to adequately examine her, an urgent panendoscopy was performed. This confirmed the cobblestone/ulcerated region on the posterior pharyngeal wall, also involving the left arytenoid and left border of epiglottis. Biopsies were taken from these 3 sites, histologically reported as demonstrating no evidence of dysplasia or malignancy. No further histological review was performed on these specimens. One week later she required a short admission due to exacerbation of her symptoms. Examination confirmed the previous findings, also with frank pus on the posterior pharyngeal wall, and again she was intolerant of FNE. After a short course of antibiotics, she was discharged home.

Six weeks after this panendoscopy and biopsy she was re-admitted for management of progressive symptoms including inadequate oral intake and subsequent weight loss. A repeat panendoscopy was performed, with biopsies from the posterior pharyngeal wall and uvula demonstrating dense and diffuse lymphoid infiltrate. These tissue samples were sent to the Regional Haematological Malignancy Diagnostic Service for further investigation, and here we will discuss the relevance of their findings (Figure 1).

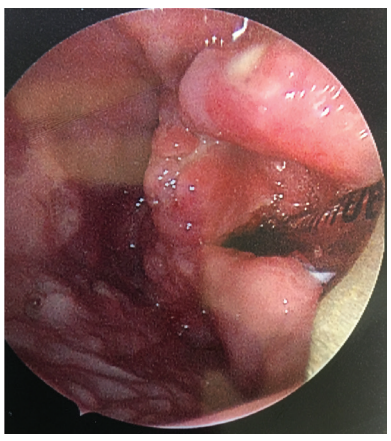

Figure 1: Panendoscopy of cobblestone/ulcerated appearance

Investigations

Initial serological testing demonstrated a chronically elevated C-reactive protein, being 78 mg/L on admission for symptom control. There were no clinical indicators of infection, and the rest of her serological testing was essentially normal.

CT imaging of the neck and thorax demonstrated thickening of the walls of the uvula, oropharynx, aryepiglottic folds and false vocal cords. No significant lymphadenopathy was identified.

Histological assessment of the diagnostic biopsies demonstrated focal areas of necrosis with a highly proliferative population of large cells. These cells had abnormal NK/T cell phenotype. Immunohistochemistry was CD2+, CD3+, CD4-,CD5-, CD56+, CD57-, CD7+, CD8-, Granzyme B+, Ki67 70%, and evidence of Epstein Barr Virus (EBV) infection (LMP1+).

As LMP1 was positive suggestive of EBV infection along with other immunohistochemistry findings this was in keeping with a diagnosis of Extranodal NK/T-cell lymphoma, nasal type (ENKTL).

In situ hybridization for EBV encoded mRNA (EBER), although the most reliable way of detecting the presence of EBV in lymphoma is not mandatory for a diagnosis according to the WHO classification system [2]. Indeed, local laboratory guidelines recommend EBER only if immunohistochemistry fails to show LMP1+.

Further serological testing demonstrated findings consistent with a previous EBV infection (EBV IgG positive, EBV IgM negative). There was no evidence of previous Cytomegalovirus (CMV), Hepatitis B/C or Human Immunodeficiency virus (HIV) infection. EBV PCR was not performed prior to commencing treatment to assess tumour load.

A staging PET/CT scan demonstrated multiple occult areas of high uptake including the nostrils, left nasopharynx, uvula, oropharynx, left level II lymph node and a right upper paratracheal node. Her lymphoma was subsequently staged as Ann Arbor stage IIE. More disseminated spread had been excluded through a negative bone marrow biopsy.

Differential diagnosis

- Initial infective process with subsequent oropharyngeal pus and pain.
- Reactive lymphoid process in the post nasal space mimicking malignancy.
- Granulomatous disease, including polyangiitis (formerly Wegner's granulomatosis), lymphoid granulomatosis or granulomatous infections (leishmaniasis or syphilis) [3].
- Head and neck malignancies including squamous cell carcinoma, nasopharyngeal carcinoma or a variety of lymphomas.
- Necrotising intranasal lesions secondary to trauma (including surgery) and infection can often be the initial presentation of such malignancies [4].

Treatment

There have been no randomised controlled trials for treatment of extranodal NK/T-cell lymphoma, nasal type (ENKTL). The British Committee for Standards in Haematology (BCSH) have published considerations for treatment using data from phase I/II studies and retrospective review [5]. These studies (usually involving small number of patients) showed the best outcomes with stage I/II disease are from using 'involved field radiotherapy (IFRT)' and that the use of standard CHOP (cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisolone) chemotherapy agents did not add any real benefit [6]. Another study of 82 patients showed that early radiotherapy was the only independent prognostic factor [7]. Since then chemotherapy regimens containing L-asparaginase such as SMILE regime (dexamethasone, methotrexate, ifosfamide, L-aspraginase and etoposide) have shown more promising results, but no studies directly comparing this regime to CHOP have been published [8,9].

Outcome and follow-up

Our patient was transferred to the regional haematological cancer centre to commence radiotherapy and SMILE chemotherapy. It is too early to assess her response to treatment.

Discussion

The presentation of our patient with a rare, aggressive extra-nodal NK/T cell lymphoma, nasal type (ENKTL) was unusual in a number of ways. Firstly, the patient demographics were outside those typically expected in three key areas. This disease is more common in men of East Asian, Latin and South American origin where it represents 7-10% of Non-Hodgkin's Lymphoma (NHL) cases, whereas our patient was both female and Caucasian (in whom it contributes to less than 1% of NHL cases) [10,11]. Additionally, her age at 65 was outside the typical median of 50-55 years reported in this form of lymphoma [12]. However, the most unusual element of this case was the main presenting symptom of odynophagia. A literature search has only confirmed one other reported case with a similar presentation [13]. Classically, the presenting features of ENKTL are those reflecting rhinosinusitis, predominantly nasal obstruction, rhinorrhoea and epistaxis [1,14-16]. Less frequently, presentation can consist of mid-facial inflammation or necrosis (typically after surgical intervention), neck masses, orbital symptoms, fever and weight loss [3,17]. Our patient did demonstrate these more typical features of nasal obstruction and mid-facial inflammatory process after surgical intervention (FESS), although her main concern was always the odynophagia with increasing severity.

Diagnosis of this form of malignancy can be difficult, with resultant delayed treatment. As discussed above, the typical presenting features are non-specific with a benign appearance. Rarely do patients present with suspicious findings of either clinical or radiologically detectable intranasal mass, or signs of disease progression [18,19]. Compounding this, although most patients have undergone pre-operative imaging and surgery for presumed benign disease (often FESS), biopsies are often not diagnostic [11,16]. Histological tissue examination often demonstrates extensive ischaemic tissue necrosis with few malignant cells, necessitating multiple deep repeat biopsies in order to achieve a tissue diagnosis [3,16]. This further contributes to the delay in diagnosis and treatment. Previous publications have reported an average delay of 8.9 months from onset of symptoms to presentation to a medical professional, and a total of 12.8 months for diagnosis from onset [1,16]. Due to these well-documented difficulties, the role of immunophenotyping has become increasingly vital in the diagnosis of ENKTL [3]. Pathologically unique characteristics include expression of cytoplasmic CD3, CD56 and cytotoxic molecules such as TIA-1, and positivity for EBV [20].

The importance of striving for more timely recognition and diagnosis of this condition is due to the potential for remission in over 50% of those with localised disease, if treatment is commenced promptly [21]. As clinicians we must respect the symptoms that patients report, and consider a more sinister diagnosis in those who do not improve with conservative and operative management in similar circumstances to those discussed. This is especially true in cases with mid-facial inflammation after surgical intervention, as diagnosis of ENKTL has been reported post-FESS [3]. For any patients with necrotic lesions affecting the nose and pharynx, multiple deep biopsies are necessary to diagnose an underlying ENKTL [1]. Negative investigations or biopsies for the first time should assure clinicians of lack of serious pathology. However, if patients continue to be symptomatic, especially those who further deteriorate, repeat biopsies for the second or third time may be necessary to confirm this NK/T cell lymphoma.

This case provides a learning opportunity for clinicians, re-emphasising the importance of acknowledging and investigating persistent and progressive symptoms in their patients. It is also a prime example of the traditional approach in medicine that strives to find a single diagnosis to explain a collection of symptoms. We recommend that for patients presenting with a similar spectrum of symptoms, not responding to appropriate management, consideration of a panendoscopy and examination under anaesthetic of the post nasal space is appropriate. In such instances, multiple and deep biopsies of even healthy appearing tissues would not be unreasonable. Through prompt identification and diagnosis, access to the newly advanced treatment options has the potential to improve patient outcomes and overall morbidity of such conditions.

Learning Points

- Benign nasal symptoms not responding to adequate treatment should be further investigated for the possibility of an occult malignancy.
- Consideration of panendoscopy and examination under anesthesia of the post-nasal space is recommended in those few patients with progressive odynophagia and background rhinitis symptoms, irrespective of the lack of red-flag symptoms.
- Negative biopsies are not reassuring in the setting of persistent or worsening symptoms. In such cases, further biopsies should be taken with the consideration of multiple-site, deep specimens.
- Mid-facial inflammation and necrosis is concerning, particularly post-operatively, and should prompt further biopsies.

References

1. Yanagi H, Nakamura Y, Takagi D, Kubota K (2012) Extranodal natural killer/T-cell lymphoma: a diagnostic dilemma. Rhinology 50: 325-331.
2. Swerdlow S, Campo E, Harris N, Pileri S, Stein H, et al. (2008) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Fourth edition. World Health Organization, Geneva, Switzerland.
3. Batra P, Shah N, Mathur S (2003) Midline lethal granuloma- A clinical enigma. Indian J Dent Res 14: 174-183.
4. Sharma A, Dandekar M, Deshmuk S, Dabholkar J (2011) Nasal extranodal natural killer T cell lymphoma: An atypical presentation. J Laryngol Otol 125: 1181-1184.
5. Dearden C, Johnson R, Pettengell R, Devereux S, Cwynarski K, et al. (2013) Guidelines for the Management of Mature T-cell and NK-cell Neoplasms (Excluding cutaneous T-cell Lymphoma). Br J Haematol 153: 451-485.
6. Li Y, Yao B, Jin J, Wang W, Liu Y, et al. (2006) Radiotherapy As Primary Treatment for Stage IE and IIE Nasal Natural Killer/T-Cell Lymphoma. J Clin Oncol 24: 181-189.
7. Huang MJ, Jiang Y, Liu WP, Li ZP, Li M, et al. (2008) Early or Up-Front Radiotherapy Improved Survival of Localized Extranodal NK/T-Cell Lymphoma, Nasal-Type in the Upper Aerodigestive Tract. Int J Radiat Oncol Biol Phys 70: 166-174.
8. Yamaguchi M, Kwong Y, Kim W, Maeda Y, Hashimoto C, et al. (2011) Phase II Study of SMILE Chemotherapy for Newly Diagnosed Stage IV, Relapsed, or Refractory Extranodal Natural Killer (NK)/T-Cell Lymphoma, Nasal Type: The NK-Cell Tumor Study Group Study. J Clin Oncol 29: 4410-4416.
9. Kwong Y, Kim W, Lim S, Kim S, Tang T, et al. (2012) SMILE for natural killer (NK)/T-cell lymphoma: analysis of safety and efficacy from the Asia Lymphoma Study Group. Blood 120: 2973-2980.
10. Au W, Ma S, Chim C, Choy C, Loong F, et al. (2005) Clinicopathologic features and treatment outcome of mature T-cell and natural killer-cell lymphomas diagnosed according to the World Health Organization classification scheme: a single center experience of 10 years. Ann Oncol 16: 206-214.
11. Quintanilla-Martinez L, Kremer M, Keller G, Nathrath M, Gamboa-Dominguez A, et al. (2001) p53 Mutations in Nasal Natural Killer/T-Cell Lymphoma from Mexico: Association with Large Cell Morphology and Advanced Disease. Am J Pathol 159: 2095-2105.
12. Lee J, Kim W, Park Y, Park S, Park K, et al. (2005) Nasal-type NK/T cell lymphoma: clinical features and treatment outcome. Br J Cancer 92: 1226-1230.
13. Kidwa S, Parasher A, Lin F (2015) An unusual presentation of NK/T-cell lymphoma, nasal-type in the United States. Am J Otolaryngol 36: 80-83.
14. Tababi S, Kharrat S, Sellami M, Mamy J, Zainine R, et al. (2012) Extranodal NK/T-cell lymphoma, nasal type: report of 15 cases. Eur Ann Otorhinolaryngol Head Neck Dis 129: 141-147.
15. Ladeb S, Gaulard P, Othmen T, Abd Alsamad I, Delfau-Larue M, et al. (2013) Nasal NK/T lymphoma. A case report. Ann Pathol 23: 149-152.
16. Yen T, Wang R, Jiang R, Chen S, Wu S, et al. (2012) The diagnosis of sinonasal lymphoma: a challenge for rhinologists. Eur Arch Otorhinolaryngol 269: 1463-1469.
17. Gaal K, Sun N, Hernandez A, Arber D (2000) Sinonasal NK/T-cell lymphomas in the United States. Am J Surg Pathol 24: 1511-1517.
18. Hung L, Chang P, Lee T, Hsu Y, Chen Y, et al. (2012) Extranodal natural killer/T-cell lymphoma, nasal type: Clinical and computed tomography findings in the head and neck region. Laryngoscope 122: 2632-2639.
19. Ou C, Chen C, Ling J, Chai J, Wu C, et al. (2007) Nasal NK/T-cell lymphoma: computed tomography and magnetic resonance imaging findings. J Chin Med Assoc 70 207-212.
20. Wang H, Zhang S, Shi Q (2008) Advances in studies of Nasal Type NK/T-cell Lymphoma. Chin J Cancer Prev Treat 15.
21. Matsuura K, Aral C, Shimura E, Osafune H, Edamatsu H, et al. (2015) Two cases of extranodal NK/T-cell lymphoma, nasal type (ENKL). Oto-Rhino-Laryngology 58.