The Journal of Laryngology & Otology
September 2005, Vol. **119,** pp. 740–742

Orbital cellulitis or lymphoma? A diagnostic challenge

Aysha Salam, FRCSEd, Manual Saldana, FRCS, FRCOphth*, Naeem Zaman, FRCS, FRCOphth†

Abstract
We present a case report of an aggressive natural killer T cell lymphoma in a police officer who presented with combined features of orbital cellulitis and mid-facial destruction. However, his initial diagnosis was confused with other disease conditions that had overlapping features. This emphasizes the significance of clinical alertness and adequate tissue sampling; this can have a great impact on early diagnosis and treatment.

Key words: Natural Killer Cells; Lymphoma; Wegener's Granulomatosis; Orbital Cellulitis

Introduction

The extra-nodal natural killer T cell lymphoma is predominantly an extra-nodal lymphoma characterized by a broad morphological spectrum. Although it is localized to the upper aerodigestive tract, it can disseminate to various other sites and mimic vasculitic and granulitic pathologies. It makes up 3 per cent of all the primary ocular lymphoproliferative lesions in reported cases.[1]

We report the case of a police officer who presented with combined features of orbital cellulitis and mid-facial destruction.

Case report

A 33-year-old man was referred by the ENT department with a history of epiphora and a soft-tissue swelling along the right lacrimal sac area.

A diagnosis of acute dacryocystitis was made and the patient was treated with oral antibiotics, following which the acute episode resolved.

A few months later, the patient suffered another episode of acute dacryocystitis accompanied by nasal obstruction, a swollen nose (that was later found to be secondary to a massive right-sided nasal polyp causing distortion of the lateral wall of nose) and obstruction to the tear flow. However, despite antibiotics the nasal swelling progressed to involve the mid-facial region and the periorbital tissues bilaterally. It was accompanied by offensive rhinorrhoea, severe facial pain and high-grade fever.

Examination revealed bilateral marked periorbital oedema with inability to open both eyes. There was a marked proptosis of the right eye with visual acuities of 6/18 OD and 6/6 OU. There was no afferent pupillary defect.

Nasal and conjunctival swabs grew Streptococci with gram-positive and anerobic rods, following which the patient was started on parenteral flucloxacillin and cefataxime.

An urgent computed tomography (CT) scan of the orbits and paranasal sinuses showed extension of inflammatory tissue from the ethmoid and sphenoid sinuses into the right orbit, with displacement of the inferior and medial recti. There was also marked effusion in the left maxillary and frontal sinuses, with mucosal thickening but no air–fluid levels.

Despite the intensive antibiotic treatment, the periorbital and facial swelling progressed. Twenty-four hours following the CT scan, the patient developed severe, right-sided epistaxis along with bleeding from the right medial canthus. It was found that the right lateral wall and part of the floor of the nose, along with the nasal septum, had undergone necrosis. The necrotic tissue was debrided along with extensive facial exenteration (Figure 1a) and was sent for histopathological examination, which showed extensive coagulative necrosis along with thrombotic and fibrinoid material around the vessel walls. Despite the

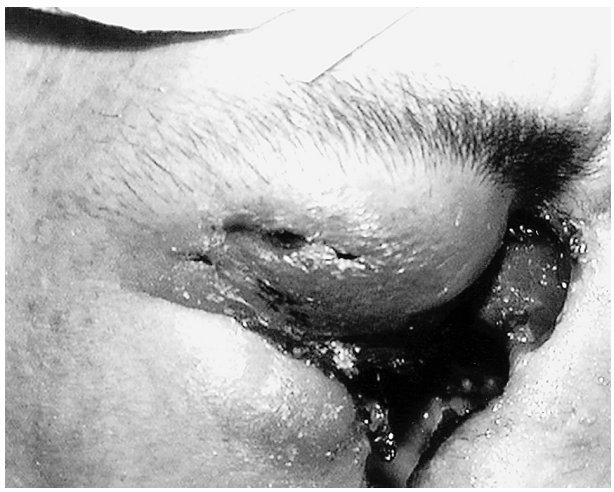

Fig. 1
Facial appearance after extensive soft tissue and bony debridement. There is removal of the septum, right lateral wall and floor of the nose.

From the Southampton Eye Unit, Southampton General Hospital, Southampton, the *Department of Ophthamology, Leeds General Infirmary, Leeds, and the †Department of Ophthamology, Hull Royal Infirmary, Hull, UK.
Accepted for publication: 21 April 2005.

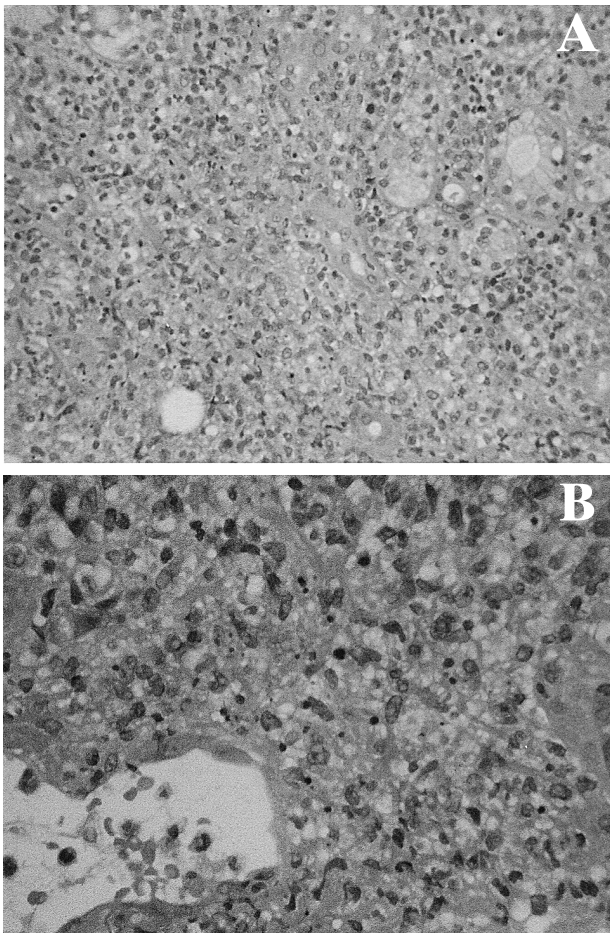

FIG. 2

(a) Histological section of the necrotic tissues, showing extensive coagulative necrosis with active inflammatory cells (haematoxylin & eosin, 10×4). (b) Higher magnification showing addition infiltration with large lymphoid cells and irregular eosinophilic nucleoli (haematoxylin & eosin, 10×10).

absence of granulomas, a histopathological diagnosis of Wegener's granulomatosis (WG) was made.

A trial of steroids and cyclophosphamide under an antibiotic cover was started. The patient's response to steroids was encouraging, with some temporary improvement, but the proptosis failed to resolve, the facial swelling extended and the left eye also developed marked proptosis.

After being reviewed by the clinicians, in the presence of negative anti-cytoplasmic neutrophilic autoantibody (cANCA) serology and a suspicious histopathology, the diagnosis of Wegener's granulomatosis was considered untenable. The tissue samples were sent back to the laboratory for further immunohistochemical analysis.

The results showed tissue infiltration with large lymphoid cells containing irregular nuclei and eosinophilic nucleoli. There was extensive invasion and destruction of blood vessels (Figure 2). The majority of cells were found to be latent membrane protein (LMP-1) positive. The biopsy features were confirmed to be those of an extra-nodal natural killer (NK)/T cell lymphoma of the nasal type with an atypical NK cell phenotype (CD 2+, CD3−, CD 56+,CD20, LMP-1+).

The patient was transferred to the oncology department for curative chemotherapy, where he was started on the cyclo phosphamide, doxorubicin, vincristine, prednisolone (CHOP) chemotherapy regime, with three phases over the next two months.

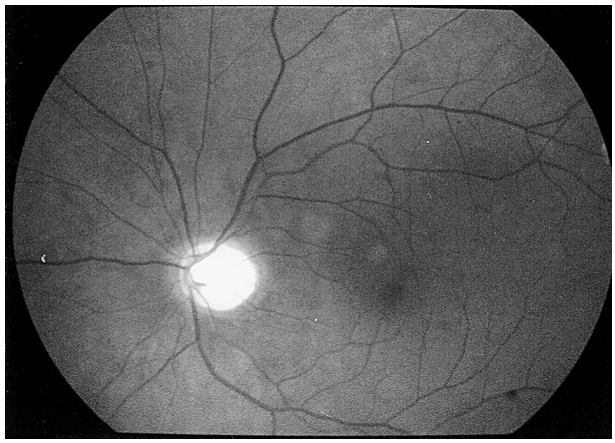

FIG. 3

Complete optic atrophy.

The patient's proptosis, pain and nasal discharge settled, but over the next three months he suffered complete loss of sight with optic atrophy in the left eye, most probably due to infiltration of the nerve by the underlying disease process (Figure 3).

At the time of writing, the patient had had an encouraging response to chemotherapy, and facial reconstruction was planned pending his recuperation from radical facial exenteration.

Discussion

The clinical features of nasal NK lymphoma can closely mimic those of other disease entities, and an early diagnosis can present a challenge to both the clinician and the pathologist. Both NK cell lymphoma and WG can cause destructive lesions often localized to the upper aerodigestive tract at presentation.

The histological features of an NK-cell lymphoma include widespread coagulative necrosis, heavy inflammatory infiltrate and atypical pleomorphic cells. However, in the presence of extensive necrosis, the paucity of these cells can make diagnosis very difficult.[2] Similarly, there may also be a heavy admixture of inflammatory cells, including small lymphocytes, plasma cells, histiocytes and eosinophils, which can mimic an inflammatory process - hence the previously popular term 'polymorphic reticulosis'.[3]

For these reasons, the diagnosis of WG was made in conjunction with measurements of cANCA, which was reported by Savage *et al*. to have a specificity of 99 per cent by immunohistochemical techniques and 98 per cent by enzyme-linked immunosorbent assay (ELISA).[4] The sensitivity ranges from 96 per cent in active generalized disease to 67 per cent in patients with active locoregional symptomatology.

The distinctive features of WG include vasculitis; small arteries and veins show acute inflammation and necrosis of blood vessels. There is deposition of fibrinoid material and occasionally thrombosis. Both WG and NK/T cell lymphoma are known to cause destructive lesions over the midline structures, including the nasal cavities, paranasal sinuses and the nasopharynx.

Hon *et al*. reported a high incidence (25 per cent) of sight-threatening complications, namely uveitis and orbital infiltration. Patients with orbital infiltration present with proptosis, severely limited ocular motility and disc-swelling leading to optic pallor.[1] The condition can also present with bilateral hypopyons resulting from direct lymphoma involvement. However, the distinction of clonal versus

https://doi.org/10.1258/0022215054797880 Published online by Cambridge University Press

reactive T or B cells in aqueous or vitreous aspirates can be difficult.[5,6] The disease is unique in causing relentless visual loss and destroying the anatomic structures involved, hence its eponym 'lethal midline granuloma'.

- **This paper reports a case of an aggressive natural killer T-cell lymphoma presenting with features of orbital cellulitis and mid-facial destruction**
- **The case is a reminder that mid-facial neoplasms, typically lymphomas, can mimic non-neoplastic conditions, including Wegener's granulomatosis and virulent infection**

Our patient was initially diagnosed as having orbital cellulitis secondary to pansinusitis. However, failure to respond to parenteral antibiotics probably implied another pathology, which was responsible for persistent proptosis and later resulted in complete loss of sight in the left eye. The tissue sections done at the time of surgery needed to be processed and reviewed by the histopathologist. A sampling error due to inappropriate tissue selection or storage was a likely possibility. As an intense inflammatory appearance complicates the histologic picture with proliferation of histiocyes induced by the neoplastic process, repeat biopsies are often required.[7] Clinicians must have very good knowledge and take into account the clinical features, serology and immunohistochemical techniques in order to take a rational approach to diagnosis and therapy. Perhaps an aggressive disease of this nature should mandate a high degree of suspicion from the outset to exclude a neoplastic pathology. The possibility of dissemination must always be entertained, and appropriate studies (including peripheral blood smear, liver-function tests, and CT scans of the skull, chest, and abdomen) should be carried out.[7]

Finally, clinical alertness, along with adequate tissue sampling, is indispensable for correct diagnosis and treatment.

References

1 Hon C, Kwok AK, Skek TW, Chim JS, Wingy Y, Au WY. Vision-threatening complications of nasal T/NK cell lymphoma. *Am J Ophthalmol* 2002;**134**:406-10
2 Chen HL, Cheng PW, Tsai CC. Pathology quiz case. Nasal T/NK cell-lymphoma. *Arch Otolaryngol Head Neck Surg* 2003;**129**:1135–6
3 Chan JKC, Jaffe ES, Ralfkiaer E. Extranodal NK/T-cell lymphoma, nasal type. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, eds. *WHO Classification of Tumours: Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues*. Lyon: France International Agency for Research on Cancer (IARC), 2001;204–8
4 Savage CO, Winerals CG, Jones S, Marshall PD, Lockwood CM. Prospective study of radioimmunoassay for antibodies against neutrophil cytoplasm in diagnosis of systemic vasculitis. *Lancet* 1987;**i**:1389–93
5 Hon C, Kwok AK, Shek TW, Au WY. Unusual locations of involvement by malignancies: Case 4. Bilateral hypopyon heralding CNS relapse of cutaneous natural killer cell lymphoma. *J Clin Oncol* 2003;**21**:3373–4
6 White VA, Gascoyne RD, Paton KE. Use of polymerase chain reaction to detect B- and T-cell gene rearrangements in vitreous specimens from patients with intraocular lymphoma. *Arch Ophthalmol* 1999;**117**:761–5
7 Pickens JP, Modica L. Current concepts on the lethal midline granuloma syndrome. *Otolaryngol Head Neck Surg* 1989;**100**:623–30

Address for correspondence:
Miss Aysha Salam,
Southampton Eye Unit,
Southampton General Hospital,
Tremona Road,
Southampton, SO16 6YD, UK.

Fax: 02380794120
E-mail: aysha_salam@yahoo.com

Miss A Salam takes responsibility for the integrity of the content of the paper.
Competing interests: None declared