CASE REPORT

Ocular presentation of natural killer/T-cell lymphoma in a Caucasian man

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Accepted 12 April 2016

SUMMARY

Natural killer/T-cell (NK/T-cell) lymphoma—nasal subtype, is a rare form of non-Hodgkin's lymphoma, most common in South East Asia, and can have an ophthalmological presentation. This report describes a 51-year-old Caucasian man with uveitis, recurrent retinal detachment and paraneoplastic features subsequently diagnosed as NK/T-cell lymphoma.

BACKGROUND

This case describes a rare presentation of an uncommon disease. Natural killer/T-cell (NK/T-cell) lymphomas are rare outside of South East Asia, comprising less than 1.5% of all non-Hodgkin's lymphomas worldwide. We report a case of NK/T-cell lymphoma in a Caucasian man with unusual systemic manifestations, whereby the ocular features preceded the lymphoma diagnosis. We believe that this case carries with it many clinical pearls for your readership, not least of which is the ability of this disease to mimic a plethora of alternative pathological processes.

CASE PRESENTATION

A 51-year-old man presented to the eye casualty of a tertiary referral hospital, with a 2-day history of a painless decrease in vision in the left eye. His medical history included gout. His ophthalmic history included panuveitis of the left eye (no cause identified), and concurrent superotemporal retinal detachment of unknown aetiology, for which he had undergone vitrectomy surgery 3 months previously.

He was found to have an exudative detachment of the left eye, and was managed on oral prednisolone. After failing to improve after 2 months of therapy, he was managed with surgical intervention to reattach the retina (encircling scleral band placement and vitrectomy with silicon oil insertion). The vitreous was biopsied at the time of surgery. It did not demonstrate lymphoma, and was negative for Epstein-Barr virus, herpes simplex virus and cytomegalovirus. The retina remained flat postoperatively.

The patient did not attend for follow-up in the ensuing 5 months, reporting that he was 'unwell'. He reported malaise, fever, arthralgia and rhinorrhoea, with the sensation of a blocked nose, numbness in his left leg and lateral aspect of his right leg and foot, and a limp. Examination revealed left ptosis, and multifocal mononeuropathy—most predominantly involving the right common peroneal

nerve resulting in a right foot drop. He was admitted to hospital for investigation.

INVESTIGATIONS

Blood tests included full blood count, liver and renal function, antineutrophil cytoplasm antibody (ANCA), and antibody markers of paraneoplastic retinopathy and neuropathy.

The patient was pancytopenic: haemoglobin 10.4 g/dL, white cell count $2.7 \times 10^9/L$ and platelets $707 \times 10^9/L$. Liver and renal function were normal. ANCA was negative. Investigations for paraneoplastic cerebellar atrophy and neuropathy, and paraneoplastic retinopathy, were negative: Anti-MAG antibody (antimyelin associated glycoprotein antibody), Purkinje cell antibody (anti-yo), neuronal nuclei antibody (anti-Hu/ri), amphiphysin antibody, anti-CV2/CRMP-5, anti-PNMA2 (ma2/Ta), anti-Tr and anti-ganglioside (GM1).

Imaging included CT of the thorax, abdomen and pelvis (CT TAP), and brain MRI. This revealed a small pericardial effusion, adrenal adenoma and mild splenomegaly with no lymphadenopathy. The brain MRI, showed non-specific scattered foci of periventricular and subcortical T2 and fluid attenuated inversion recovery hyperintensity with sparing of the corpus callosum—suspicious—not confirmatory for demyelination.

Electromyogram showed mononeuritis multiplex with axonal features (tibial, sural, ulnar, radial, median nerves). This made demyelination/sarcoidosis unlikely, but was suggestive of an acute vasculitis. Muscle and nerve biopsy showed non-specific type II fibre atrophy, myelin degradation and almost total loss of large myelinated fibres, but neither myositis, dystrophy nor vasculitis.

Lumbar puncture and bone marrow aspirate and trephine were performed. The patient had acellular, culture-negative cerebrospinal fluid. The bone marrow demonstrated trilineage haematopoiesis with no evidence of an infiltrate. Ziehl-Nielsen staining was negative, and there was no evidence of lymphoma.

The patient subsequently developed a red eye with evidence of scleritis, and was started on intravenous methylprednisolone with a working diagnosis of ANCA-negative vasculitis. He developed fluctuant fevers with early morning (6:00) peaks. His lactate dehydrogenase measured 885 IU/L, and blood culture for cytomegalovirus/Epstein Barr virus (CMV/EBV) IgM/IgG and PCR revealed an EBV viral load of $>700\,000$ copies/mL. He described a worsening sensation of a blocked nose, and underwent a nasal turbinate biopsy. This

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To cite: Hughes E, Fogarty H, Fortune A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-215089

was negative for vasculitis. Immunostaining was strongly positive for CD 56, and weakly positive for CD3. EBV encoded RNA (EBER) staining for EBV was also strongly positive. The histology confirmed a diagnosis of non-Hodgkin's lymphoma, NK-T-cell nasal subtype, stage II.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included systemic inflammatory disease (eg, vasculitis or sarcoidosis) in light of the history of panuveitis, fever and malaise. Infective causes were also considered—Lyme disease, HIV, tuberculosis, herpes simplex virus and brucella. The patient's multifocal mononeuropathy and ptosis raised suspicion for a concurrent neurological disorder such as Guillain-Barre syndrome or demyelination. Lastly, paraneoplastic retinopathy, paraneoplastic cerebellar atrophy and paraneoplastic neuropathy from an undiagnosed neoplasm were considered.

TREATMENT

The patient was referred to haematology for SMILE chemotherapy (dexamethasone, methotrexate, ifosfamide, L-asparaginase and etoposide). He is undergoing this treatment at present.

OUTCOME AND FOLLOW-UP

The patient is undergoing chemotherapy at present, and the retina has remained attached.

DISCUSSION

This case describes a rare presentation of an uncommon disease. NK/T-cell lymphomas are uncommon outside of South East Asia, comprising less than 1.5% of all non-Hodgkin's lymphomas worldwide. They are typically found in the nasal cavity, and >95% are associated with evidence of EBV infection (mechanism unknown). They often mimic a vasculitic disease process, for example, Wegener's granulomatosis, as was the case in the history presented here. There are reports of an ocular presentation of NK/T-cell lymphoma. Cimino *et al*¹ reported a case of bilateral panuveitis with vitreous positivity for CD 56 staining. The connection between the lymphoma and ophthalmic pathology is presumed in this case, as the vitreous biopsy did not demonstrate lymphoma. However, the nature of the recurrent detachment and subsequent course of systemic features strongly support the link. Similarly, recalcitrant sinusitis with adjacent scleritis from orbital involvement of the nasal lymphoma has been reported.² Kase *et al*³ described a case of anterior uveitis, where an aqueous tap was positive for both CD56 and EBER staining. The largest case series was published in Hong Kong, in 2002—6 of 24 patients with nasal NK/T-cell

lymphoma had vision-threatening complications.⁴ The authors divided these into two categories: uveitis, or orbital infiltration. Two of the 25 patients developed a rhegmatogenous retinal detachment, preceded by uveitis—similar to that seen in the case discussed here. Sclerouveitis as the presenting feature of central nervous system and peripheral lymphoma has also been described.^{5 6} Classically, these patients experience a painful reduction in vision. This contrasts with the case presented here, in which the patient developed scleritis months after the initial presentation, with a painless loss of vision secondary to uveitis and retinal detachment.

Learning points

- ▶ Natural killer/T-cell (NK T-cell) lymphoma must be included in the differential diagnosis of uveitis and retinal detachment, even when initial vitreous biopsy is negative.
- ▶ NK T-cell lymphoma is a rare presentation in a Caucasian patient, but must not be overlooked.
- ▶ NK T-cell lymphoma is a mimicker of vasculitis, and a serum measurement of EBV IgM/IgG is useful in its diagnosis.

Acknowledgements The authors thank Dr Niall Mulligan, MB FCAP, Department of Pathology, Mater Misericordiae University Hospital, Eccles St, Dublin 7, Dr Peter Kelly, MB, Department of Neurology, Mater Private Hospital, Dublin 7.

Contributors EH was the primary author of this work. The additional authors provided intellectual material and assisted in the editing of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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