

Case study

Title : Bilateral combined retinal vascular occlusion following treated non-Hodgkins lymphoma

Abstract

Aim: We describe an atypical ocular presentation of central nervous system involvement in non-Hodgkins lymphoma (NHL)

Presentation: A 63 year old man with past history of relapsed Non Hodgkin Lymphoma (NHL) in remission with R-CHOP chemotherapy presented with sequential acute loss of vision in right eye and left eye without any systemic manifestations of relapse. On ophthalmological evaluation, was found to have a mixed central retinal artery and central retinal vein obstruction. CSF (cerebro-spinal fluid) study showed diffuse large B cell lymphoma (DLBCL) cells. The Central nervous system (CNS) lymphoma was managed with triple intrathecal chemotherapy

Discussion: Non-Hodgkin's lymphoma is the most common type of ocular lymphoma, which may often be the first manifestation of systemic relapse in previously treated NHL. Combined vascular occlusion secondary to NHL is extremely rare. We are unaware of any previous reports of bilateral combined vascular occlusion neither due to DLBCL, nor of any cases of vascular occlusion associated with ophthalmoplegia.

Conclusions: Re-relapse as isolated CNS lymphoma at second remission in a patient with systemic NHL is quite rare. Although unlikely, bilateral combined central retinal vein occlusion and central retinal artery occlusion may be the first manifestation of central nervous system lymphoma. Clinicians should have a raised index of suspicion particularly with sudden, total loss of vision.

Key words: Bilateral central retinal artery and vein obstruction, Non Hodgkin Lymphoma

Introduction:

We describe an atypical ocular presentation of profound, sequential, total loss of vision in a patient with previously treated diffuse large B-cell non-Hodgkins lymphoma (NHL) and previously unreported associated retinal findings and ophthalmoplegia.

Case Presentation

A 63 year old gentleman presented to general casualty with acute loss of right eye vision. He had a four day history of headaches, which were diagnosed as migraine by his General Practitioner, and prescribed sublingual Nifedipine. One hour after the treatment he experienced rapid loss of right eye vision and his left eye vision was unaffected. No obvious lymphadenopathy was noted. A previous medical history of non-Hodgkins lymphoma (NHL),

being in remission following CHOP chemotherapy and Parkinson's disease was noted. A computed tomography (CT) scan of the brain was arranged to exclude cerebral haemorrhage, infarction or space occupying lesion, and inflammatory blood serum markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were sent to exclude giant cell arteritis. The CT scan was reported as normal and the inflammatory makers were not elevated. The patient was allowed home with instructions to attend the eye casualty the following day.

The patient was seen in eye casualty the next morning (day 1) and overnight he noticed pain on moving the right eye. Visual acuity was no perception of light (NPL) in the right eye and 6/6 unaided in the left eye. A right relative afferent papillary defect (RAPD) was present. He was noted to have mild right eye restricted eye movements in all directions of gaze, a 1mm ptosis and 2mm exophthalmos. Fundoscopy revealed a swollen right disc, four quadrant flame haemorrhages, a pale macula with cherry-red spot and 'cattle trucking' of the major vessels (fig.1). Left eye examination was entirely normal.

Right eye features were compatible with a generalised vascular stasis - a mixed central retinal vein occlusion (CRVO) and central retinal artery occlusion (CRAO). A working diagnosis of right orbital apex syndrome was made, with differential diagnosis of scleritis and central nervous system (CNS) involvement from NHL. The CT scan from the previous day was reviewed, but lacked contrast or fine 3mm cuts of the orbits. Therefore Magnetic Resonance Imaging (MRI) was requested, but this was subsequently delayed and changed, by the radiology department, to fine cut CT of orbits with contrast, which was subsequently reported as normal.

Treatment with high dose steroids was contemplated and discussed with the medical retina consultant. However, the patient had a history of neutropenic sepsis following two separate episodes of CHOP chemotherapy and in the absence of radiological evidence of optic nerve compression or raised inflammatory serum markers it was felt that high dose steroids should be avoided. The patient was referred to the haematologists and admitted to exclude recurrence of NHL. There were no systemic manifestations to suggest recurrence or relapse of NHL.

The next day (day 2) the patient woke to find he had lost vision in his previously unaffected left eye. The haematologists administered intravenous methylprednisolone 1g and an urgent MRI was requested. Later that morning he was reviewed by the medical retina consultant. The patient's vision was now bilateral NPL, with a complete right ptosis and gross ophthalmoplegia bilaterally. The appearance of the right fundus was unchanged (fig.1), and unexpectedly the left fundus appeared normal. Revised differential diagnoses included CNS relapse of NHL (eg anterior visual pathways and cortical blindness from occipital lobe involvement) and non-arteritic anterior ischaemic optic neuropathy (NA-

AION), secondary to a toxic reaction to CHOP chemotherapy. Fine cut CT of orbits with contrast was performed later that afternoon and subsequently reported as normal. Lumbar puncture was requested. Repeat inflammatory blood serum markers (ESR, CRP) were not elevated.

The following day (day 3) a second dose of IV methylprednisolone 1g was administered. The patient was reviewed with both eyes NPL and with dilated unresponsive pupils. Both optic discs were now swollen with a similar fundal appearance in both eyes was present (figs.1 and 2). MRI was performed that afternoon and reported as 'bilateral optic neuritis, possible optic atrophy, no compression, no evidence of lymphoma'. Lumbar puncture was requested and performed by haematologists with preliminary results being normal.

Fundus fluorescein angiogram was performed (fig.3). This showed total absence of perfusion of the retinal vasculature, with only a slight flush of fluorescein at the cup of the optic discs after 6 minutes. Choroidal perfusion was not patchy or delayed.

Cerebro-spinal fluid (CSF) results were available the following day (day 4) and revealed large B-cell lymphoma cells. A diagnosis of CNS lymphoma was confirmed and intrathecal chemotherapy was commenced; high dose methotrexate 7.6g, cytarabine 50mg and hydrocortisone 50mg. One week after chemotherapy the patient developed pancytopenia and neutropenic sepsis. He died, shortly afterwards, two weeks after his initial presentation with loss of vision.

Discussion

Whereas Hodgkin lymphoma very rarely causes ocular disease, non-Hodgkin lymphoma (NHL) is the most common type of ocular lymphoma. Depending on the site of involvement, ocular lymphoma can be either intraocular or orbital and adnexal. The haemopoietic and lymphoid neoplasms have been classified by the World Health Organisation based on the predominant cell type and defining phenotypic, molecular or cytogenetic characteristics. These five principal categories are non-Hodgkin lymphomas (subdivided into mature B-cell, mature T-cell and natural killer cell neoplasms), the Hodgkin lymphomas and the immune-deficiency associated lymphomas. The mature B-cell neoplasms account for more than 85% of all lymphomas¹.

Our patient originally presented with lymphadenopathy, a year prior to his ophthalmic symptoms, and was diagnosed with a low grade systemic marginal zone B-cell lymphoma. This was treated with six cycles of R-CVP chemotherapy; rituximab (a B-cell specific monoclonal antibody), cyclophosphamide, vincristine and prednisolone. The lymphoma subsequently transformed to the more aggressive 'diffuse large B-cell lymphoma', which was treated with R-CHOP chemotherapy; rituximab, cyclophosphamide,

hydroxydaunorubicin, Oncovin (vincristine) and prednisolone. Following his fourth cycle the patient was noted to be in remission both clinically and radiologically. This was four weeks prior to his presentation with visual loss.

Ocular lymphoma is often the first manifestation of systemic relapse in previously treated NHL.² However, optic nerve and chiasmal disease is unusual. The literature reports several cases of optic disc swelling secondary to lymphomatous infiltration of the optic nerves,³ but combined vascular occlusion secondary to NHL is extremely rare. We are aware of four case reports with this type of presentation; three cases describe unilateral combined vascular occlusion and a mixed cell lymphoma was diagnosed in the bilateral involvement case. We are unaware of any previous reports of bilateral combined vascular occlusion due to DLBCL, nor of any cases of vascular occlusion associated with ophthalmoplegia.

The pattern of infiltration in ocular lymphoma gives some important clues to the source of the neoplastic cells. Ocular lymphoma associated with systemic disease often presents with involvement of the anterior segment or with uveal masses due to presumed haematological spread through the choroidal circulation. In contrast, CNS lymphomas tend to present with retinal masses, vitritis or with optic nerve and/or retinal vascular infiltration. In a series of 32 patients, intraocular lymphoma was associated with CNS involvement in 56%, systemic lymphoma in 16%, CNS and systemic lymphoma in 6% and no extraocular lymphoma in 22%. The CNS, systemic and primary ocular lymphomas have very different treatment strategies, so it is very important to try and establish the distribution of disease. This may be done clinically, radiologically and cytologically, both from blood and CSF. Ocular-CNS NHL is poorly responsive to corticosteroid treatment, but is sensitive to external beam radiotherapy and systemic/intrathecal chemotherapy.

Sudden, dramatic loss of vision from 6/6, beyond perception of light (PL), to NPL is most unusual for both arteritic and non-arteritic AION. Therefore, clinicians should have a raised index of suspicion for relapse of CNS lymphoma in such cases.

References:

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164 Fig.1. Montage of right fundus –swollen right disc, four quadrant flame haemorrhages, a
165 pale macula with cherry-red spot.



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169 Fig.2. Montage of left fundus–swollen left optic disc, fewer retinal haems, pale macula with
170 cherry-red spot.

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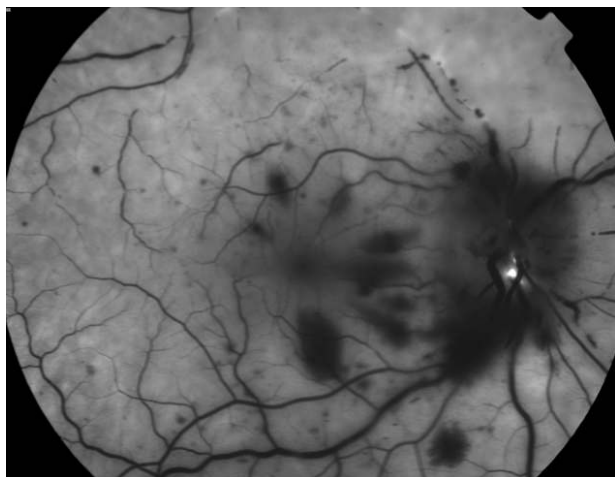


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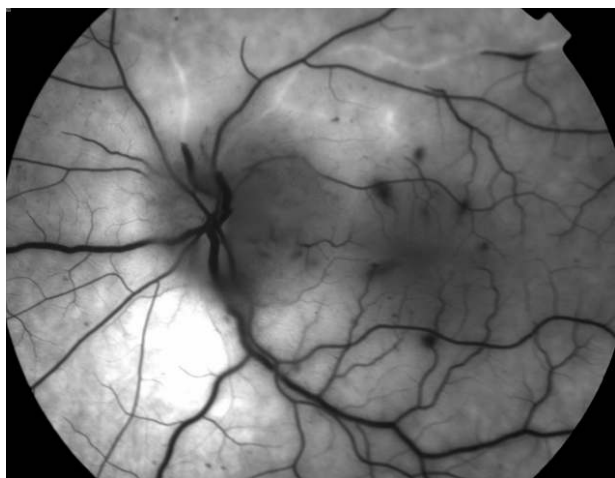
174 Fig.3. Fluorescein angiogram of (a) right eye and (b) left eye demonstrating choroidal filling
175 and lack of filling along arterioles and venules at 8 minutes.

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