

Ophthalmic Manifestations of Haematological Disorders

KS Charles¹, N Leelah², L Boodoo², DC Murray³

ABSTRACT

Five case histories are presented. Waldenstrom's macroglobulinaemia caused bilateral central retinal vein occlusion, proptosis was the presenting feature of retro-orbital plasmacytoma in relapsed multiple myeloma, a red painful eye was due to neovascular glaucoma in primary polycythaemia, bilateral VIth nerve palsy caused convergent squint and diplopia in meningeal relapse of acute lymphoblastic leukaemia and lymphoma of the eyelid caused complete ptosis. Interdisciplinary management is described. Ophthalmological lesions in haematological disease should be promptly recognized and managed. Collaboration between ophthalmology and haematology departments may be effective for palliative management.

Key words: Haematological, manifestations, ophthalmological

Manifestaciones Oftálmicas de Trastornos Hematológicos

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RESUMEN

Se presentan cinco historias de casos. La macroglobulinemia de Waldenström causó la obstrucción bilateral de la vena central de la retina; la proptosis fue la primera manifestación del plasmacitoma retro-orbital en la recaída del mieloma; un ojo enrojecido con dolor debido a un glaucoma neovascular en una policitemia primaria; la parálisis del 7mo nervio bilateral causó estrabismo convergente y diplopía en la recaída meníngea de la leucemia linfoblástica aguda; y un linfoma del párpado causó ptosis total. Se describe el tratamiento multidisciplinario. Es necesario reconocer y tratar lo antes posible las lesiones oftalmológicas en las enfermedades hematológicas. La colaboración entre los departamentos de oftalmología y hematología puede ser efectiva a la hora de buscar tratamientos paliativos.

Palabras claves: Hematológica, manifestaciones, oftalmológica

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INTRODUCTION

Haematological disorders are associated with numerous manifestations in the eye (1). Severe anaemia due to iron, folate or vitamin B₁₂ deficiencies could cause 'anaemic retinopathy' with intraretinal haemorrhages, Roth's spot haemorrhages, cotton wool spots, retinal exudates, venous dilatation and optic

nerve pallor. Proliferative retinopathy in sickle cell anaemia may be complicated by retinal detachment or vitreous haemorrhage. Severe thrombocytopenia causes intraretinal haemorrhages. Leukaemias and lymphomas may infiltrate structures in the eye or cause changes associated with hyperviscosity, anaemia or thrombocytopenia. Thrombophilic states like antithrombin deficiency, protein S deficiency, protein C deficiency and the antiphospholipid antibody syndrome cause venous or arterial occlusion. Plasma cell dyscrasias cause the hyperviscosity syndrome and may infiltrate structures. Myeloproliferative neoplasms such as primary polycythaemia and primary thrombocythaemia cause hyperviscosity, vascular occlusions, haemorrhages and glaucoma.

The potential for visual impairment complicating the course of a chronic, debilitating illness is real. Neurophthalmic/central nervous system (CNS) signs often signal a poor prognosis necessitating prompt diagnosis, counselling and interdisciplinary management (1). Five cases of ophthalmolo-

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gical manifestations in haematology disorders and their management are presented.

CASE REPORTS

Case 1: A 61-year old male presented to the ophthalmologist with a two-month history of blurred vision in the right eye and reduced vision in the left eye. He had no history of hypertension, diabetes or hyperlipidaemia and was a non-smoker. He had been investigated for transient thrombocytopenia three years prior to this presentation. Best corrected visual acuity was 20/40 in the right eye and 20/200 in the left. Funduscopy revealed dilated veins and multiple retinal haemorrhages bilaterally (Figs. 1a, 1b) consistent with bilateral central retinal

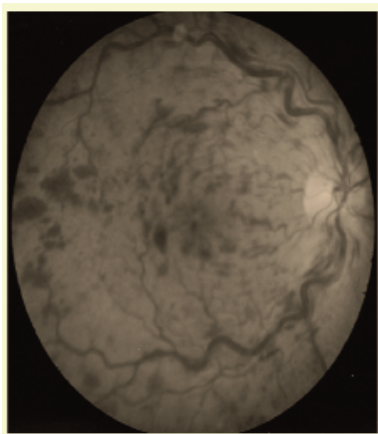


Fig. 1a: Right eye funduscopy showing venous dilatation and retinal haemorrhages due to central retinal vein occlusion in case 1.

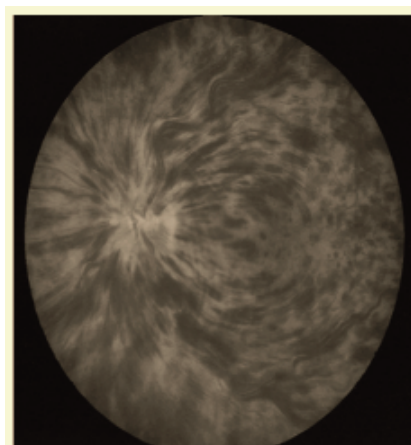


Fig. 1b: More marked haemorrhages and venous dilatation from simultaneous central retinal vein occlusion in the left eye.

vein occlusion (CRVO). There was a left relative afferent pupillary defect (RAPD). He was referred to the haematology department for further investigations. He reported weight loss in the preceding six months and episodes of nocturnal fever. He was found to have mild anaemia (Hb 11.6 g/dL), bone mar-

row lymphocytosis and intra-abdominal lymphadenopathy on computed tomography (CT) scan. Biopsy of an inguinal lymph node showed diffuse infiltration with small lymphocytes. The presence of a large serum IgM monoclonal protein (Fig. 1c) confirmed a diagnosis of Waldenstrom's macroglobulinaemia.

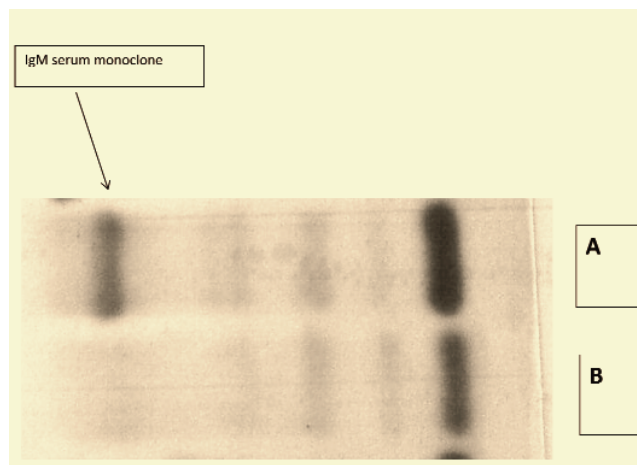


Fig. 1c: Serum protein electrophoresis showing a strong monoclonal IgM band consistent with Waldenstrom's macroglobulinaemia.

He was treated with six monthly courses of cyclophosphamide, hydroxydaunorubicin, vincristine (oncovin) and prednisolone (CHOP). He achieved complete remission from Waldenstrom's macroglobulinaemia and best corrected visual acuity improved to 20/32 in the right eye and 20/40 in the left. He subsequently developed immune thrombocytopenia and died from relapsed and refractory Waldenstrom's macroglobulinaemia nine years after initial diagnosis.

Case 2: A 59-year old man was diagnosed with IgA multiple myeloma on the basis of a serum IgA monoclonone, lytic bone lesions on radiological survey and bone marrow plasmacytosis > 60%. Remission was attained with infusional chemotherapy (vincristine, adriamycin and dexamethasone) of which he received six cycles. Two months after cycle 6, he presented with "bulging right eye" for one month. Visual acuity was 20/32 in the right eye and 20/10 in the left. There was a right RAPD and both horizontal and vertical diplopia. He had non-axial proptosis with inferotemporal displacement of the right globe. Intraocular pressure was normal (09 mmHg) bilaterally and fundus examination was normal. Computed tomography scan showed a right retro-orbital mass invading the sphenoid sinus with bone destruction (Fig. 2). Biopsy confirmed plasmacytoma. Despite surgical decompression, following which proptosis resolved significantly, and recommencement of anti-myeloma therapy, he succumbed to refractory myeloma within four months.

Case 3: A 72-year old female presented to her ophthalmologist with a one-week history of a painful, red right eye. She was

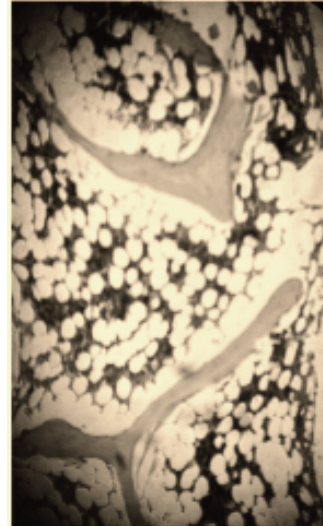


Fig. 2: Computed tomography scan of orbit showing right retro-orbital plasmacytoma and eroding into the paranasal sinuses in case 2.

with erythroid hyperplasia and iron depletion confirming a myeloproliferative neoplasm, primary polycythaemia with iron depletion. The myeloproliferative disorder was controlled using hydroxyurea tablets for myelosuppression and aspirin for antiplatelet activity.

Ophthalmological treatment was with latanoprost drops to the right eye, prednisolone 1%, atropine 1%, brimonidine, timolol 0.5% and latanoprost drops to the left eye and acetazolamide tablets 250 mg orally four times daily. She had bilateral panretinal photocoagulation. Visual acuity in the right eye decreased by one line to 20/100 but improved to 20/40 in the left. Intraocular pressures improved to 17 mmHg and 23 mmHg, respectively. Simultaneously, haematological remission was achieved. Unfortunately, the patient died of secondary acute myeloblastic leukaemia two years after initial diagnosis.



Case 4: A 21-year old man was referred for extreme leukocytosis, anaemia and thrombocytopaenia. Total white cell count was $106 \times 10^9/L$, haemoglobin 5.5 g/dL and platelets $18 \times 10^9/L$. Both peripheral blood film and bone marrow aspirate showed small, round malignant lymphoblasts with high nucleocytoplasmic ratio, round nuclei and indistinct nucleoli. Cerebrospinal fluid (CSF) analysis was normal. A diagnosis of acute lymphoblastic leukaemia (ALL) was made and he was treated on a modified ECOG/LARSON chemotherapy protocol. This included intrathecal methotrexate (ITMTX) and cranial irradiation to protect against CNS relapse. He had achieved complete remission and was receiving maintenance treatment when he experienced visual blurring and ‘crossing’ of the eyes (Fig. 4a). Examination revealed bilateral nasal deviation and limitation of abduction of both eyes. He had diplopia in all directions of gaze. Visual acuity was 20/15 in the right eye with light perception only in the left. Examination of the CSF showed the presence of small lymphoblasts (Fig. 4b). There was bilateral VIth (abducens) cranial nerve

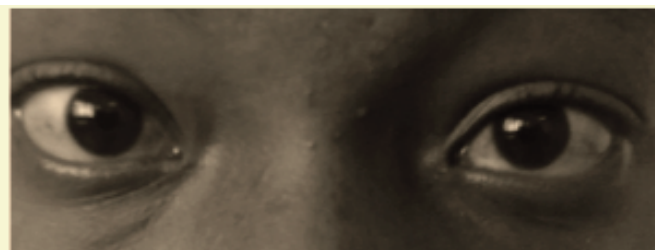


Fig. 4a: Bilateral convergent strabismus in case 4.



Fig. 5: Complete ptosis of left upper eyelid infiltrated by lymphoma in case 5.

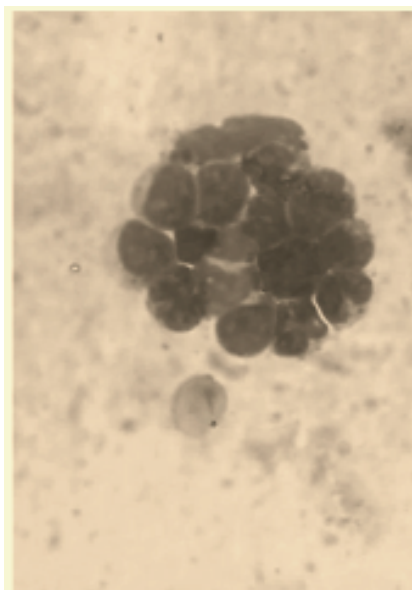


Fig. 4b: Malignant lymphoblasts in cerebrospinal fluid.

palsy secondary to leukaemic infiltration of the meninges. He was treated with ITMTX and systemic re-induction chemotherapy. After six weekly injections of ITMTX, the CSF was normal and eye signs had resolved significantly. Visual acuity was now 20/15 in the right eye and 'counting fingers' in the left. Unfortunately, 19 months after initial diagnosis, he presented with headache, facial twitching and vomiting. He had severe leukocytosis, anaemia and thrombocytopenia. Combined CNS and bone marrow relapse was confirmed. He succumbed within days.

Case 5: A 72-year old woman was referred to the ophthalmology clinic for progressive swelling over the left upper eye lid over a 10-month period. She had no systemic symptoms. There was complete closure of the left eye (Fig. 5) but normal extra-ocular motility. Visual acuity was 20/15 in the right eye and 20/40 in the left. Eye lid biopsy revealed CD20 positive small cell lymphoma and she was referred to the haematology department. Clinical staging with CT scan of chest, abdomen, pelvis and bone marrow examination showed no evidence of lymphoma elsewhere. She has so far received eight cycles of cyclophosphamide 100 mg orally daily for two weeks every month. Although visual acuity has not been rechecked since

starting treatment, there has been a significant reduction in lid swelling and a return to eye opening.

DISCUSSION

Waldenstrom's macroglobulinaemia is a clonal disorder of lymphoplasmacytoid cells which is diagnosed by the finding of bone marrow lymphocytosis and a serum IgM monoclonal protein. Central retinal vein occlusion is caused by hyperviscosity associated with high circulating concentrations of the large pentameric IgM molecule. Nevertheless, bilateral CRVO seen in case 1 is a rare presenting feature with only a few cases reported in the literature (2). Acute treatment is with plasmapheresis followed by chronic suppression of IgM production with chemotherapy, purine analogues, monoclonal antibody therapy or autologous stem cell transplantation. Median survival for Waldenstrom's macroglobulinaemia is in the region of five years. As a result of concurrent systemic and local ophthalmological treatment, case 1 survived for nine years after diagnosis with preserved vision.

Orbital plasmacytoma are rare plasma cell tumours which may be solitary or occur as part of systemic multiple myeloma (3). These may arise from bone (osseous) or soft tissue (extramedullary). Such tumours may cause proptosis as the presenting feature of myeloma, during its course or at relapse (4). Orbital plasmacytoma in IgA myeloma is rare and has been reported only a few times in the literature (5). Therapeutic options include orbital surgery and radiotherapy along with systemic myeloma therapy. The patient in case 4 declined radiotherapy for fear of blindness. Complete surgical resection was not possible because of the location and infiltration of the orbital plasmacytoma. Its occurrence so early after initial treatment for myeloma suggested chemoresistance. Failure of response to subsequent treatment was predictable in this situation.

Myeloproliferative neoplasms like primary (essential) thrombocythaemia and primary polycythaemia cause vascular occlusion, neovascularization and neovascular glaucoma. As in case 3, laser panretinal photocoagulation, glaucoma medications and myelosuppressive therapy could preserve sight (6).

Cranial nerve palsies in patients with ALL should raise the possibility of meningeal infiltration and prompt examination of the CSF (7). Leukaemic infiltration of the meninges was demonstrated as the cause of bilateral abducens nerve

palsy in case 4. The majority of patients with meningeal relapse of ALL attain CSF clearance with treatment. However, bone marrow relapse is inevitable, and response to treatment and overall survival is poor (8).

Small cell lymphoma of the eyelid is uncommon (9). Where disease is localized, radiotherapy is effective but carries the risks of redness, swelling, dry eyes, infections, corneal scarring, glaucoma, cataracts and damage to the retina or optic nerve (10). The patient in case 5 has responded favourably to an oral alkylating agent with no side effects. Monoclonal anti-CD20 therapy is an option in the event of relapse.

In conclusion, five cases of haematological disorders manifesting in the eye have been presented. Combined ophthalmological and haematological management to preserve quality of life in patients already stricken with chronic, malignant or debilitating disease is highlighted. Correctable or treatable visual loss should be detected and attended to (11). The possibility of an underlying haematological disorder should be considered in cases of apparent primary ophthalmological disorders.

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