Case report

Subjective intermittent colour vision loss as the initial presentation of chronic myeloid leukemia

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ABSTRACT

Purpose: To report a case of subjective intermittent loss of bilateral colour vision and episodic white-out vision in a patient with undiagnosed chronic myeloid leukemia (CML).

Observations: A patient initially diagnosed with diabetic retinopathy presented with a chief complaint of subjective intermittent loss of colour vision in both eyes, as well as intermittent bilateral white-out vision. These symptoms previously went uninvestigated until a thorough history revealed concurrent constitutional symptoms including recent night sweats and fevers. Closer fundus examination revealed that the lesions previously thought to be diabetic retinal hemorrhages were Roth spots.

Conclusions: and Importance: An unusual chief complaint of colour vision loss and multiple Roth spots in the context of chronic night sweats and fevers prompted further workup. A CBC with differential revealed a markedly increased WBC count and the patient was diagnosed with CML. Cytoreduction therapy led to complete resolution of the patient’s visual symptoms and a return to normal WBC count at the most recent follow up appointment. We report, to our knowledge, the only case of colour vision loss as the initial presenting symptom of CML in the current literature, and reiterate the importance of a thorough history, neuro-ophthalmic examination and relevant investigations in patients with unusual visual symptoms, including intermittent loss of colour vision. In this case, we speculate that hyperviscosity syndrome secondary to CML was the cause of this patient’s peculiar visual disturbance.

1. Introduction

Leukemia encompasses several malignant proliferative disorders of leukopoietic bone marrow stem cells. It is characterized by overcrowding of neoplastic leukocytes in the bone marrow, with subsequent widespread infiltration of organs, tissues and peripheral blood. Ocular involvement may be a result of direct infiltration by neoplastic cells or secondary hematologic abnormalities associated with the disorder, which can lead to anemia and hyperviscosity syndrome.

Chronic myeloid leukemia (CML) is one such variant of leukemia that results in increased proliferation of granulocytic cells lines. CML is estimated to account for 15–20% of adult leukemias, with an incidence rate of 1.9 cases per 100,000 people per year, and a median age of diagnosis of 65 years. There is a slight male predominance.

Ophthalmologists play a unique role in caring for these patients in that ocular manifestations may rarely be the only presenting sign of CML in this population. Furthermore, patients who have ophthalmic manifestations of CML have been reported to have lower 5-year survival rates, underscoring the importance of prompt investigation and treatment in these patients. Clinical signs include vascular changes, such as retinal vein tortuosity or obstruction, dot-blot hemorrhages, flame-shaped hemorrhages, and Roth spots. We present, for the first time in the English literature, a case of a patient with undiagnosed CML who initially presented to the ophthalmology clinic with bilateral subjective intermittent loss of colour vision and episodic white-out vision.

2. Case report

A 70-year-old man initially presented to the ophthalmology service at the University of Ottawa complaining of sudden bilateral decrease in vision to a best-corrected visual acuity (BCVA) of 20/40 OD and 20/50 OS. The ophthalmologist noted mild non-proliferative diabetic retinopathy, including microaneurysms, dot blot hemorrhages, and macular edema and referred the patient to a retina specialist. The patient then presented to the neuro-ophthalmology subspecialty clinic, having been referred months before for a separate complaint of convergence disturbance.
insufficiency, which had resolved by this time. It was at this appointment, however, that a thorough history and further investigations were pursued due to a new, unusual visual complaint along with a more detailed fundus examination revealing previously undetected findings.

The patient had a complex medical history, including type 2 diabetes, hypertension, dyslipidemia, coronary artery disease with a history of 2-vessel coronary artery bypass, and a lung adenocarcinoma treated with lobectomy.

He complained of a few-month history of bilateral intermittent blurry vision, as well as a unique complaint of a 2-month history of subjective total colour vision loss upon waking, which would then gradually return to his baseline blurry vision throughout the day. Initially, the loss of colour and difficulty with distinguishing hues lasted 1.5–2 hours but had progressed over the past 2 months to lasting half a day. He also complained of a few episodes of gradual onset of white-out vision lasting 7 hours before returning to baseline.

On review of systems, the patient endorsed jaw claudication, occasional fevers of 101°F 1–2 times per week for the past few weeks, and drenching night sweats for the past few years. He denied fatigue, weight loss, or anorexia. There were no other focal neurological symptoms, headache, scalp tenderness, or new arthralgias or myalgias.

On examination, BCVA was 20/50 OU, there was no afferent pupillary defect, and colour vision testing using Ishihara plates were normal OU. The remainder of the neuro-ophthalmic examination, including confrontational visual fields, extraocular muscle function, saccades, smooth pursuit, cranial nerve and anterior segment examinations were within normal limits. There was no nystagmus. On fundoscopy, the optic nerve demonstrated cup-to-disc ratios of 0.3 OD and 0.4 OS, with mild temporal pallor and a temporal slope, respectively. There was bilateral macular edema. Notably, there were multiple scattered Roth spots consisting of intraretinal hemorrhages surrounding white dots in the posterior pole of both eyes. (Fig. 1A and B).

Humphrey Visual Field 30-2 was within normal limits.

Given the unusual history of subjective intermittent loss of colour vision and white-out vision lasting several hours to half a day, chronic night sweats, new fevers, and Roth Spots on posterior segment examination, the neuro-ophthalmologist was concerned about a lymphoproliferative process. A CBC with differential was ordered that same day. Although less likely, the jaw claudication in a patient this age raised the suspicion for giant cell arteritis as well, and an ESR and CRP were also ordered.

The patient was called by the emergency department later that evening to be assessed by hematology. His WBC was 330.1 × 10⁹/L with 16.51 × 10⁹/L blasts. ESR was 23 mm/hr and CRP was 28.2 mg/L. The patient was admitted to hospital, and a bone marrow biopsy confirmed the diagnosis of chronic myeloid leukemia (CML) in the chronic phase. Marrow cytogenetics revealed Philadelphia chromosome positivity. Leukapheresis was done 1 day after admission. He was started on hydroxyurea for initial rapid cytoreduction, and later switched to imatinib mesylate.

At his 2-month ophthalmology follow-up, BCVA was 20/40 OU, and his symptoms of intermittent colour vision loss and white-out vision had resolved completely. He continued to be followed by the retina service for anti-VEGF injections for diabetic macular edema, as well as his hematologist. His latest bloodwork in March 2017 showed a WBC count of 6 × 10⁹/L.

3. Discussion

Ocular manifestations of leukemia, first described by Liebreich in 1863, may be seen in up to 40–50% of patients at the time of diagnosis, though they are often asymptomatic. In CML, only 5–10% of patients present with ocular symptoms. In his review of ocular manifestations of leukemia, Rosenthal included tortuous dilated retinal vessels, retinal vascular sheathing, hard exudates, cotton wool spots, retinal hemorrhages, microaneurysms, neovascularization, and lid, orbital, optic nerve, retinal and choroidal infiltration as possible signs. Indeed, several studies reporting these findings as the initial presenting symptoms of CML or symptoms in association with CML have been published.

Rosenthal noted that intraretinal hemorrhages may contain a white dot within their center, also known as Roth spots, which could represent cellular debris, capillary emboli or accumulation of leukemic cells. In a study by Dhasmana et al. looking at 102 patients diagnosed with leukemia, the most commonly noted posterior segment finding was intra-retinal hemorrhages without white dot centers in 31.9%, followed by Roth spots in 25.4%. Our patient exhibited multiple Roth spots in the posterior pole of both eyes, which was initially mistaken for diabetic retinopathy, given that the patient had a 25-year history of type 2 diabetes and other diabetic findings, including macular edema.

Our patient presented with complaints of waking up with subjective loss of colour vision in both eyes, with gradual resolution back to his baseline of slightly blurry, but full colour vision throughout the day. This initially lasted for 1.5–2 hours daily but progressed to lasting half a day by the time he presented to the neuro-ophthalmology clinic. Of note, the Ishihara colour test was normal because his colour vision had returned to normal at the time of the clinical assessment. Additionally, he experienced intermittent whitening out of his entire visual field in both eyes, which often lasted up to several hours. We speculate that these symptoms, along with the finding of Roth spots, were due to hyperleukocytosis and hyperviscosity syndrome. These states are known to cause sludging of circulating leukemic blasts within the microvasculature, leading to mechanical obstruction and decreased circulation within small vessels. We hypothesize that this sludging, potentiated by laying supine during sleep, may have led to intermittent ischemia of the optic nerves. The visual cortex, specifically the bilateral occipitotemporal regions, may have been affected although it is less likely given the

Fig. 1. A, B - Colour Fundus Photos - Right and left eyes, respectively, showing multiple intraretinal hemorrhages located in the posterior poles. Notably, some of these hemorrhages display white centers, consistent with Roth Spots.
absence of other concurrent visual defects such as visual field abnormalities or visual agnosia. Color vision may have been predominantly affected because it is an especially sensitive psychophysical parameter, thus making it more susceptible to ischemic pathology earlier on when compared to other afferent processes.

Intermittent loss of colour vision with greyscale upon waking and intermittent white-out of vision in association with CML has not yet been reported in the literature. It is an unusual and esoteric complaint that may easily be dismissed in a busy ophthalmology clinic. In our case, a thorough history and neuro-ophthalmic examination revealed that these peculiar symptoms appeared in the context of constitutional symptoms and the presence of Roth spots. This raised the suspicion for a myeloproliferative disorder, and a CBC with differential was promptly ordered. Had this patient’s otherwise atypical symptoms not been seriously considered and investigated, it is likely that delayed diagnosis of his CML would have led to a poorer prognosis, especially if the disease had presented in the acute blast crisis phase. Ophthalmologists play a vital role in being able to diagnose CML if there are initial ocular presenting signs and symptoms. It is thus important to be aware of these associations and undertake appropriate systemic investigations in these cases.

Patient consent

1. This report does not contain any personal information that could lead to the identification of the patient.

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