

Case report

A unique case of chronic myeloid leukemia presenting as monocular vision loss with unilateral retinopathy

Mark P. Seraly^{a,*}, Sumeet K. Gupta^a, Inderjit Mehmi^{a,b}, Lauren Veltri^{a,b}, Ghassan R. Ghorayeb^a^a West Virginia University School of Medicine, 1 Medical Center Dr, Morgantown, WV, USA^b West Virginia University Cancer Institute, Section of Hematology/Oncology, 1 Medical Center Dr, Morgantown, WV, USA

ARTICLE INFO

Keywords:

BCR-ABL1

Chronic myeloid leukemia

Hasford

Imatinib

Monocular vision loss

Sokal

Unilateral retinopathy

ABSTRACT

Purpose: To report a case of unilateral leukemic retinopathy secondary to chronic myeloid leukemia (CML).
Observations: Patient presented to clinic with a visual acuity (VA) of 20/200 in the right eye (OD) after several months of progressive monocular vision loss and was found to have dense pre-retinal hemorrhage. Patient underwent 23-gauge pars plana vitrectomy to clear the preretinal hemorrhage along with a complex macula-off retinal detachment repair to address retinal tear and multilayer retinal hemorrhage. The patient was subsequently diagnosed with CML as she was found to be positive for the fusion protein of break point cluster gene (BCR) with Abelson tyrosine kinase (ABL1), BCR-ABL1, upon systemic work-up. Imatinib therapy resulted in complete hematologic and cytogenetic resolution after one month, however, the patient's vision remained unchanged six months after surgery.

Conclusion and importance: To the authors' knowledge, this is the first reported case of unilateral leukemic retinopathy secondary to low risk CML, as determined by the Sokal and Hasford prognostic scoring systems. CML should be included in the differential diagnosis of patients with progressive monocular vision loss with suspicious multi-layer retinal compromise.

1. Introduction

Retinopathy secondary to leukemic neoplasia consists of an extensive list of ocular manifestations that have been well described over the past 50 years.¹ Leukemia alters the integrity of retinal and choroidal vasculature, which leads to neovascularization, hemorrhage, and neoplastic infiltrate in potentially all ocular structures.¹ Chronic myeloid leukemia (CML) is an indolent neoplasia often characterized by a 9/22 chromosomal translocation which results in subsequent fusion of the break point cluster gene (BCR) with the Abelson tyrosine kinase (ABL1) resulting in BCR-ABL1, a fusion protein and oncogene.² Patients with CML often present with fatigue, weight-loss, and hepatosplenomegaly while isolated ocular findings occur in only a small minority.^{1,3} Tyrosine kinase inhibitor (TKI), Imatinib, and other new generation (NG)-TKIs such as Nilotinib, Dasatinib, and Radotinib are considered first line therapy in the management of patients with CML.⁴ Clinical decisions are often guided by the Sokal and Hasford prognostic scoring systems, which utilize their respective validated algorithms based upon patient age, spleen size, platelet count, and several peripheral cell counts to stratify patients into low, intermediate, and high risk disease categories.^{5,6} NG-TKIs have been shown to be superior to Imatinib in high-

risk CML patients.⁴

To date, nine cases have been reported in which the ocular manifestations of CML were the only presenting signs of the disease, however, in all of these cases, ocular involvement was described bilaterally.^{7–11} In addition, the disease risk stratification of these patients with CML and symptomatic ocular presentations was not discussed. To the best of our knowledge, this is the first reported case of leukemic retinopathy secondary to low risk CML, as determined by the Sokal and Hasford scoring systems, which manifested as monocular vision loss with unilateral ocular involvement that included retinal detachment and multi-layer hemorrhage.

2. Case report

A 63-year old Caucasian woman was referred to the West Virginia University Eye Institute after one month of progressive vision loss in the right eye (OD), associated with dark reticular curtain-like floaters. The patient's extraocular movements were intact and her visual acuity was 20/200 OD and 20/40 in the left eye (OS). The patient had an afferent pupillary defect OD and visual field testing of that eye revealed extensive scotoma with only minimal sparing of the inferior field.

* Corresponding author. 13 Willow Lane, Morgantown, WV, 26505, USA.

E-mail address: mpseraly@mix.wvu.edu (M.P. Seraly).

<https://doi.org/10.1016/j.ajoc.2019.02.003>

Received 18 July 2018; Received in revised form 8 November 2018; Accepted 6 February 2019

Available online 15 February 2019

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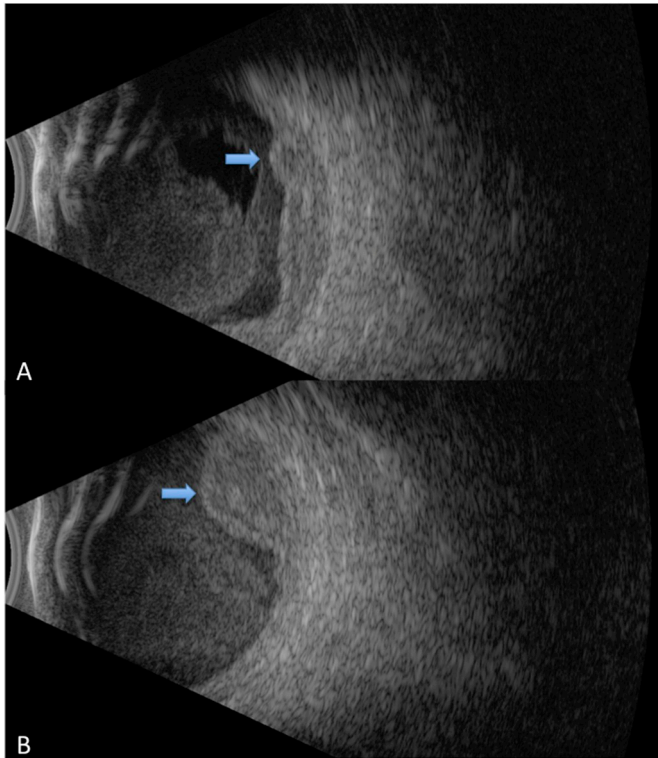


Fig. 1. Pre-operative B scan ultrasonography of the right eye (OD) revealing multi-layer hemorrhage A) and a lesion concerning for localized intraocular mass or subretinal hemorrhage B).

Examination of the anterior segment revealed evidence of vitreous hemorrhage OD. Dilated fundoscopic examination was limited secondary to the presence of a dense preretinal hemorrhage and B-scan ultrasonography raised the additional concern of a subretinal lesion (Fig. 1). Examination of the fellow eye was unremarkable.

The next day, the patient underwent 23-gauge pars plana vitrectomy. Upon clearance of the preretinal hemorrhage, the surgeons made note of a localized subretinal mass or hemorrhage with additional inferior retinal tears, and an associated retinal detachment. Internal and external drainage were unsuccessful in completely draining the subretinal blood. Vitreous samples obtained from the procedure were sent for cytology and while malignant cells were not discovered, the vitreous humor appeared suspicious, and not characteristic of a simple hemorrhage. Flow cytometry was not obtained. Due to the additional concern, the patient was referred for oncologic work up.

The patient underwent systemic oncologic evaluation with appropriate labs and imaging studies. The patient was found to have a leukocytosis of 126,500 with elevated absolute counts of neutrophils, lymphocytes, and basophils. One-year prior, the patient's blood work demonstrated normal blood counts. The diagnosis of CML was confirmed with genetic testing which revealed BCR-ABL1 showing a major (P210) protein, BCR-ABL1 IS positivity of 61.57%, and a bone marrow aspirate which revealed maturing granulocytic and erythroid precursors with rare cells suspicious for megakaryocytes. The patient's imaging studies did not reveal systemic disease and she was categorized as low-risk with Sokal and Hasford scores of 0.73 and 676.57, respectively.

The patient's past cardiac and pulmonary comorbidities were relative contradictions to Nilotinib and Dasatinib. The patient was started on 400mg Imatinib daily and demonstrated complete hematologic response with normalization of blood counts at one month. The patient's hematologic response was sustained at 3 months and her cytogenetic response was adequate with BCR-ABL1 at 5.26%, well below the 10% threshold considered therapeutic. At six months, BCR-ABL1 was

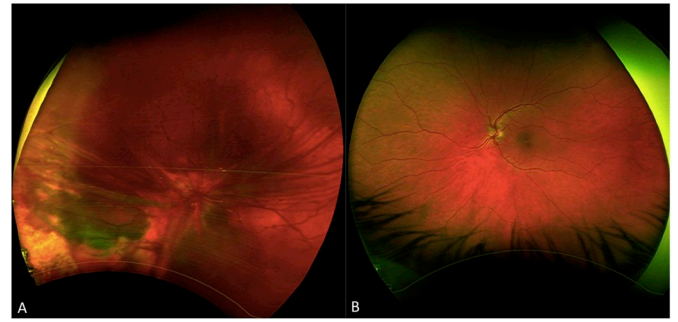


Fig. 2. Fundus photograph taken one-month status post surgical intervention demonstrating stable retinal scar OD A) and normal healthy retina in the left eye (OS) B).

positive at 0.8514%, which again demonstrated sustained therapeutic response.

The patient's one-month postoperative eye exam revealed a submacular scar and the patient had no improvement in visual acuity (Fig. 2). Optical coherence tomography demonstrated loss of foveal depression and severe disruption the macular architecture (Fig. 3). Ultimately, seven months after the surgery the patient developed a total retinal detachment secondary to subretinal oil infiltration, a surgical complication. Further surgical care was deemed of minimal prognostic value for further visual recovery.

3. Discussion

This case report highlights a patient who presented with monocular vision loss and a unique combination of unilateral multi-layer hemorrhage, retinal tear, and retinal detachment secondary to CML. The patient had low risk disease per the Sokal and Hasford scoring systems, and attained hematologic normalization and major cytogenetic response after one month of Imatinib therapy. Hochaus et al. demonstrated the long term efficacy of Imatinib therapy in the management of patients with CML.¹² 49.1% of patients achieved complete cytogenetic response (CCyR) at 6 months post treatment and 82.8% of patients retained CCyR after 11 years. Interestingly, the overall survival rate of patients with high Sokal scores was only 68.6% compared to patients with intermediate and low Sokal scores who had overall survival rates of 80.3% and 89.9%, respectively.¹² The Hasford scoring system has

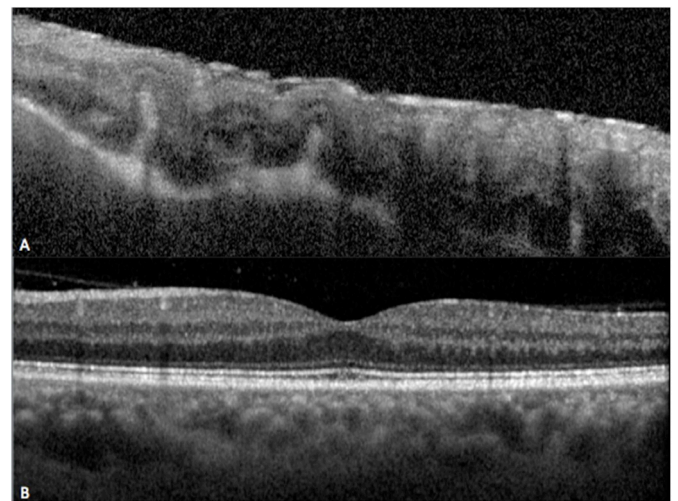


Fig. 3. Heidelberg optical coherence tomography revealing an apparently attached retina with epiretinal membrane, loss of foveal depression, disruption of macular architecture, and underlying choroidal folds OD A) Foveal depression intact with normal macular architecture OS B).

also demonstrated great strength in prognosticating patients with CML into low, intermediate, and high risk disease groups.⁶ Patients with low risk CML had a median survival rate of 96 months compared to median survival durations of 65 months and 45 months for the intermediate and high risk groups, respectively.⁶

While the Sokal and Hasford scoring systems have reliably predicted therapeutic response and survival rates in patients with CML, the scores have never been correlated with the ocular manifestations of the disease.^{5,6} In patients with CML who present with isolated ocular manifestations, TKI therapy with concomitant ocular surgical intervention has often resulted in improvement in visual acuity and other ocular symptoms.^{7–11} Huang et al. reported a case of 30 year old male who presented with bilateral multilayer retinal hemorrhage with visual acuities of 20/20 OD and 20/100 OS.⁷ After 12 months of cytoreductive therapy, the patient had complete hematologic and cytogenetic responses along with improvement of visual acuity to 20/30 OS.⁷ Similarly, TKI therapy with concomitant pars plana vitrectomy, endophotocoagulation, and gas-air exchange resulted in VA improvement of 20/25 in both eyes, in a patient with CML who presented with bilateral optic disk neovascularization.¹¹

Ocular manifestations of CML have been associated with poor overall survival, as demonstrated by Ohkoshi et al., who found that the five-year survival rate was only 21.4%; meanwhile the five-year survival in patients without ocular manifestations was over twice as high.¹³ There is a great paucity of evidence in the literature, however, for which factors determine visual prognosis in patients with ocular CML. Our patient had 20/200 vision OD with unilateral retinal detachment, retinal tear, and multilayer retinal hemorrhage. Despite complete hematologic resolution and therapeutic cytogenetic response after Imatinib treatment, the patient's VA remained poor at 20/200 for seven months until her ultimate total retinal detachment secondary to surgical complication. It is important to note that the patient had experienced vision loss for nearly one month prior to receiving surgical intervention. The size and duration of the patient's retinal detachment likely affected the patient's visual outcome, as these are known risk factors for poor visual prognosis.¹⁴ This case demonstrates that despite appropriate medical and surgical management, ocular improvement may not always be feasible given the duration and extent of retinal damage in eyes affected by CML retinopathy.

4. Conclusion

To the authors' best knowledge, this represents the first reported case of unilateral leukemic retinopathy secondary to low risk CML, as predicted by the Sokal and Hasford scoring systems. CML should be included in the differential diagnosis of patients with progressive monocular vision loss with suspicious unilateral multi-layer retinal compromise. Further investigation is required to elucidate the connection between CML ocular manifestations, visual prognosis, and disease risk stratification.

Patient consent

Informed consent was obtained from this patient in writing for publication of her case details.

Conflicts of interest

The authors have no financial disclosures.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Funding

No funding or grant support.

Acknowledgements

None.

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