



## Bilateral vision loss as initial presentation of chronic myeloid leukemia in a young adult: A case report and review of the literature

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### ABSTRACT

**Purpose:** To report a case of bilateral vision loss as the primary presenting symptom of chronic myeloid leukemia in a young adult.

**Observations:** The 28-year-old male patient presented to clinic with visual acuity of 20/200 in both eyes after several months of episodic bilateral vision loss. Intraretinal and pre-retinal hemorrhages were appreciated, as well as Roth spots and peripheral neovascularization. Initial lab findings were consistent with a diagnosis of acute myeloid leukemia, later, upon bone marrow examination, the diagnosis was edited to chronic myeloid leukemia. Dasatinib therapy resulted in a complete hematologic resolution after six weeks. After intravitreal injections of bevacizumab in both eyes, visual acuity improved to 20/25 in the right eye and 20/20 in the left eye.

**Conclusion and importance:** After review, this is one of only a few reported cases of bilateral blurry vision as the primary presenting symptom of chronic myeloid leukemia in a young adult. Because visual disturbances occur more frequently in acute myeloid leukemia, and lab results may be inconclusive, careful consideration should be given to differentiate myelogenous leukemias, as the acute and chronic subtypes may present similarly.

### 1. Introduction

Chronic myeloid leukemia (CML) is classified as a myeloproliferative neoplasm most commonly characterized with the Philadelphia chromosome t(9; 22).<sup>1</sup> This translocation results from a fusion of the Abelson tyrosine kinase gene on chromosome 9 with the breakpoint cluster gene on chromosome 22.<sup>1</sup> CML affects the bone marrow and peripheral blood and is classified into either the blast, accelerated, or the most common, chronic phase.<sup>2</sup> Typical presenting symptoms of CML may include fatigue, night sweats, malaise, weight loss, low fever, weakness, and left upper quadrant discomfort.<sup>3,4</sup>

Less frequently, leukemic retinopathy, secondary to choroidal and retinal vascular disturbances, can lead to neovascularization, retinal detachment, retinal hemorrhage, and direct leukemic infiltration of the retina.<sup>5</sup> Patients with these changes have been well documented for decades; however, few cases have reported bilateral blurry vision as the primary presenting symptom of CML in a young adult.<sup>5-16</sup> We present a rare case of a young adult patient with recently diagnosed CML whose primary presenting symptom was bilateral blurry vision. We also include a review of other reported cases of CML with ocular findings as the

initial presentation.

### 2. Case report

The patient is a 28-year-old male with a history of shingles and hypertension who presented to urgent care with concerns about recurrent episodes of blurred vision lasting three to four weeks. The first episode of blurred vision began in the right eye (OD) three months before presentation. Interestingly, the patient reported that blurred vision OD began after taking 12.5mg of diphenhydramine and resolved within four weeks of discontinued use. The second episode began three weeks before presentation in the top right quadrant OD, which the patient also associated with diphenhydramine use. After taking the same medication on the morning of the presentation, he noticed blurred vision of the top left quadrant of his left eye (OS) with persistent OD symptoms. He denied a significant history of eye disease. Family history was notable for colon cancer. On the physical exam, his visual acuity (VA) without correction was 20/200 in both eyes (OU). He was then referred to ophthalmology.

On ophthalmic examination, visual acuity was initially noted as counting fingers at three feet OD and five feet OS. The confrontational

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fields were restricted. The anterior segment exam was within normal limits; however, sub-inner limiting membrane, intraretinal and pre-retinal hemorrhages were noted OU. The vitreous revealed scant hemorrhage, settling inferiorly (Fig. 1). The vessels were tortuous, with thick boxcarring and beading OU. Macular pre- and intraretinal hemorrhages were also present OU. The periphery revealed white-centered hemorrhages (Roth spots) and neovascularization of the retina. Initial work-up by the ophthalmologist suggested concern for acute bacterial endocarditis, lupus, diabetes, leukemia, or other infectious causes. The patient was referred to the emergency room for further hematologic workup and evaluation with expected admission to the hospital.

Upon physical exam at the emergency department, the liver was palpated approximately 2 cm below the costal margin, and non-tender splenomegaly was appreciated. Furthermore, the patient admitted to recent excessive alcohol intake due to significant life stressors.

A comprehensive metabolic panel, complete blood count with differential and several other lab tests were performed. White blood cells (258.59 K/ $\mu$ L) and absolute segmented neutrophils (90.51 K/ $\mu$ L) were elevated, while normal levels of red blood cells (4.53 M/ $\mu$ L) and platelets (161 K/ $\mu$ L) were observed. Percent metamyelocytes (14.0%), myelocytes (6.0%), promyelocytes (9.0%) and blasts (3.0%) were elevated. Laboratory results were highly indicative of myelogenous cancer, and the diagnosis was edited from endocarditis to acute myeloid leukemia (AML). After a consultation with hematology-oncology, he was started on tretinoin 40 mg once daily as well as hydroxyurea 2 g once daily. Because further management was not available at the hospital, and there was a concern for an acute hemorrhage, the patient was transported via medical air ambulance to a higher acuity hospital.

The peripheral blood smear and bone marrow examination were subsequently received and consistent with the chronic phase of chronic myeloid leukemia. Beyond that, the Philadelphia chromosome was present in all examined cytogenetic samples. The previous diagnosis of AML was edited to CML, and the patient was started on the tyrosine kinase inhibitor dasatinib 100 mg orally once daily.

Two weeks after admission to the hospital, a follow-up ophthalmology consultation was completed. The VA improved to 20/60 OD and 20/100 OS. Upon fundus exam, the optic discs, vessels, macula, and periphery were stable OU. The intraretinal and vitreous hemorrhages showed signs of improvement OU, and the vascular sheathing resolved completely OU.

One month after the first follow-up appointment, the patient presented to a retinal specialist due to an incomplete resolution of vitreous hemorrhage OU. Fluorescein angiography revealed early neovascularization, intra and pre-retinal hemorrhages, and inferiorly settling vitreous hemorrhage. At the time of visit, VA had significantly improved to 20/20 OD and 20/25 OS. Vitreous and macular hemorrhages were still present OU with moderate improvement (Fig. 2);

however, the patient had developed macular edema and a macular pucker OU.

Peripheral retinal hemorrhage had resolved OU, while peripheral neovascularization persisted. Microaneurysms and dot blot hemorrhages OU were still appreciated in the periphery. Due to these changes, the patient was recommended and elected to receive an intravitreal injection of bevacizumab 1.25mg/0.05mL OU. His visual acuity transiently worsened between injections but stabilized after the second injection to 20/25 OD and 20/20 OS. The patient in follow-up continues to receive intermittent bevacizumab injections for cystoid macular edema and now has some mild peripheral fibrosis; however, no peripheral nonperfusion has been noted.

### 3. Discussion

In this report, we describe a 28-year-old male patient with bilateral blurry vision as the primary presenting symptom of CML. In the United States, it's more common for adults to present with CML, with a median age of onset around 67 years.<sup>2</sup> Among this population, there is a slight male predominance.<sup>3</sup> Our patient is male, but he was only 28 years old at the time of presentation without any significant hematologic abnormalities or pertinent past medical history.

Typical presenting symptoms of CML may include fatigue, night sweats, malaise, weight loss, low fever, weakness, left upper quadrant discomfort, and in the advanced phase; bone pain, lymphadenopathy, skin infiltration and chloroma.<sup>3,4</sup> In 40–50% of cases, splenomegaly is reported while hepatomegaly is an unusual finding.<sup>3</sup> In rare cases, symptoms of priapism, thrombosis, bleeding, upper gastrointestinal ulceration, and retinal hemorrhage may be present.<sup>3,4</sup> Our patient presented with bilateral blurry vision while otherwise asymptomatic, with splenomegaly later appreciated on physical exam. To date, this is one of only a few reported cases of bilateral blurry vision as the primary presenting symptom of CML in a young adult.<sup>6–16</sup>

Presenting visual disturbances seen in CML are secondary to choroidal and retinal vascular changes.<sup>5</sup> Of the eleven mentioned cases, vitreous hemorrhage, preretinal hemorrhage, optic disc hemorrhage, macular hemorrhage, dot and blot hemorrhage, flame-shaped hemorrhage, Roth spots, intraretinal hemorrhage and subhyaloid hemorrhage have all been documented.<sup>6–16</sup> Other reported initial ocular abnormalities include tortuous and dilated veins, neovascularization of the retina, optic disc edema, retinal detachment, and leukemic infiltrates, which were less common than retinal hemorrhage.<sup>6–16</sup> Kincaid and Green<sup>5</sup> suggested that microaneurysms and retinal neovascularization, comparable to what is seen in sickle cell anemia, could be specific to the chronic leukemia subtypes. Our patient presented with vitreous hemorrhage, sub-inner limiting membrane hemorrhage, dilated tortuous vessels, macular hemorrhage, Roth spots, peripheral neovascularization,

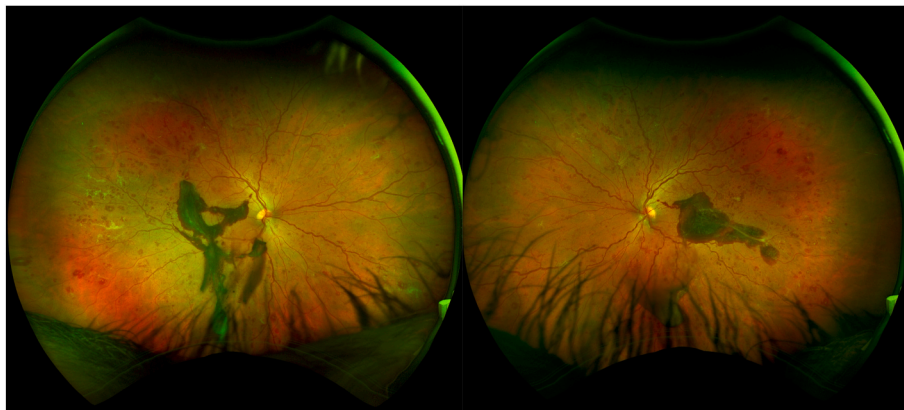
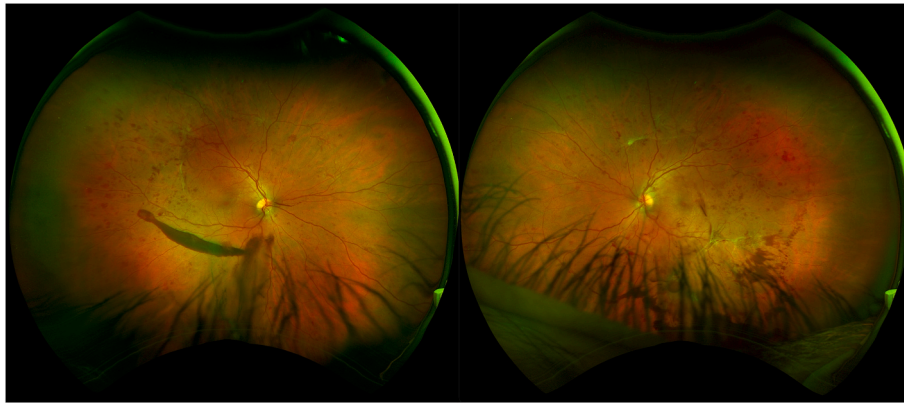


Fig. 1. Fundus photos taken upon initial presentation of the right eye A) and left eye B) demonstrating pre-macular subhyaloid hemorrhage, diffuse intra-retinal hemorrhage, Roth spots throughout with venous beading and very early areas of peripheral neovascularization OU.



**Fig. 2.** Fundus photos taken 6 weeks after the initial presentation of the right eye A) and left eye B) demonstrating improvement in macular and peripheral hemorrhage with newly developed macular edema and macular pucker OU.

and intraretinal and pre-retinal hemorrhages. The pre-retinal macular hemorrhage is a likely cause of our patient's bilateral blurry vision. It is possible there was an impending central retinal vein occlusion OU; however, the patient's vision cleared to 20/25 OD and 20/20 OS as the hemorrhages were clearing on systemic treatment, making it difficult to discern.

In cases where ocular involvement was not the only presenting sign or symptom, cotton-wool spots, flame-shaped hemorrhage, nuclear sclerosis, opportunistic infections, choroidal infiltrates, peripheral microaneurysms, and gray-white streaks have been documented.<sup>5,19–21</sup> In rare cases, hyperviscosity has been reported secondary to leukocytosis and may present as priapism, cerebrovascular accidents, tinnitus, and confusion.<sup>22</sup>

Retinal hemorrhages are commonly observed in an ophthalmology clinic and can be a manifestation of trauma, hypoxia, vascular disease, and hematological disorders.<sup>23</sup> The types of hemorrhages can help identify the specific systemic process at work. Roth spots were once believed to be pathognomonic for acute bacterial endocarditis but have since been reported in anemia, leukemia, and high altitude retinopathy.<sup>17,23,24</sup> To our knowledge, the presence of Roth spots in patients with visual disturbances as the only presenting symptom has only been reported in CML<sup>6,8,10,13,14</sup>; however, several types of retinal hemorrhages can present in leukemic retinopathy, which may mimic other pathologies.<sup>24,25</sup>

It has been documented that ocular involvement is present in acute leukemias much more frequently than in chronic subtypes, which can make the diagnosis more difficult.<sup>5</sup> This issue was consistent with our patient as the suspected diagnosis of acute bacterial endocarditis was initially attributed to AML after consultation with hematology-oncology, review of the comprehensive metabolic panel, complete blood count, and other labs. Thus, caution should be given before differentiating leukemic subtypes in patients who present with sudden vision loss. In the case of life-threatening hematologic disorders, testing for chromosome-specific abnormalities has shown to be beneficial to correctly make the diagnosis of myelogenous leukemias.<sup>6,7,9,10,12,13,18,21,26</sup> Further research is needed to improve the classification of retinal hemorrhages and ocular disturbances found in CML and AML.

First-line treatment for chronic phase CML includes tyrosine kinase inhibitors imatinib, nilotinib, or dasatinib.<sup>4</sup> Of the eleven cases where bilateral vision loss was the presenting symptom of CML, three used imatinib, two used dasatinib, one used bosutinib, three used systemic chemotherapy, one was untreated and one treatment was unknown.<sup>6–16</sup> When tyrosine kinase inhibitors were available, a significant resolution of retinal hemorrhage and improved visual acuity was documented in all but one patient, where preretinal hemorrhage in the fovea caused maculopathy.<sup>6–10,12–14</sup> In some severe cases, surgical intervention was

indicated to prevent irreversible vision loss. Panretinal photocoagulation was demonstrated to successfully resolve retinal neovascularization.<sup>8</sup> In two separate cases, pars plana vitrectomy was chosen to address multilayer retinal hemorrhages and retinal tear<sup>7,27</sup>; however, after one month post-operation there was no improvement in VA and severe disturbances in the macular architecture were observed.<sup>7</sup> With treatment, our patient's VA improved to 20/25 OD and 20/20 OS six weeks after admittance to the hospital and administration of dasatinib 100 mg orally once daily.

#### 4. Conclusion

To our best knowledge, this is one of only a few reported cases of bilateral blurry vision as the primary presenting symptom of CML. CML should be considered in patients who present with bilateral blurry vision associated with multi-layer retinal hemorrhages, even if otherwise asymptomatic. Further research should be conducted to better categorize retinal hemorrhages and ocular disturbances found in CML and AML.

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#### Authorship

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

#### Patient consent

The patient provided written consent to the publication of personal information and case details.

#### Declaration of competing interest

The authors have no conflicts of interest to disclose.

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