

Sudden Visual Loss as an Initial Manifestation of Chronic Myeloid Leukemia

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ABSTRACT

Chronic myelogenous leukemia (CML) is a pluripotent stem cell disease characterized by anemia, granulocytosis and granulocytic immaturity, basophilia, thrombocytosis and splenomegaly. It is associated with a reciprocal chromosomal translocation t (q34; q11), resulting in a breakpoint cluster region–Abelson fusion gene (Philadelphia chromosome). Ophthalmic manifestations as the first and the only presentation of CML in patients are very rare. Ocular lesions in CML patients are frequently asymptomatic, and thus all patients should undergo an eye evaluation at the initial diagnosis. Here, we report a previously healthy 36-year-old Saudi male who initially presented with progressive loss of vision. On examination, he was found to have a bilateral retinal hemorrhage. The investigations revealed findings consistent with CML. The patient was treated with tyrosine kinase inhibitors, and he had complete remission, including full recovery of his vision.

Key words: Chronic myelogenous leukemia, retinal hemorrhage, Saudi, visual loss

INTRODUCTION

Among all age groups of Saudis patients with cancer, leukemia is the third most common cancer in males, the fifth in females and fourth in both genders.^[1] Chronic myelogenous leukemia (CML) is a rare type of leukemia, accounting for 14% of all leukemias in the United States and 15.3% of all leukemias in Saudi Arabia.^[1,2] CML is a proliferative disorder of the hematopoietic stem cell and it is a genetic disease characterized by the presence of the Philadelphia chromosome, which results from a reciprocal translocation between the chromosomes 9 and 22.^[3,4]

About 85% of CML patients are diagnosed in the chronic phase, of which 40% are asymptomatic.^[2,3] The breakpoint cluster region–Abelson (BCR–ABL) will disrupt tyrosine kinase activity because of its effect

as an oncoprotein, leading to the increased survival of malignant cells.^[3] Tyrosine kinase inhibitor (TKI) inhibits the action of BCR–ABL, leading to the death of malignant cells containing the abnormal Philadelphia chromosome.^[3,5]

CASE REPORT

The present case reports a 36-year-old Saudi male who presented with loss of vision in the right eye. The patient had no history of cardiac and autoimmune diseases as well as had no family history of blood diseases such as sickle cell anemia, thalassemia or leukemia. The physical examination findings were not suggestive of splenomegaly, lymphadenopathy, cardiac arrhythmias or murmurs.

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The patient was referred from the Ophthalmology Clinic at the King Fahd Hospital of the University because the white blood count (WBC) was $543 \times 10^3/L$. It was stated that the patient had poor vision in the right eye with central opacity.

The patient had a progressive visual loss in the left eye for 2 weeks before presentation. The visual loss was not associated with pain, fever, redness or any other symptoms. After being seen and examined by a medical team, fundoscopic examination showed findings consistent with bilateral retinal hemorrhage and dilatation of blood vessels.

Blood tests were requested, including renal function test, liver function test, blood sugar, calcium and magnesium; all these blood tests were normal as were the coagulation tests. However, complete blood counts revealed profound leukocytosis: WBC count $543 \times 10^3/L$. The manual differential count showed 60% polymorph, 11% band, 1% lymph, 1% monocyte, 3% eosinophil, 2% basophil, 9% myelocyte, 3% promyelocyte and 3% blast. Red blood cell count was $4 \times 10^3/L$ (range: 4.5–6.6), hematocrit was 24% (40–54) and platelet count was $526 \times 10^3/L$ (140–440). Bone marrow biopsy and peripheral blood film showed hypercellular bone marrow composed of atypical myeloid cells, as shown in Figure 1. In addition, chromosomal analysis was positive for the t(9;22) translocation, as shown in Figure 2. Fluorescence *in situ* hybridization identified the BCR–ABL gene fusion. Based on these findings, the patient was diagnosed with CML.

DISCUSSION

CML is a myeloproliferative disorder that results from expression of the fusion gene BCR–ABL following a

chromosomal translocation in the hematopoietic stem cell.^[5] The diagnosis of CML is established by increased bone marrow cellularity and identifying a reciprocal translocation between chromosomes 9 and 22 in a hematopoietic stem cell, as shown in Figures 1 and 2.

The clinical onset of a disease like CML can be considered as insidious, and some CML patients are diagnosed by chance during their routine checkups.^[6] Some presenting symptoms of CML such as angina pectoris, pulmonary insufficiency, priapism and visual loss are not common symptoms. Only 5–10% CML patients present with eye symptoms as the initial presentation at the time of diagnosis.^[7]

On clinical examination, splenomegaly is the most common physical finding in a patient with CML.^[6] However, in our patient, the spleen was not palpable clinically. In asymptomatic leukemia patients, ocular lesions are often detected, which has led several authors to suggest inclusion of eye examination in the routine evaluation.^[7,8] Our patient had progressive and painless visual loss in the right eye for about 2 weeks before diagnosis. He had an eye examination by the ophthalmologist, and bilateral retinal hemorrhage was diagnosed secondary to CML. The ophthalmic manifestations of CML vary drastically and include intraretinal, subhyaloid and vitreous hemorrhages; nerve fiber layer infarcts; Roth's spots; infiltration of the optic nerve; ischemia and papilledema secondary to raised intracranial pressure.^[6-8] In addition to the eye manifestation, it has been reported that CML patients with ophthalmic manifestations have a 5-year lower survival rate than those without these manifestations.^[2]

Treatment options for patients with CML are varied and include a potential cure with allogeneic hematopoietic

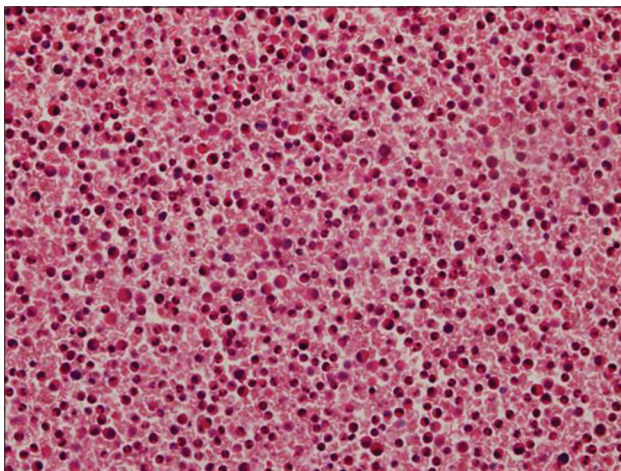


Figure 1: Increased bone marrow cellularity with a shift to the left



Figure 2: Philadelphia chromosome positivity

Table 1: Definitions of response to tyrosine kinase inhibitors therapy in chronic myelogenous leukemia

Definitions of response	
Response	Definition
Clinical response	Disappearance of all symptoms and signs
Complete hematological response	WBC $<10 \times 10^3/L$ Basophil $<5\%$ No myelocyte, promyelocyte, myeloblast Platelets $<450 \times 10^3/L$ Spleen nonpalpable
MMR	Detectable disease with ratio of BCR–ABL to ABL $\leq 0.1\%$ (≥ 3 log reduction)

MMR – Major molecular response; WBC – White blood cells

Table 2: Patients response to tyrosine kinase inhibitors (imatinib)

Date	WBC	HG (g/dl)	MMR
2006	552×10^3	8	NA
2008	6×10^3	11	NA
2010	6×10^3	12	NA
2012	6×10^3	12.8	0.0031
2014	6×10^3	12	0.0043
2016	9×10^3	13	0.00037

MMR – Major molecular response; WBC – White blood cell; HG- Hemoglobin

cell transplantation, disease control without a cure using TKIs or palliative therapy with cytotoxic agents.^[9]

The treatment of CML depends on the phase of the disease and other factors such as age, response and ability to tolerate therapy, availability of donor and medical comorbidities. The response to TKIs was defined according to clinical, hematological and molecular response, as shown in Table 1.

Assessment of response and follow-up evaluation

The patient was treated with imatinib 400 mg daily. He responded very well to therapy and within 3 months he was not complaining of symptoms. The retinal hemorrhages were healed completely with complete visual recovery. He had a complete hematologic response: complete normalization of peripheral WBC count ($<10 \times 10^3/L$) and platelet count ($<450 \times 10^3/L$) sustained for the past

10 years, as shown in Table 2. In the first 5 years, BCR–ABL transcript monitor was not available; however, during the last 5 years, the PCR/ABL monitor became available, and subsequently it was measured every 6 months. The last reading of PCR/ABL monitor was 0.00037, as shown in Table 2.

In summary, this study reports a patient who presented with retinal hemorrhages secondary to CML that lead to blindness as the first manifestation of CML. This case illustrates that CML should be considered as a possible etiology in patients with visual loss. Therefore, ophthalmic evaluation is needed in these patients for early identification and treatment to restore visual function.

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None

Conflicts of interest

There are no conflicts of interest.

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