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Unusual Retinal Hemorrhages as A First Sign of Chronic Myeloid Leukemia: A Case Report

Dorian Laslo[1*], Ivana Franić Šimić[2], Vlatka Periša[1,3]

[1]Faculty of Medicine Osijek, University Josip Juraj Strossmayer Osijek, Osijek, Croatia

[2]Cinical Hospital Centre Osijek, Clinic of Internal medicine, Department of haematology, Osijek, Croatia

[3]Clinical Hospital Centre Zagreb, Clinical department for laboratory diagnostics, Zagreb, Croatia

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[*]**Corresponding author:** Dorian Laslo, Faculty of Medicine Osijek, University Josip Juraj Strossmayer Osijek, Osijek, Croatia

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ABSTRACT

Chronic myeloid leukemia (CML) is clonal disorder characterised by reciprocal translocation t(9, 22). About half of the patients are asymptomatic. Unilateral vision disturbance is very rare symptom of CML and we present the second case report. A 34-year-old, previously healthy, man presented with complaints of blurring in right eye. The visual acuity was 0.5 in the right eye, with normal vision on the left. Intraretinal hemorrhage in the right eye was confirmed by fundoscopy and optical coherence tomography. A hemogram showed a total leukocyte count of 178,3 $x10^9$/L. He had a splenomegaly without other bleeding manifestations. Cytogenetics revealed a karyotype of 46, XY, t (9;22). FISH analysis proved Philadelphia chromosome in 96% of cells and the patient was diagnosed as CML and started imatinib therapy. All patients presented with retinal bleeding wihtout clear reason should performe blood tests, because it is the only way to rule out CML.

Keywords: BCR-ABL Positive chronic myelogenous leukemia; Imatinib mesylate; Retinal hemorrhage; Vision disorders

INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative hematopoietic disorder characterized by the uncontrolled proliferation of myeloid cells. CML is caused by reciprocal translocation of the c-ABL1 gene from chromosome 9 to the BCR gene on chromosome 22. The fusion gene BCR-ABL1, also known as the Philadelphia chromosome, produces constantly active tyrosine kinase which promotes uncontrolled proliferation of myeloid cells. About fifty percent of the patients with CML are asymptomatic. The most common symptoms of CML are symptoms of anemia, splenomegaly and weakness. Retinal hemorrhage is a rare symptom. It manifestation starts when leukemic cells disrupt the vascular integrity of the retinal and choroidal vascular structures, which leads to bleeding and retinal

infiltration.[1] The first line of therapy is the use of tyrosine kinase inhibitors, usually imatinib. An ocular manifestation as the first sign of CML has been described in only ten different cases, while only one reported unilateral ocular manifestation secondary to CML.[2] We report the second case of a patient with the first presentation of CML as unilateral retinal hemorrhages.

CASE REPORT

A 34-year-old man without any comorbidities had noticed blurring in the right eye 3 days before visiting an ophthalmologist. He did not have a history of other symptoms of neurological or ophthalmological disturbances or bleeding manifestations. The ophthalmologist had performed an examination and established visual accuracy of 0,5 in the right eye and normal vision on the left. Fundoscopy and optical coherence tomography (OCT) confirmed intraretinal hemorrhage within the anterior layers of the macula with stable boundaries in the right eye (Figure 1a). The anterior chambers of both eyes were normal. The ophthalmologist's recommendation was to perform complete blood analysis. The next day the patient's blood was analyzed in the ambulance of his family medicine doctor. A hemogram showed a total leukocyte count of 178,3 x 109/L, hemoglobin of 112 g/L and a platelet count of 238 x 109/L. Because of leukocytosis the patient was admitted at the Department of Hematology, for further diagnostic procedures, on the same day. The patient was afebrile with pale visible mucosa and skin. He reported weakness and weight loss in the past few months. He had splenomegaly of 5 cm below the left costal margin. There were no signs of lymphadenopathy or bleeding manifestations. Differential leukocyte count was suggestive of the left shift with the prominence of myeloid precursors. The patient started a cytoreductive therapy by taking hydroxyurea on the same day when he was admitted. The bone marrow was hypercellular with plentiful granulocytopoesis of all developmental stages and it was suggestive of CML in the chronic phase. Conventional cytogenetics revealed a karyotype of 46, XY, t (9; 22) (Figure 2a). Fluorescent *in situ* hybridization analysis proved the Philadelphia chromosome in 96% of cells (Figure 2b). Qualitative reverse transcriptase-polymerase chain reaction for BCR-ABL1 translocation showed a fusion transcript of b2a2 encoding for major transcript p210. According to Sokal-Hasford scoring system he has intermediate-risk disease. Two weeks after hospitalization at the Department the patient has started on 400 mg imatinib daily and achieved a total hematological remission after one month of imatinib therapy. He attained complete cytogenetic remission after 6 months of imatinib therapy and his visual acuity on the right eye was normal (Figure 1b).

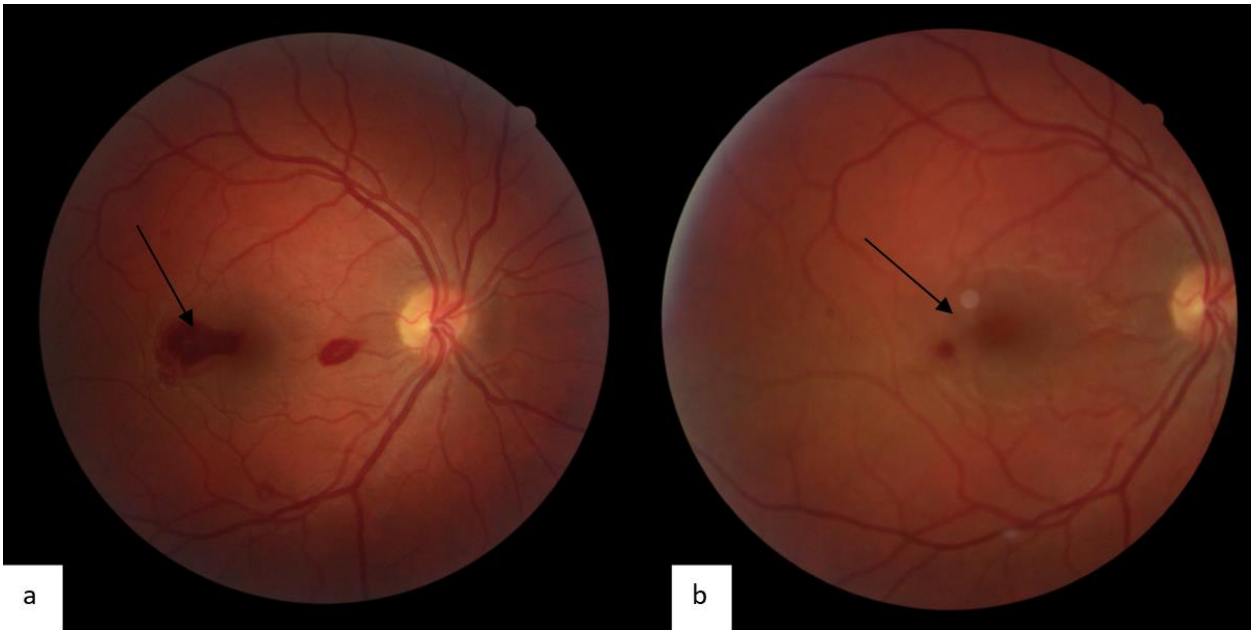

Figure 1: a) Picture shows bleeding in the anterior layers of the macula (arrow) in the right eye. b) Picture shows withdrawal of the bleeding in the right eye (arrow).

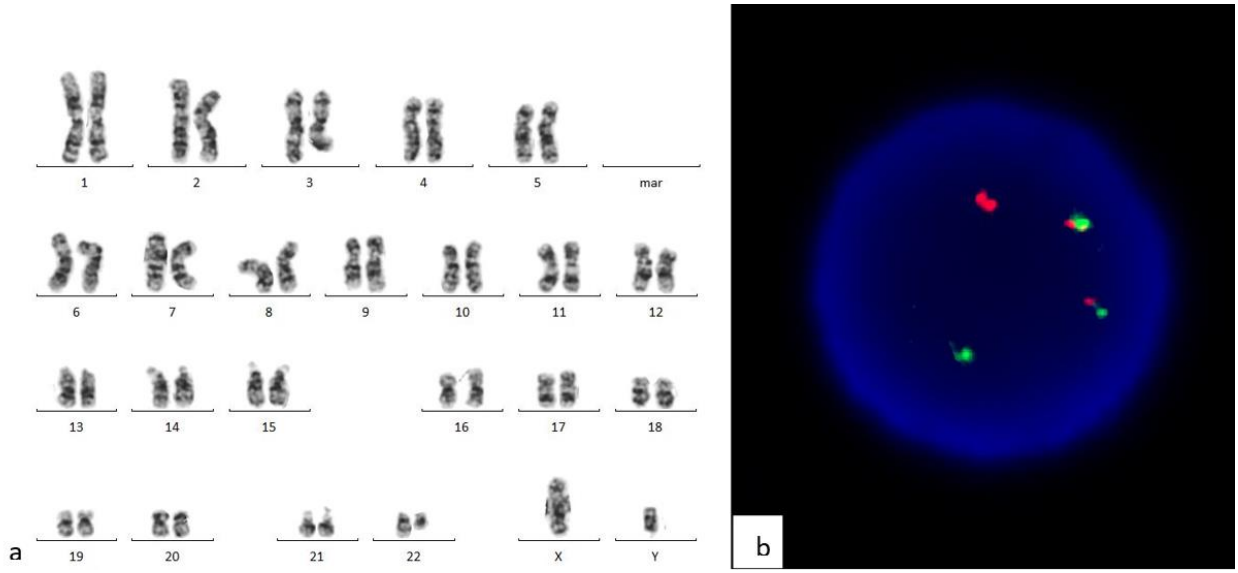

Figure 2: a) Figure shows karyotype of 46, XY, t (9; 22). b) Figure shows FISH analysis and proof of t(9; 22).

DISCUSSION

The long term efficiency of imatinib therapy in CML patients was estimated in the study provided by Hochhaus et al. In the study 49, 1% of the patients achieved complete cytogenetic remission within 6 months and 82, 8% within 11 years. The overall survival rate of the patients classified as intermediate-risk disease was 80,3 %, while those

with low-risk and high-risk disease was 89,9% and 68,6%. This study has proved that the Sokal-Hasford scoring system is excellent in the prediction of the therapeutic response of a patient to imatinib treatment, however the Sokal-Hasford scoring systems do not correlate with the ocular manifestations of CML.[3,4,5] In the study provided by Ohkoshi and Tsiaras the patients who had ophthalmological manifestations of a leukemia had significantly lower 5-year survival rate, on the other hand this study was provided on children who were treated for acute leukemias.[6] There is a lack of data in the literature on the impact of ocular manifestations in the overall survival of adult patients with CML. Additionally there is a lack of any scoring system that could predict ocular outcomes in patients with ocular manifestations of CML.

In the case reported by Serali et al, the patient was experiencing gradual vision loss on the right eye through a month before she started any treatment. She had a clot and retinal bleeding secondary to CML. She had been operated in an attempt to remove the clot and started on imatinib therapy. Despite imatinib therapy and surgical procedure her visual acuity on the right eye was 20/200.[2] Huang and Sanjay reported a case of a 30-year-old male patient presented with preretinal hemorrhage and white-centered hemorrhage in his left eye and visual acuity of 20/20 OD and 20/100 OS. After 12 months of cytoreductive therapy using only hydroxyurea his visual acuity improved to 20/30 in his left eye and there was no systemic recurrence.[7] In our case the patient has been using cytoreductive therapy since 4th day after the first sign of vision loss started. After 6 months his visual acuity has been back to normal on the right eye and he attained complete cytogenetic remission. Based on these three case reports we can assume that the outcome of an ocular manifestation secondary to CML depends on neither the type of a cytoreductive therapy nor the surgical procedure. It is more likely that the outcome of an ocular manifestation, secondary to CML depends on the prompt start of a cytoreductive therapy.

CONCLUSION

Any patient presented with retinal hemorrhage without clear cause should perform usual blood tests. CML, although in rare cases, can cause retinal bleeding. In those cases a quick response of an ophthalmologist and a hematologist is necessary because the outcome of an ocular manifestation depends on the prompt start of cytoreductive therapy.

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