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Case Report

Visual Loss as Initial Presentation of Chronic Myelogenous Leukemia

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A B S T R A C T

A previously healthy 17-year old girl presented with sudden visual loss in both eyes. Visual acuity on the right eye was 0.3 and on the left eye 0.1. Fundoscopic examination showed bilateral optic disc edema, retinal venous tortuousity and dilatation, retinal blot and flame-shaped hemorrhages, Roth spots and on the left eye dark blot preretinal hemorrhage covering the fovea. Laboratory evaluation showed white blood cell count of 455×10^9 L. Bone marrow biopsy confirmed the diagnosis of chronic myelogenous leukemia. Chemotherapy was initiated and led to the improvement of visual acuity. Fundus changes had resolved except for the preretinal hemorrhage on left eye which decreased in size. Preretinal hemorrhage in fovea caused maculopathy on the left eye. Three months after admisson visual acuity was 1.0 on the right eye and 0.3 on the left eye. Leukemia should always be included in the differential diagnosis of optic disc edema and retinal hemorrhages.

Key words: *CML, visual loss, symptoms and signs*

Introduction

Ocular manifestations as a presenting sign of leukemia, especially chronic, are rare. Leukemia may present on the anterior and posterior segment of eye and it can involve the orbita as well. Ocular changes may be induced by direct infiltration of leukemic cells in the orbit such as iris, chorioid, retina or optic nerve or by vascular and hematological abnormalities such as anemia, thrombocitopenia, hyperviscosity states affecting the retina. Ocular changes may present as intraretinal hemorrhages, white centered hemorrhages, cotton wool spots, subhyaloid hemorrhages and vitreous hemorrhages and neuro-ophthalmic signs as papilloedema secondary to a raised intracranial pressure and isolated cranial nerve palsies[1].

Case Report

A 17-year old girl presented with a sudden visual loss in both eyes. She reported a few days of moderate headaches and no other symptoms. Examination revealed a visual acuity of 0.3 in the right and 0.1 in the left eye. The slit lamp examination showed that the anterior segments were normal and the vitreous was clear in both eyes. Fundus examination revealed bilateral optic disc edema, dilated and tortuous retinal vessels, retinal blot hemorrhages, Roth spots and on the left eye dark blot preretinal hemorrhage covering the fovea (Figure 1 and 2). Medical history revealed that her father died at the age of 30 of heart attack and we first suspected a vascular disease or hypercoaguabile state. Differential diagnosis included malignant hypertension, diabetes, elevated intracranial pressure, central retinal vein obstructions, leukemia and lymphoma. Her blood pressure was 115/70 mmHg. A full cell blood count revealed a white blood cell count of 455×10^9 L. Red blood cell count and thrombocyte count were normal, as well as initial routine biochemistry tests. She was hospitalized on the Pediatrics departement and diagnosed with chronic myelogenous leukemia. Physical examination revealed hepatosplenomegaly confirmed by abdominal ultrasound examination. Her bone marrow biopsy showed hypercellularity (G:E = 95:1) with reduced eritropoesis and induced granulocitopoesis, kariotype (ISCN 1995): 46,XX, t(9;22), molecular analyse (ISH/FISH) showed 90% Ph+ cells and immunophenotypic marker studies were consistent with the diagnosis [CD 13+ 64%, CD 33+ 99%].

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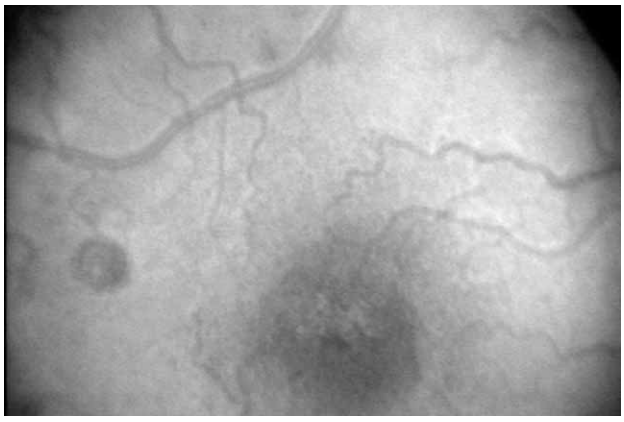

Figure 1. White centered retinal hemorrhage on the right eye-Roth spot.

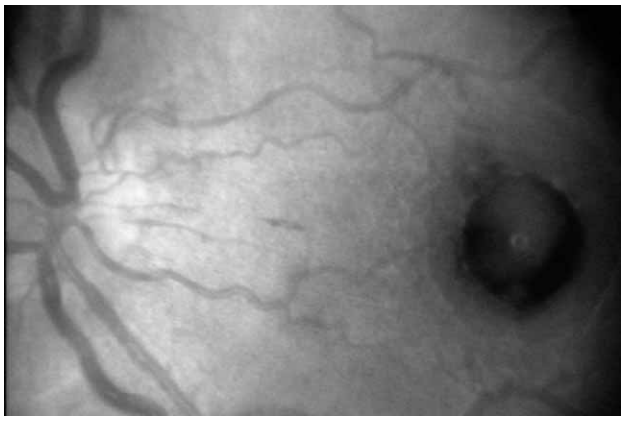

Figure 2. Optic disc edema, flame-shaped hemorrhages, tortuous and dilated vessels and preretinal hemorrhage covering the fovea on the left eye.

Induction therapy with hydroxyurea and interferon was initiated and general improvement of the disease was observed. Magnetic resonance imaging, although done 6 days after chemotherapy was induced (her white blood cell count felt to 319×10^9 L by that day), still demonstrated a 1 mm enhancing lesion in the left optic nerve. No optic nerve irradiation was performed. On fundoscopic examination two weeks after admission the optic disc swelling was less prominent. Retinal vascular changes had resolved. All retinal haemorrhages had cleared except the left foveal preretinal hemorrhage, which was about one fourth of its original size. Visual acuity was l.0 in the right and 0.1 in the left eye. Her WBC count was 97×10^9 L. On the next follow-up, three weeks after admission, both optic nerves were normal, with no signs of vein stasis. In the left fovea residual bleeding and dehemoglobinised blood was still present. Intraretinal hemorrhages were seen along both inferior arcades. Three months after admisson maculopathy caused by preretinal hemorrhage developed in the left eye. The patient's visual acuity gradually improved to 1.0 in the right and 0.3 in the left eye. Her WBC count was 12×10^9 L. She responded well to α interferon and hydroxyurea and her vision was preserved without irradiation therapy. She is currently being prepared for an imatinib tretment and allogenic stem cell transplant.

Discussion

Our patient presented with bilateral sudden vision loss as initial symptom of CML. Visual impairment as the initial symptom of leukemia, especially chronic myelogenous leukemia, is rare. Clinically evident ocular involvement is common in patients with leukemia and has been described in up to half of patients at the time of diagnosis[2–4]. It is more common in acute than in chronic forms of leukemia[2–5] and is seen as a primary leukemic infiltrate in 3% of patients and as secondary complications in 39% of patients[6].

Eye symptoms are, though, present in only about 5–10% patients at initial diagnosis[3,4]. Although retinal involvement during leukemia is frequent, a leukemic macular lesion and leukemic optic nerve infilltration are exceptions[7]. Fundus examination in our patient revealed bilateral optic disc edema, dilated and tortuos retinal vessels, retinal blot and flame-shaped hemorrhages, Roth spots and on the left eye dark blot preretinal hemorrhage covering the fovea. The mechanism of optic disc edema is not completely understood. It may be a sign of CNS involvement or direct leukemic cell infiltration of the optic nerve[8]. It will tipically lead to relatively rapid and potentially irreversible vision loss. Sometimes, if therapy induced early, treatment can result in remarkable recovery. CNS leukemia most commonly affects cranial nerves III through VII[9]. Kincaid and Green found, in an autopsy series of 384 leukemic patients that 18% with acute leukemia and 16% of chronic leukemia had optic nerve involvement[10].

In our patient, no optic nerve irradiation was performed, because the patient showed a very good reaction to chemotherapy. Three weeks after induction of chemotherapy fundoscopic examination showed no more sign of disc edema and patient's visual acuity rapidly recovered. The restoration of visual function after radiation therapy is generally poor. Some authors reported radiation therapy did cause shrinkage of the infiltrate in every instance, but failed to improve vision in 90% of patients[11,12]. Other authors reported resolution of leukemic infiltration and return of visual recovery after radiotherapy[13,14].

The retinal findings had cleared almost completely by three weeks after initiation of chemotherapy same as reported by some authors[8,12]. Hemorrhages may be found at any anatomical level and probably come about as a result of the associated anemia and thrombocytopenia. While our patient had normal count of red blood cells and thrombocyts, retinal hemorrhages can be explained due to hyperviscosity syndrome caused by leucocytosis.

On the examination performed three weeks after admission some new hemorrhages were present along both inferior arcades. The toxic effect of chemotherapy

on the microvasculature is likely to be an important factor in this mechanism. Thrombocytopenia which was present along chemotherapy can be also cause of these hemorrhages. Maculopathy developed in the left fovea due to long lasting preretinal bleeding. Many authors showed prognostic importance of ophthalmic manifestations, especially in childhood leukemia[15–17]. Ohkoshi showed that a 5 year survival rate of patients with ophthalmic manifestations was 21.4% which is significantly lower than that of those who lacked ophthalmic manifestations 45.7%[15]. This case underlines the importance of high clinical suspicion in the early diagnosis of leukemia. Work-up in a patient with swollen optic disc and retinal hemorrhages should always include full blood cell count to exclude myeloproliferative disorders.

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GUBITAK VIDA KAO PRVI SIMPTOM KRONIČNE MIJELOIČNE LEUKEMIJE

SAŽETAK

Prethodno zdrava 17-godišnja djevojka javila se zbog naglog gubitka vida na oba oka. Vidna oštrina na desnom oku je bila 0,3, a na lijevom 0,1. Fundoskopija je pokazala obostrani edem papile vidnog živca, proširene i izvijugane vene, mrljasta i plamičasta krvarenja, Rothove pjege i na lijevom oku preretinalno krvarenje u području makule. Pregledom krvne slike nađe se visoki broj leukocita od 455×10^9 L. Punkcijom koštane srži utvrđena je dijagnoza kronične mijeloične leukemije. Uvedena je kemoterapija na koju je pacijentica dobro reagira i uz pad broja leukocita došlo je i do poboljšanja vidne oštrine i povlačenja edema papile vidnog živca i krvarenja na mrežnici. Preretinalno krvarenje na lijevom oku se smanjivalo. Tri mjeseca od postavljanja dijagnoze na lijevom oku posljedično je nastala makulopatija. Vidna oštrina na lijevom oku je 0,3, a na desnom oku vidna oštrina je 1,0. Kod nalaza edema vidnog živca i krvarenja na mrežnici u diferencijalnoj dijagnozi treba misliti na leukemiju.