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Case Report

Decreased Vision as Initial Presenting Symptom of Acute Lymphoblastic Leukemia: A Case Report

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Keywords

Acute lymphoblastic leukemia · Visual disorder · Optical coherence tomography · Serous macular detachment

Abstract

This case illustrates that hematologic disorders must be considered as a potentially life-threatening cause for vision loss. Proper laboratory workup and timely interdisciplinary approach are essential to ensure the best possible care for ophthalmic patients. Historically, before the use of bone marrow biopsy, the ophthalmologist was often asked to assist in the diagnosis of leukemia. Since ophthalmological symptoms may be the initial presenting signs of leukemia as highlighted in this case, the ophthalmogist is still of crucial importance.

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Introduction

Potentially life-threatening systemic diseases like hematologic disorders can initially present with isolated ocular symptoms. Therefore, accurate ophthalmologic assessment and prompt ancillary testing facilitates timely diagnosis and subsequent therapy in undefined cases.

Thus, we report of a patient presenting with isolated decreased monocular vision. Ophthalmic and clinical workup led to the diagnosis of acute lymphoblastic leukemia (ALL). Only a sparse number of similar cases have been reported in the literature [1–5]. We would like to elucidate the striking correlation between the amount of subretinal fluid, total leukocyte count and visual acuity.

Case Presentation

The 28-year-old female patient presented with decreased central vision in her right eye since getting up that morning. She reported no other symptoms and stated to be in good health. Her family, social and past medical history revealed no relevant findings.

The initial corrected visual acuities were 20/40 (OD) and 20/20 (OS), but it dropped to 20/200 (OD) on day 5 of clinical follow-up.

Ophthalmic examinations of the anterior segment of both eyes showed no pathological findings. Fundus examination showed a vital optic nerve head, but the macula of the right eye presented with a prominent center-involving serous neurosensory retinal detachment and whitish-yellowish choroidal infiltrations. It was less prominent in the central macula of the left eye, but extensive serous detachment was present in the area of the papillomacular bundle (fig. 1) at the inferotemporal vascular arcade. Optical coherence tomography (OCT) confirmed prominent subretinal fluid overlying an area of choroidal thickening. Fluorescein angiography detected multifocal areas of leakage at the level of the retinal pigment epithelium (fig. 1).

Due to her initial findings, the primary care ophthalmologist considered central serous retinopathy or chorioretinitis of unknown origin as potential differential diagnoses. Follow-up on day 3 revealed further deterioration of symptoms despite proper treatment with oral prednisone and ketorolac eyedrops. Upon referral, immediate laboratory workup was initiated. The leukocyte count (normal range in parentheses) was found to be substantially increased to a total of 38.2 g/l (4.0–10.0) [erythrocytes 4.65 g/l (3.8–4.2), thrombocytes 30 g/l (150–380), blasts 87% (0.0) and increased LDH 645 U/l (100–250)]. Considering this life-threatening situation, the patient was admitted to the department of hematology. Upon further enquiry and more detailed medical history, the patient remembered an ill-defined swelling of several lymph nodes.

Ancillary clinical testing confirmed the diagnosis of common B-cell ALL. The Bcr/ABL oncogene was tested to be negative. Chemotherapy was inducted on day 5 according to the GMALL 03/07 study protocol [6]. On consecutive ophthalmic examinations, her vision dropped in both eyes as shown in figure 2. The clinical findings and OCT images demonstrated a striking relationship between visual acuity, amount of subretinal fluid and leukocyte count. To depict this significant correlation, the thickness of submacular fluid was measured and compared to vision and leukocyte count (fig. 2).

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Discussion

Leukemia is a potential life-threatening malignant disease characterized by uncontrolled proliferation and accumulation of mature and premature malignant leukocytes in the bone marrow with a subsequent peripheral distribution. Different forms of leukemia can be classified by their cell of origin and by their time of duration. Detailed subclasses are described by their genetic and immunochemical characteristics [7, 8]. The overall incidence rate of ALL is 1.28/100,000 per year showing a bimodal distribution with higher rates in younger (0–14 years) and older patients (over 54 years) [9].

Ocular involvement of ALL can affect all intraocular structures. Direct leukemic manifestations as infiltrates have been reported of the optic nerve, choroid, retina, iris, ciliary body and anterior chamber. Indirect leukemic manifestations such as central serous chorioretinopathy overlaying choroidal infiltrations, retinal vascular sheathing and subconjunctival, anterior chamber, intraretinal, or intravitreal hemorrhages have been found. These findings may be related to accompanying anemia, thrombocytopenia or hyperviscosity states [10].

Histopathology of postmortem specimens performed by Kincaid and Green [10] at the Wilmer Ophthalmological Institute between 1923 und 1980 found ocular involvement in 82% of patients with ALL. However, ocular examinations at the time of diagnosis show less frequent ocular manifestations. Reddy et al. [11] reported ocular findings in 35.4% of 288 newly diagnosed cases of leukemia in children and adults, but obvious clinical symptoms were only present in 10%. Ocular involvement in hematologic disease entities may benefit from immediate systemic chemotherapy of ALL as they are usually not treated directly [10].

The leukemic infiltrates were found in almost any location in the eye; however, they are most frequent in the choroid with primary or compressive involvement of the adjacent choriocapillaris [1]. Blood dyscrasia and leukemic cell infiltration may cause focal choroidal ischemia. The consecutive dysfunction of the retinal pigment epithelium and the outer blood-retina barrier may ultimately lead to serous retinal detachment as observed in our patient [12, 13]. These findings correlate well with the multifocal areas of leakage at the level of the retinal pigment epithelium shown by fluorescein angiography in our case. Similar pathomechanisms are discussed in central serous retinopathy or paraproteinemic maculopathy [14]. Mansour et al. [14] proposed another potential pathomechanism contributing to serous retinal detachment. They suggested that an increased osmotic gradient caused by subretinal accumulation of high-molecular-weight immunoglobulins induces exudation.

Due to immediate induction of chemotherapy by the department of oncology and hematology, the leukocyte count of the patient declined adequately. Upon her last visit to the department of ophthalmology her visual acuity improved to 20/40 (OD) and 20/20 (OS), and the reduction of subretinal fluid showed an evidently positive correlation with regressing leukocyte counts (fig. 2). In line with the therapeutic response to chemotherapy, her ocular biomicroscopic examination, OCT and fluorescein angiography had resolved back to normal (fig. 3).

Statement of Ethics

This case report was conducted in accordance with good clinical practices. The authors state to have full control of all primary data and have no ethical conflicts to disclose.

Disclosure Statement

The authors have declared no conflicts of interest.

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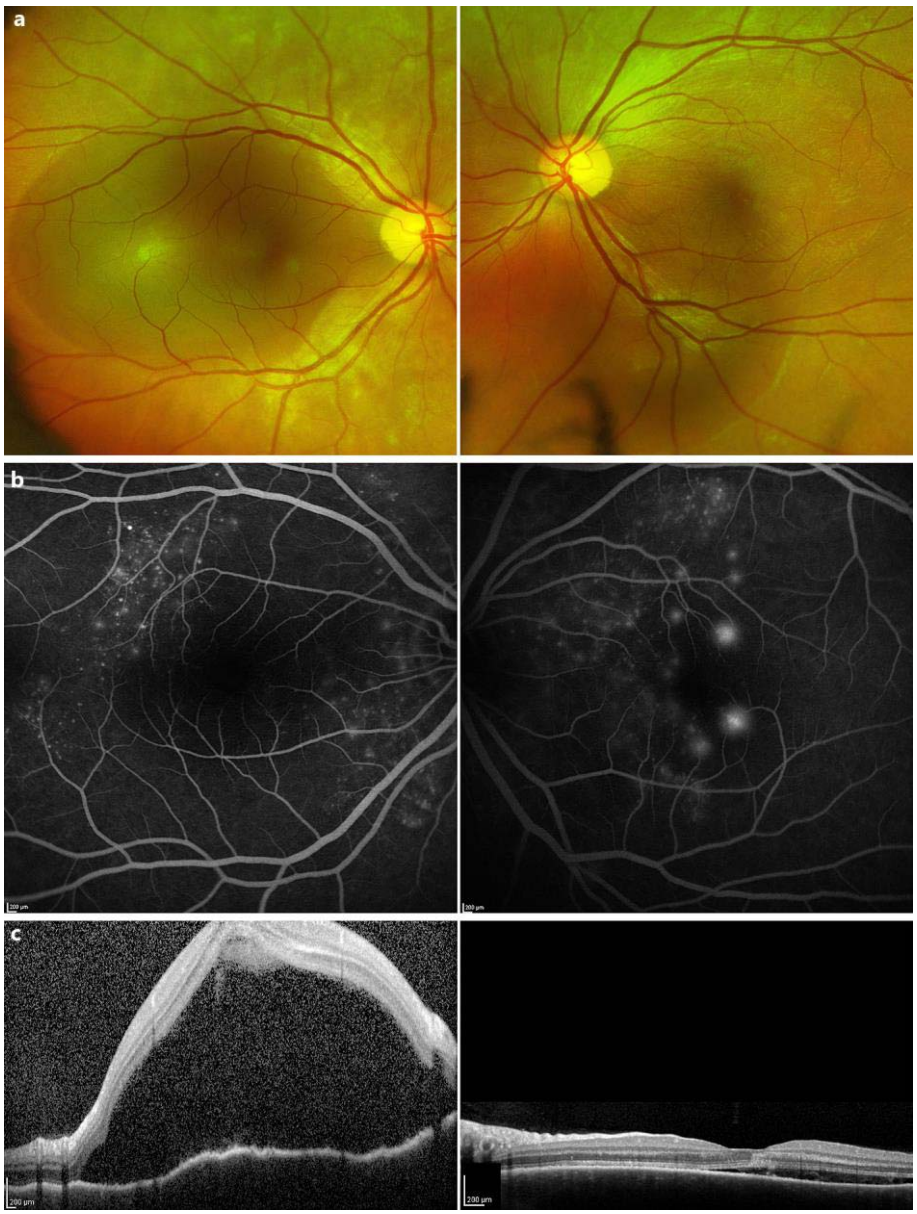

Fig. 1. **a** Fundus photographs of the right eye (left) and the left eye (right) showing bilateral serous retinal detachment on day 4. **b** Fluorescein angiography detects a 'Milky-Way pattern' of diffuse small punctate hyperfluorescence with increasing size and brightness on both eyes as the study progresses on day 1. **c** OCT shows more prominent submacular fluid on the right eye compared to the left eye with maximal detection on day 4.

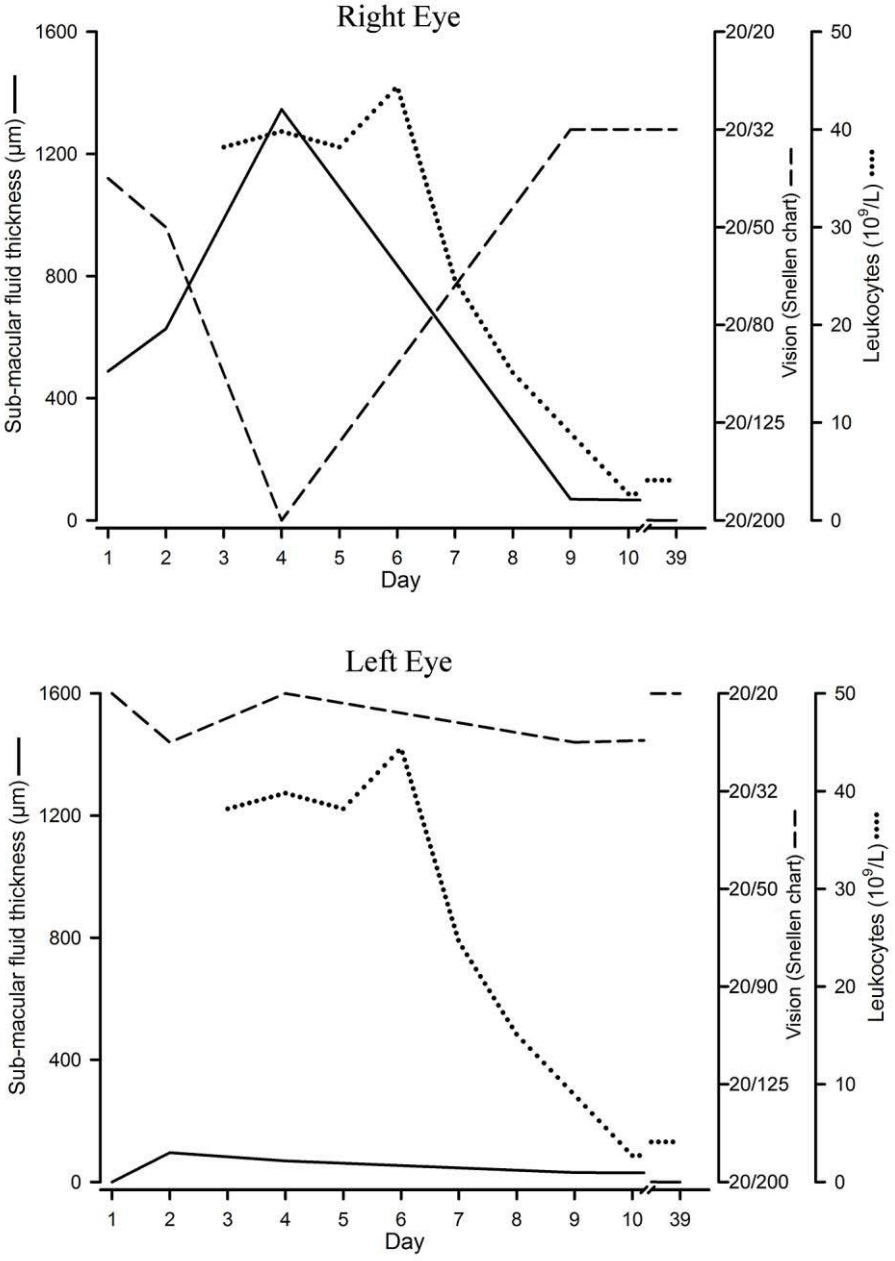

Fig. 2. These figures demonstrate the correlation of best corrected visual acuity (BCVA – measured by the Snellen chart; – –), amount of submacular fluid (––––) and leukocyte count (••••) of the right eye (above) and the left eye (below). On day 3, lab work is initiated. After induction of chemotherapy, leukocyte count drastically declines, whereas BCVA significantly improves due to decreased submacular fluid. Additionally, these figures demonstrate the unilateral onset of vision deterioration. Examinations reveal a central onset of increased submacular fluid on the right eye compared to the more peripheral onset on the left eye. Hence, the effect on central vision should be worse on OD compared to OS.

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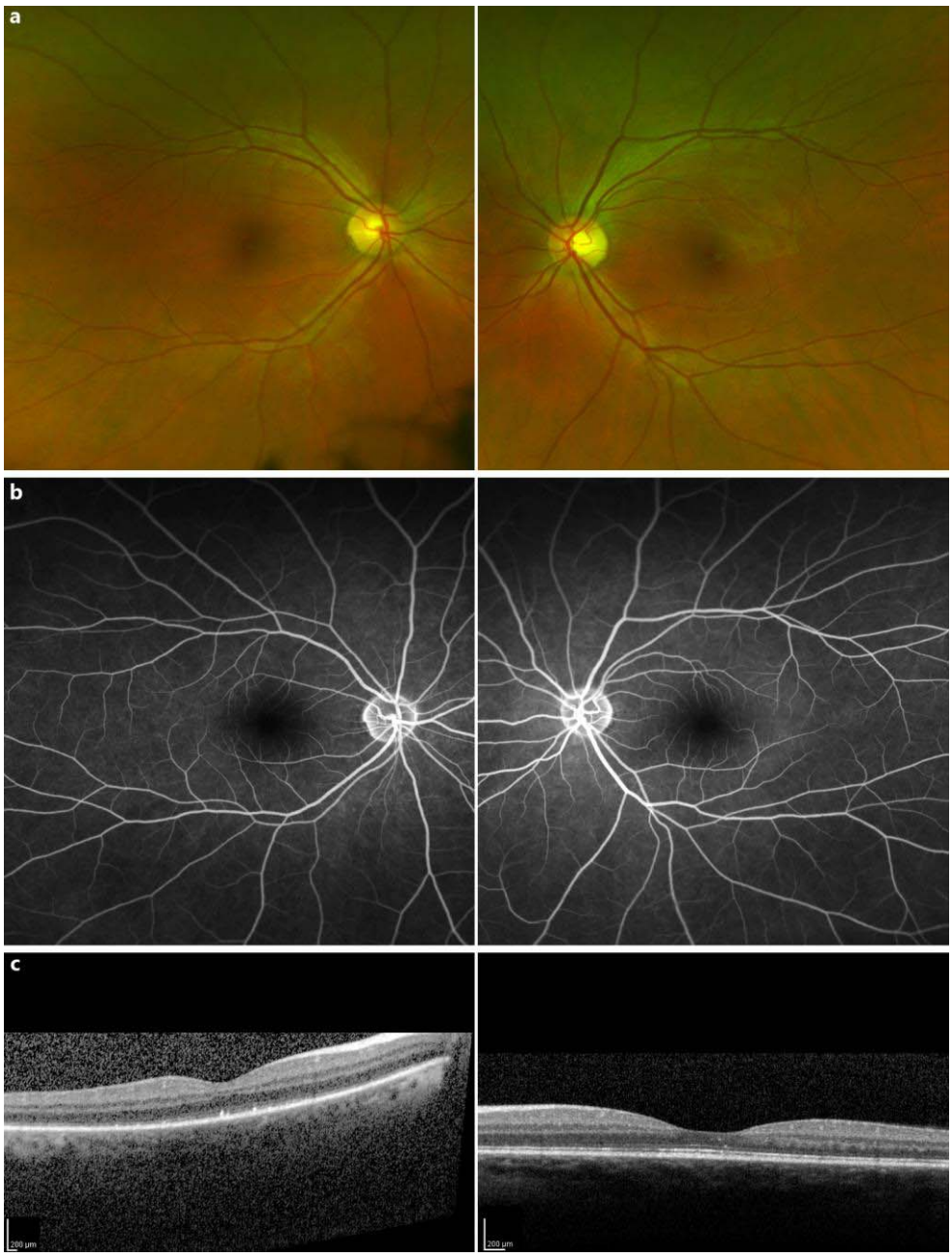

Fig. 3. **a** Fundus photographs of the right eye (left) and the left eye (right) together with fluorescein angiography (**b**) and OCT (**c**) have resolved back to normal on day 39. Only small exudates are discernible after complete resorption of submacular fluid.