Serous retinal detachment as a presenting sign of acute lymphoblastic leukemia: A case report and literature review

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ABSTRACT

Purpose: To describe a unique case of unilateral serous retinal detachment as the presenting sign of B-cell acute lymphoblastic leukemia (ALL).

Observations: A 74 year old woman presented with right eye blurry vision and was found to have an underlying serous retinal detachment, along with cotton wool spots, inner retinal hemorrhages, and retinal pigment epithelial changes throughout her bilateral fundi. Fluorescein angiography demonstrated bilateral vasculitis and ultrasonography revealed asymmetric thickening and enhancement of the affected eyes’ choroid. This prompted a systemic workup and results were suspicious for an underlying hematologic malignancy. The patient was admitted to the hospital for bone marrow biopsy confirming B-cell ALL, underwent intensive intravenous and intrathecal chemotherapy, and was discharged one month later. Follow up appointment in the ophthalmology clinic demonstrated functional and anatomic improvement in the serous retinal detachment and choroidal thickening suggestive of infiltration in her right eye.

Conclusions: SRDs are an uncommon ocular manifestation of leukemia, and even less common as a presenting sign of the disease. A comprehensive literature review demonstrated 11 other cases reported worldwide. We present the first such case with additional findings of leukemic retinopathy, optic nerve and choroidal infiltration, and vasculitis, as well as a complete library of ophthalmic imaging from the patient’s initial presentation. Ocular involvement has been reported in up to 90% of patients with leukemia. The most common ocular manifestation is leukemic retinopathy, characterized by white-centered hemorrhages, intraretinal hemorrhages, retinal vascular sheathing, tortuous and dilated retinal veins, leukemic infiltrates, and cotton wool spots. Other ophthalmic findings are orbital masses, optic nerve infiltrates, episcleitis, iris infiltrates, hypopyon, panuveitis, central retinal vein occlusions, retinal neovascularization, vitreous hemorrhages, retinal pigment epitheliopathy, and choroidal infiltration. Ocular changes in leukemia are most commonly secondary to direct leukemic infiltration of the ocular structures, hematologic abnormalities such as pancytopenia and hyperviscosity, opportunistic infections, or toxicity of chemotherapy used to treat the leukemia.

Serous retinal detachments (SRD) are a less common but well-documented ocular manifestation of leukemia. The majority of case reports have described SRDs as a finding after the systemic diagnosis of leukemia has been made, not as an initial sign. Furthermore, visual symptoms in general are rare as the first presenting sign of leukemia. We report a patient who presented with unilateral blurry vision due to a SRD as the initial sign of acute lymphoblastic leukemia (ALL).

1. Case report

A 74 year old female presented with right eye subacute visual decline over ten days. She denied eye pain, flashes, and floaters. Her associated C-designed article with open access under the CC BY-NC-ND license.
Fluorescein angiography (FA) showed early phase multifocal hyperlayer corresponding to the location of a large CWS in the left eye (Fig. 2). Macula in the right eye, and peripapillary thickening of the nerve fiber neurosensory retinal detachment and focal RPE changes in the superior phase diffuse small vessel peripheral leakage in both eyes. Interestingly, fluorescent spots of the macula, blockage from hemorrhages, and late (Fig. 1). Optical coherence tomography of the macula (OCT) showed a hypoafluorescent patches corresponding to CWS and hemorrhages, a stippled hyperfluorescent area in the superior macula; in the general mild hyperfluorescence of the superior macula; in the left eye, there were hypoafluorescent patches corresponding to CWS (Fig. 1). Optical coherence tomography of the macula (OCT) showed a hypersensory retinal detachment and focal RPE changes in the superior macula in the right eye, and peripapillary thickening of the nerve fiber layer corresponding to the location of a large CWS in the left eye (Fig. 2). Fluorescein angiography (FA) showed early phase multifocal hyperfluorescent spots of the macula, blockage from hemorrhages, and late phase diffuse small vessel peripheral leakage in both eyes. Interestingly, we did not observe pooling of fluorescein in the late phase (Fig. 3). Ultrasound imaging of the right eye showed no evidence of masses and a slightly thickened choroid compared to the left eye, but no sub-Tenon fluid or “T-sign”. (Fig. 4).

Due to concern for a systemic process, we instructed the patient to have labs drawn the same day, and initial complete blood count results were significant for a white blood cell count of 225.8 (normal 4–11) with blasts, hemoglobin of 5.7 (normal 11.7–15.7), and platelet count of 37 (normal 150–400). Other abnormalities included an erythrocyte sedimentation rate of 50 (normal 0–30), C-reactive protein of 1.3 (normal <0.5), lactate dehydrogenase of >1800 (normal 135–214), uric acid 12.5 (normal 2.5–5.7), and creatinine 1.1 (normal 0.51–0.95). Of note her QuantiFERON and syphilis testing were negative. We instructed the patient to present directly to the emergency department to obtain further workup for a hematologic malignancy and formal hematologic consult.

The patient was eventually admitted to the hospital for further studies. Flow cytometry demonstrated a monoclonal population suggestive of B-cell ALL and a bone marrow biopsy confirmed this diagnosis. Her magnetic resonance imaging (MRI) of the brain demonstrated enhancement of the right optic nerve suggesting leukemic infiltration. (Fig. 5). Lumbar puncture revealed an abnormal B cell population but no blasts. The patient was started on systemic chemotherapy, which consisted of intravenous (IV) cyclophosphamide, vincristine, and daunorubicin and oral prednisone. She was also initiated on intrathecal methotrexate therapy due to high suspicion for central nervous system involvement. One month following initial presentation, the patient was discharged from the hospital on a stable chemotherapy regimen and seen in the ophthalmology clinic two days later.

At follow up appointment, the patient noted overall improvement in vision in the primarily affected right eye. Visual acuity was 20/30–3 in the right eye and 20/30–2 in the left eye. Follow up OCT showed interval improvement of the serous retinal detachment in the right eye (Fig. 6). She continues to follow up in vitreoretinal clinic.

2. Discussion

We report a patient who presented with right eye subacute visual decline due to a SRD as an initial sign of B-ALL. This patient was initially
evaluated by an outside ophthalmologist, who diagnosed her with central serous chorioretinopathy (CSR) and referred her to our institution for further management. However, her demographic and history were atypical for CSR (except an underlying risk factor of stress), her exam showed CWS and hemorrhages which would be atypical for CSR. Furthermore her FA imaging not only did not show features that are characteristic for CSR (e.g. expansile dot, smokestack, late pooling), but also demonstrated bilateral small vessel vasculitis raising concern for a systemic process. An extensive lab workup to further evaluate for autoimmune, infectious, inflammatory, and malignant causes eventually led to a diagnosis of B-ALL. Thus, her exam findings were consistent with bilateral leukemic retinopathy and a unilateral SRD. Her vasculitis noted on FA may have been due to leukemic infiltration versus her underlying rheumatoid arthritis. Ultrasound imaging with enhancement and thickening of the choroid was suggestive of choroidal infiltration and MRI imaging revealed optic nerve infiltration.

SRDs are uncommon as an ocular manifestation of leukemia, and even less common as a presenting sign of disease. Though they are more common in acute (vs. chronic) leukemia, they are less common in lymphoid (vs. myeloid) subtypes, females and older patients, making our patient an unlikely suspect.

There have only been a few cases worldwide of SRDs as a presenting sign of ALL. We performed a comprehensive literature review of such case reports (PubMed advanced search terms: central serous retinopathy or serous retinal detachment or exudative retinal detachment AND acute lymphoid leukemia or acute lymphoblastic leukemia or acute lymphocytic leukemia) (Table 1). Eleven case reports were identified. Most patient were female (8/11, 72.7%) and age distribution ranged from 12 to 75 years old (median: 44). Most patients presented with a chief complaint of bilateral decreased vision. Of note, almost half of the patients did not present with any significant systemic symptoms, highlighting the importance of considering a full workup even in cases of isolated ocular findings concerning for leukemia. All authors reported a fundus exam and/or photograph, nine reported a FA, six reported an OCT, six reported an B-scan ultrasound, and none reported AF images. All patients underwent chemotherapy treatment. Among patients with published follow up data (8/11, 72.7%), all demonstrated functional and anatomic improvement of SRDs.

In considering the underlying mechanism for SRDs in leukemia, pathologic studies have shown blast cells both within and surrounding choroidal vessels. In a post-mortem study by Leonardy et al. the incidence of intravascular and extravascular ocular leukemic cell infiltration was 45.9%. Thus, though choroidal involvement is not always clinically apparent, it occurs somewhat commonly. Imaging such as enhanced depth imaging OCT (EDI OCT) can aid in evaluating choroidal thickness. Two prior studies employed EDI OCT to demonstrate increased choroidal subfoveal thickness in ALL patients with serous retinal detachments. It is postulated that leukemic infiltration of the choroid causes decreased blood flow in the choriocapillaris, either by external compression or internal stagnation of blood. This leads to ischemia of the overlying RPE and disruption of the intercellular tight junctions. The subsequent incompetence of the outer blood retinal barrier allows for subretinal accumulation of the choroidal fluid.

Along with CSR, the differential diagnosis for a SRD is extensive and includes Vogt-Koyanagi-Harada syndrome, uveal effusion syndrome, posterior scleritis, age-related macular degeneration, malignant hypertension, toxemia of pregnancy, choroidal hemangioma, metastatic neoplasm, infectious causes (tuberculosis, syphilis, Lyme, toxoplasmosis, cytomegalovirus), congenital disease (colobomas, optic nerve pits), and drug toxicity. A thorough history, review of systems, clinical
exam, and complete set of ocular imaging can aid greatly in the decision to pursue systemic workup.

Our report as well as those presented in Table 1 demonstrate that ophthalmologists can play a critical role in recognizing underlying hematologic malignancies and performing a thorough systemic workup. Of note, new SRDs in a patient without a clear underlying cause

Fig. 3. Fluorescein angiogram (FA) at initial presentation. Images of the right eye (left column) and left eye (right column) showed early phase multifocal hyperfluorescent spots of the macula, blockage from hemorrhages, and late phase diffuse small vessel peripheral leakage. No evidence of diffuse subretinal accumulation of fluorescein in the late phase.

Fig. 4. B-scan ultrasound of the right eye at initial presentation shows mildly thickened choroid and no masses.
particularly in an unusual CSR demographic should prompt further evaluation. Early intervention is correlated not only with better anatomical and functional ocular recovery, but also life-saving therapy.

3. Conclusion

In this report, we present an unusual case of unilateral SRD as a presenting sign of ALL in an elderly female, with previously unreported co-occurring signs of leukemic retinopathy, optic nerve and choroidal infiltration, and vasculitis. We are also the first to provide a complete library of ocular and brain imaging for such a case, which includes fundoscopic photos, AF, OCT, FA, B-scan ultrasound, and MRI brain. We additionally present the results of a comprehensive review on all case reports of SRDs as a presenting sign of ALL, compare and contrast their findings, describe the proposed pathologic basis of SRDs in leukemia, and highlight the important role of ophthalmologists in saving the lives of patients with this potentially lethal disease.

Patient consent

Written consent to publish this case report has not been obtained. This report does not contain any personal information that could lead to
Table 1
Literature review of cases of acute lymphoblastic leukemia (ALL) with serous retinal detachment (SRD) as presenting sign.

| Author          | Age (years) | Sex | Unilateral or Bilateral | Visual Symptoms                          | Initial Visual Acuity | Non-visual symptoms | Fundus Exam/Photo | Fluorescein Angiogram | Optical Coherence Tomography of the Macula | B Scan (Ultrasound) |
|-----------------|-------------|-----|-------------------------|------------------------------------------|-----------------------|---------------------|-------------------|-----------------------|---------------------------------------------|---------------------|
| Kim et al., 2010| 45          | F   | Bilateral              | Central scotoma, visual disturbance      | 20/100 OD, 20/25 OS   | Headaches           | Serous retinal detachment | Multifocal hyperfluorescence beneath the detachment in the early phase and diffuse subretinal accumulation of fluorescein in the late phase | Neurosensory retinal detachment with increased reflectivity of choroid layers |                       |
| Stewart et al., 1989 | 12    | M   | Unilateral             | Decreased vision, redness, pain          | 20/400 OD (20/25 OS)  | None                | Serous retinal detachment | Multifocal hyperfluorescence beneath the detachment in the early phase and diffuse subretinal accumulation of fluorescein in the late phase |                                  | No choroidal or scleral thickening |
| Lee et al., 2012  | 16         | F   | Bilateral              | Decreased vision                        | 20/200 OU             | None                | Serous retinal detachment | Diffuse subretinal accumulation of fluorescein, no stippled hyperfluorescence of leakage |                                  |                       |
| Malik et al., 2005 | 13    | F   | Bilateral              | Blurry vision                           | 20/30 OD, 20/60 OS   | Sore throat, night sweats, abdominal pain | Serous retinal detachment | Diffuse subretinal accumulation of fluorescein, no stippled hyperfluorescence of leakage |                                  |                       |
| Vieira et al., 2015 | 63    | F   | Bilateral              | Subacute vision loss                     | 20/100 OD, 20/60 OS  | None                | Serous retinal detachment | Multifocal hyperfluorescence beneath the detachment in the early phase and diffuse subretinal accumulation of fluorescein in the late phase | Subretinal fluid (macular thickness: OD 638 μm and OS 423 μm) |                       |
| Katz et al., 2014  | 46         | F   | Bilateral              | Blurry vision                           | 20/200 OU             | Abdominal pain, lumbar pain, nausea, vomiting | Serous retinal detachment, intraretinal hemorrhages | Late phase multifocal hyperfluorescence and diffuse subretinal accumulation of fluorescein | Neurosensory retinal detachment |                       |
| Chinta et al., 2012 | 36    | M   | Bilateral              | Subacute vision loss                     | 20/50 OD, 20/25 OS   | None                | Serous retinal detachment | Delayed choroidal filling and multifocal hyperfluorescence in early phase, multifocal hyperfluorescence in late phase | Subretinal fluid pockets |                       |
| Kincaid et al., 1979 | 71    | F   | Bilateral              | Subacute vision loss                     | HM OD, 20/100 OS     | Weight loss, depression | Serous retinal detachment, vascular attenuation | Multifocal hyperfluorescence beneath the detachment in the early phase and diffuse subretinal accumulation of fluorescein in the late phase |                                  |                       |
| Abdallah et al., 2005 | 42    | F   | Subacute vision loss   | None                                     |                       | Serous retinal detachment |                       |                       | Neurosensory retinal detachment |                       |
| Ortiz et al., 2010 | 44     | M   | Bilateral              | Scotoma                                  | 20/40 OU              | Malaise             | Serous retinal detachment |                       | Neurosensory retinal detachment |                       |
| Fackler et al., 2006 | 75    | F   | Bilateral              | Subacute vision loss                     | 20/126 OD, 20/250 OS | Chronic cough, headaches, fatigue, weight loss | Serous retinal detachment | Multifocal hyperfluorescence beneath the detachment in the early phase and diffuse subretinal accumulation of fluorescein in the late phase | Neurosensory retinal detachment |                       |

Abbreviations: OD = oculus dextrus (right eye), OS = oculus sinister (left eye), OU = oculus uterque (both eyes), HM (hand motion), ALL (acute lymphoblastic leukemia), IV (intravenous), IT (intrathecal), RPE (retinal pigment epithelium), IS/OS (photoreceptor inner segment/outer segment), CNS (central nervous system). Gronbech et al., 2014, Vangheluwe et al., 1990, and Walter et al., 1985 reported serous retinal detachments as a presenting sign of ALL, but were not retrievable for review. [BLANK CELL] indicates information not provided in case report or imaging not completed.
the identification of the patient.

Funding

This work was supported by the Heed Ophthalmic Foundation and Michels Fellowship Foundation awarded to Natalia F. Callaway, MD, MS.

Authorship

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

Declaration of competing interest

The following authors have no financial disclosures: MVP, NFC, QDN, DVD.

Acknowledgements

None.

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