American Journal of Ophthalmology Case Reports 23 (2021) 101142

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Case report

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

Malini Veerappan Pasricha, Natalia F. Callaway, Quan Dong Nguyen, Diana V. Do *

Byers Eye Institute, Stanford University School of Medicine, 2452 Watson Court, Palo Alto, CA, 94303, USA

ARTICLE INFO

Keywords:
Acute lymphoblastic leukemia
Acute lymphoid leukemia
Acute lymphocytic leukemia
Serous retinal detachment
Exudative retinal detachment
Central serous chorioretinopathy

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 lab 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.

Importance: A new diagnosis of serous retinal detachment(s) without any obvious cause should raise suspicion for leukemia and prompt further workup. Early recognition of this hematologic malignancy is crucial for prompt initiation of life-saving therapy.

Ocular involvement has been reported in up to 90% of patients with leukemia.[1] 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.[2] Other ophthalmic findings are orbital masses, optic nerve infiltrates, episcleritis, iris infiltrates, hypopyon, panuveitis, central retinal vein occlusions, retinal neovascularization, vitreous hemorrhages, retinal pigment epitheliopathy, and choroidal infiltration.[3–13] 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.[14]

Serous retinal detachments (SRD) are a less common but well-documented ocular manifestation of leukemia.[15–17] 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.[18–32] 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

Abbreviations: /Acronyms: Acute lymphoblastic leukemia, (ALL); optical coherence tomography, (OCT); serous retinal detachment, (SRD); fluorescein angiogram, (FA); autofluorescence, (AF); cotton wool spots, (CWS); retinal pigment epithelium, (RPE); magnetic resonance imaging, (MRI); intravenous, (IV); central serous chorioretinopathy, (CSR).

* Corresponding author. Byers Eye Institute, Stanford University Medical Center, 2452 Watson Court, Palo Alto, CA, 94303, USA.
E-mail address: dianado@stanford.edu (D.V. Do).

https://doi.org/10.1016/j.ajoc.2021.101142
Received 8 August 2020; Received in revised form 5 May 2021; Accepted 14 June 2021
Available online 22 June 2021

symptoms were dizziness, metallic taste, reduced appetite, shortness of breath, and night sweats. She denied fevers, chills, cough, fatigue, abdominal pain, chest pain, mucosal bleeding, infections, and nausea. Her medical history was significant for well-controlled hypertension (on amlodipine), pre-diabetes (last hemoglobin A1C 6.0), hyperlipidemia (on atorvastatin), and rheumatoid arthritis (minimally symptomatic, not on therapy). She denied any recent travel or animal exposures. Of note, the patient reported that she had been under stress lately due to her vision loss, as she was unable to perform her desk job and provides the sole source of income for her family. Ocular history was unremarkable.

Visual acuity was 20/50 in the right eye and 20/30 in the left eye (no improvement with pinhole bilaterally). Intraocular pressures were 13 mmHg in the right eye and 14 mmHg in the left eye. Slit lamp exam revealed no abnormalities, except for visually significant cataracts in both eyes. Fundus examination and photograph of the right eye showed a posterior vitreous detachment (PVD), blunted foveal reflex, retinal hemorrhages in the superior macula and superonasal periphery, and cotton wool spots (CWS) along the inferior arcade, peripapillary region, and superior periphery. Fundus examination and photograph of the left eye showed a PVD and CWS along the inferior arcade, superior arcade, and peripapillary region. Autofluorescence imaging (AF) of the right eye showed hypoautofluorescent patches corresponding to CWS and hemorrhages, a stippled hyperautofluorescent area in the superior macula corresponding to retinal pigment epithelium (RPE) changes, and a generalized mild hyperautofluorescence of the superior macula; in the left eye, there were hypoautofluorescent patches corresponding to CWS (Fig. 1). Optical coherence tomography of the macula (OCT) showed a neurosensory 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 hyperfluoroscent 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 hematology 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

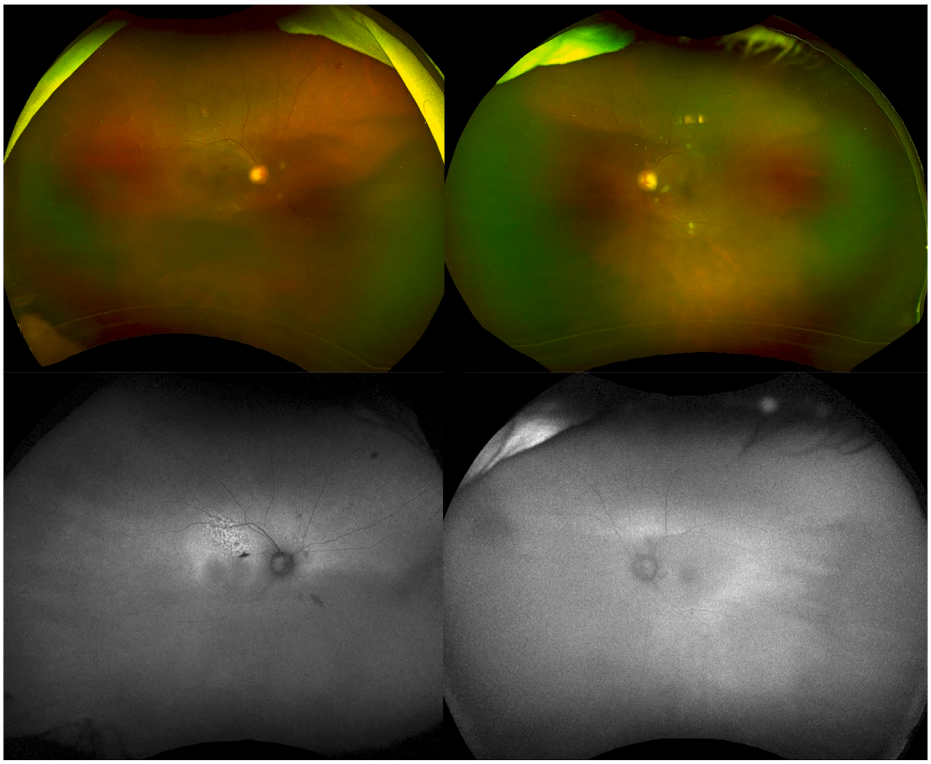

Fig. 1. Fundus photographs and autofluorescence images at initial presentation.
Top Row: Fundus photographs of the right eye (left) and left eye (right). Right eye image shows blunted foveal reflex, inner retinal hemorrhages in the superior macula and superonasal periphery, and cotton wool spots (CWS) along the inferior arcade, peripapillary region, and superior periphery. Left eye image shows CWS along the inferior arcade, superior arcade, and peripapillary region.
Bottom Row: Autofluorescence of the right eye (left) and left eye (right). Right eye image shows hypofluorescent patches corresponding to CWS and hemorrhages, a stippled hyperfluorescent area in the superior macula corresponding to RPE changes, and a generalized mild hyperfluorescence of the superior macula. Left eye image shows hypofluorescent patches corresponding to CWS.

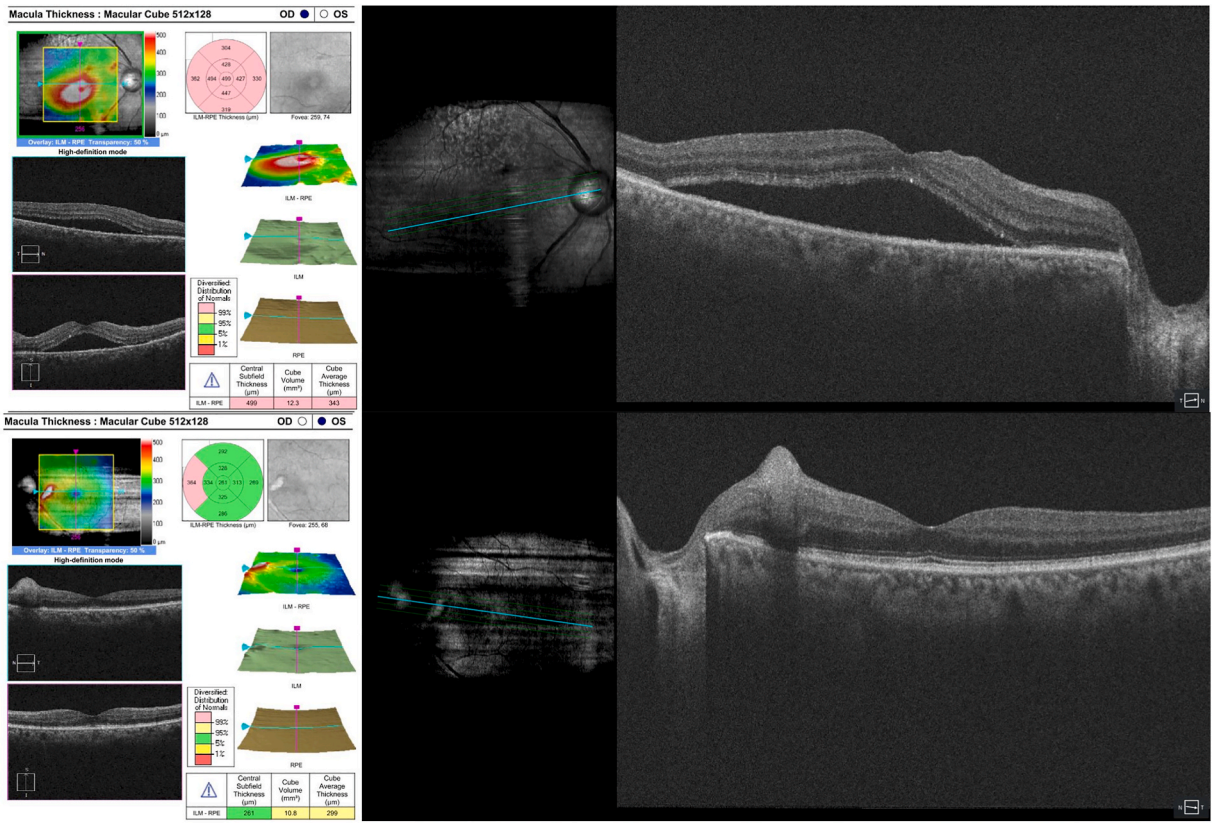

Fig. 2. Optical coherence tomography (OCT) of the macula at initial presentation.
Top Row: Right eye OCT with corresponding macular thickness map showing shallow neurosensory retinal detachment and focal retinal pigment epithelium (RPE) changes in the superior macula.
Bottom Row: Left eye OCT with corresponding thickness map showing peripapillary thickening of the nerve fiber layer corresponding to the location of a large CWS.

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.[33–41]

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).[3,14,42–53] 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, one reported a 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%.[54] 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.[55,56] 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.[54] 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.[57]

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.[47] A thorough history, review of systems, clinical

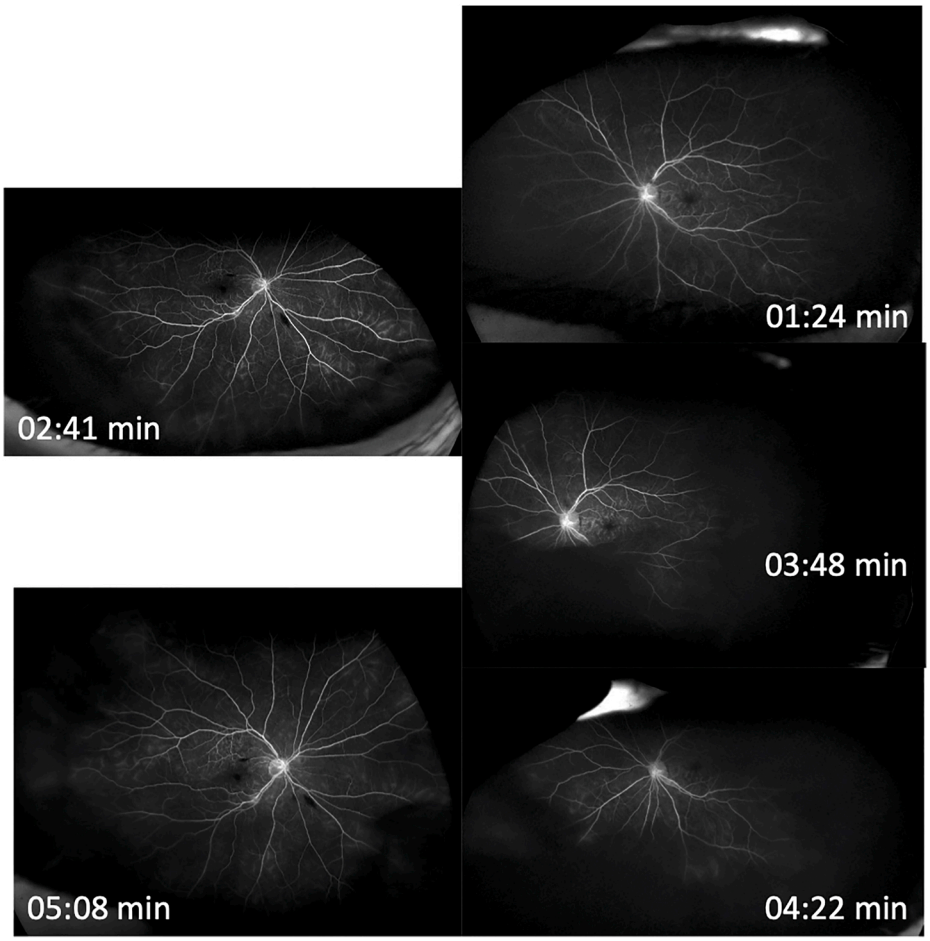

Fig. 3. Fluorescein angiogram (FA) at initial presentation.
Images of the right eye (left column) and left eye (right column) showed early phase multifocal hyperfluorescent spots of the macula, blockage from hemorrhages, and late phase diffuse small vessel peripheral leakage. No evidence of diffuse subretinal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

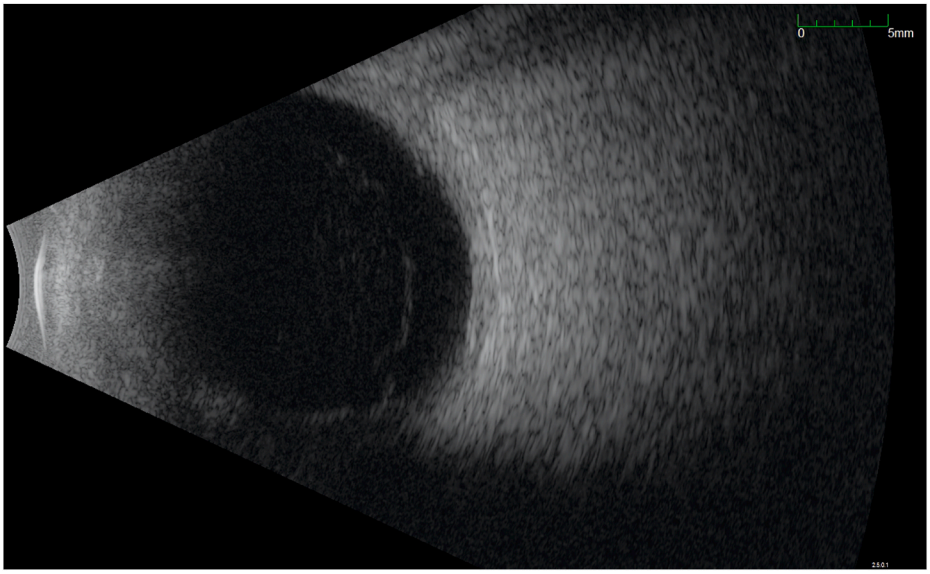

Fig. 4. B-scan ultrasound of the right eye at initial presentation shows mildly thickened choroid and no masses.

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

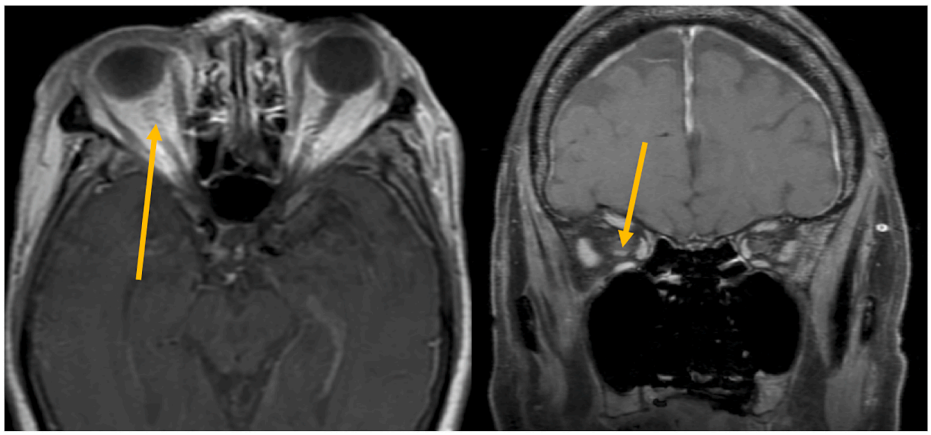

Fig. 5. Magnetic resonance imaging (MRI) of the brain at initial presentation. Axial T1 (right) and coronal T1 (left) images showing enhancement of the right optic nerve (yellow arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

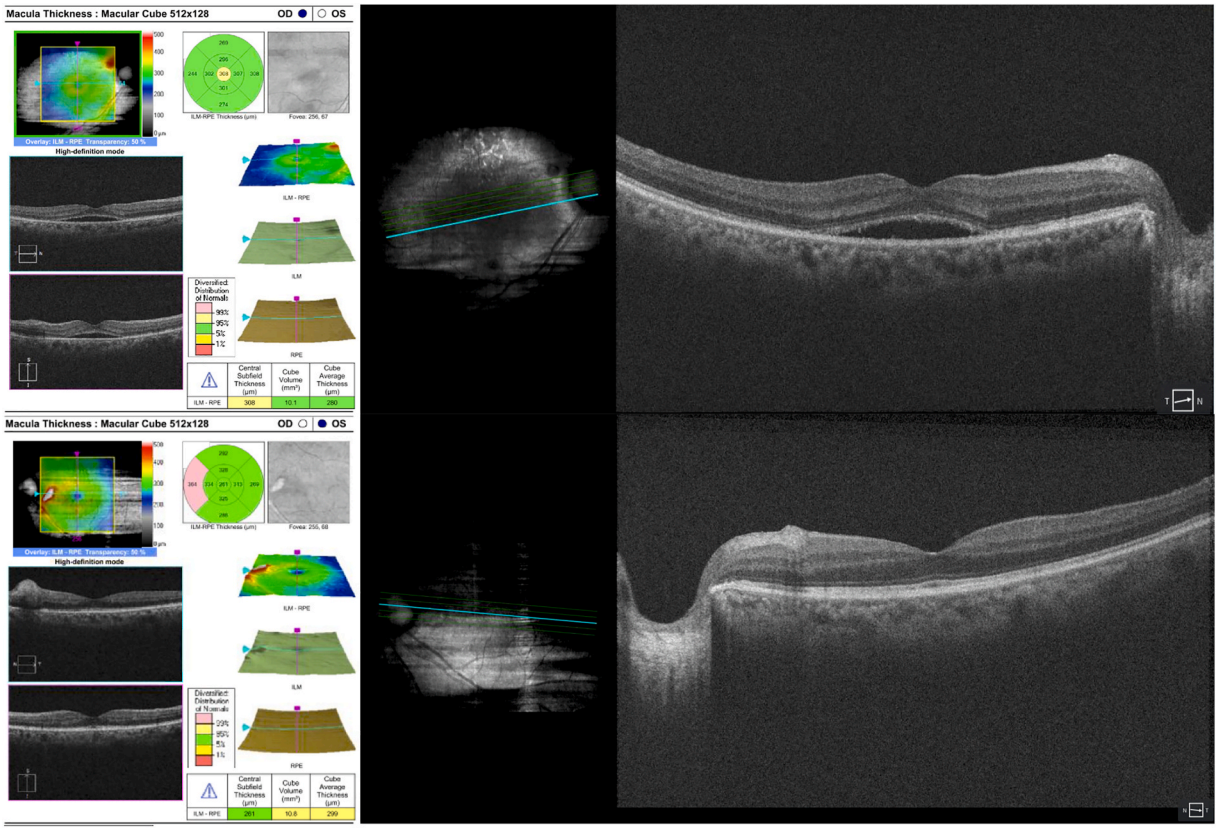

Fig. 6. Optical coherence tomography (OCT) of the macula at follow up visit, after one month of hospitalization for chemotherapy treatment.
Top Row: Right eye OCT with corresponding macular thickness map showing interval improvement in neurosensory retinal detachment.
Bottom Row: Left eye OCT with corresponding thickness map showing interval improvement in peripapillary thickening of the nerve fiber layer.

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	Fluoroscein 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 fluoroscein, no stippled hyperfluoroscence 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 fluoroscein, no stippled hyperfluoroscence 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, lumbago, nausea/ vomiting	Serous retinal detachment, intraretinal hemorrhages	Late phase multifocal hyperfluorescence and diffuse subretinal accumulation of fluoroscein	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 hyperfluoroscence 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			
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 sysem). 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.

References

1. Kincaid MC, Green WR. Ocular and orbital involvement in leukemia. *Surv Ophthalmol*. Jan-Feb 1983;27(4):211–232. https://doi.org/10.1016/0039-6257(83)90123-6.
2. Reddy SC, Jackson N. Retinopathy in acute leukaemia at initial diagnosis: correlation of fundus lesions and haematological parameters. *Acta Ophthalmol Scand*. Feb 2004;82(1):81–85. https://doi.org/10.1046/j.1600-0420.2003.00197.x.
3. Stewart MW, Gitter KA, Cohen G. Acute leukemia presenting as a unilateral exudative retinal detachment. *Retina*. 1989;9(2):110–114. https://doi.org/10.1097/00006982-198909020-00007.
4. Talcott KE, Garg RJ, Garg SJ. Ophthalmic manifestations of leukemia. *Current opinion in ophthalmology*. *Nov*. 2016;27(6):545–551. https://doi.org/10.1097/icu.0000000000000309.
5. Schachat AP, Markowitz JA, Guyer DR, Burke PJ, Karp JE, Graham ML. Ophthalmic manifestations of leukemia. *Arch Ophthalmol*. 1989;107(5):697–700. https://doi.org/10.1001/archopht.1989.01070010715033.
6. Allen RA, Straatsma BR. Ocular involvement in leukemia and allied disorders. *Arch Ophthalmol*. 1961;66(4):490–508. https://doi.org/10.1001/archopht.1961.00960010492010.
7. Bouladi M, Zerei N, Bouraoui R, El Matri L. Unilateral infiltration of the optic nerve revealing relapse of an acute lymphoblastic leukemia. *La Tunisie medicale. Mar*. 2019;97(3):504–507.
8. Patel AV, Miller JB, Nath R, et al. Unilateral eye findings: a rare herald of acute leukemia. *Ocular oncology and pathology*. *Apr*. 2016;2(3):166–170. https://doi.org/10.1159/000442951.
9. Zimmermann A, Weinand F, Lorenz B. [Unilateral loss of visual function with edema of the optic nerve in a 35-year-old male patient]. *Ophthalmologe : Zeitschrift der Deutschen Ophthalmologischen Gesellschaft*. *Nov*. 2010;107(11):1072–1076. https://doi.org/10.1007/s00347-010-2216-6. Einseitige Visusminderung mit Papillenodem bei einem 35-jahrigen Patienten.
10. Dhar-Munshi S, Alton P, Ayliffe WH. Masquerade syndrome: T-cell prolymphocytic leukemia presenting as panuveitis. *Am J Ophthalmol*. Aug 2001;132(2):275–277. https://doi.org/10.1016/s0002-9394(01)00839-x.
11. Schmiegelow K, Scherfig E, Ju Prause, Jensen OA. Isolated leukemic choroidal relapse in a child with acute lymphoblastic leukemia one year off therapy, diagnosed through transvitreal retino-choroidal biopsy. *Acta ophthalmologica*. *Feb*. 1988;66(1):33–37. https://doi.org/10.1111/j.1755-3768.1988.tb08530.x.
12. Clayman HM, Flynn JT, Koch K, Israel C. Retinal pigment epithelial abnormalities in leukemic disease. *Am J Ophthalmol*. 1972;74(3):416–419.
13. Khaja WA, Pogrebniak AE, Bolling JP. Combined orbital proptosis and exudative retinal detachment as initial manifestations of acute myeloid leukemia. *Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus*. Oct 2015;19(5):479–482. https://doi.org/10.1016/j.jaapos.2015.05.018.
14. Kim J, Chang W, Sagong M. Bilateral serous retinal detachment as a presenting sign of acute lymphoblastic leukemia. *Kor J Ophthalmol : Kor J Ophthalmol*. Aug 2010;24(4):245–248. https://doi.org/10.3341/kjo.2010.24.4.245.
15. Murphy JA, Pitts JF, Dudgeon J, Hogg RB, Harnett AN. Retinal detachments due to chronic lymphocytic leukaemia. *Clin Lab Haematol*. 1991;13(2):217–220. https://doi.org/10.1111/j.1365-2257.1991.tb00272.x.
16. Burns C, Blodi F, Williamson B. Acute lymphocytic leukemia and central serous retinopathy. *Trans Am Acad Ophthalmol Otolaryngol*. 1965;69:307–309.
17. Zimmerman L, Thoreson H. Sudden loss OF VISION IN acute leukemia. A clinicopathologic report OF two unusual cases. *Surv Ophthalmol*. 1964;9:467–473.
18. Hine JE, Kingham JD. Myelogenous leukemia and bilateral exudative retinal detachment. *Annals of ophthalmology*. *Dec*. 1979;11(12):1867–1872.
19. Miyamoto K, Kashii S, Honda Y. Serous retinal detachment caused by leukemic choroidal infiltration during complete remission. *The British journal of ophthalmology*. *Nov*. 2000;84(11):1318–1319. https://doi.org/10.1136/bjo.84.11.1318a.
20. Wu L, Calderon M, Hernandez G, Marbis J, Ramirez V. Bilateral exudative retinal detachment as the first sign of relapsing acute myelogenous leukaemia. *Clin Exp Ophthalmol*. Aug 2006;34(6):623–625. https://doi.org/10.1111/j.1442-9071.2006.01291.x.
21. Hua HU, Rayess N, Moshfeghi AA. Acute promyelocytic leukemia with sudden vision loss. *JAMA ophthalmology*. Dec 5 2019. https://doi.org/10.1001/jamaophthalmol.2019.4838.
22. Green W, Rao PK, Harocopos GJ. Extramedullary relapse of acute myelogenous leukemia presenting as a large serous retinal detachment. *Ocular oncology and pathology*. Jul 2017;3(2):95–100. https://doi.org/10.1159/000450858.
23. Yabas Kiziloglu O, Mestanoglu M, Totuk Gedar OM, Adiguzel C, Toygar O. Recurrence of acute lymphoblastic leukemia manifesting as serous retinal detachments and optic disc swelling. *International ophthalmology*. *Aug*. 2018;38(4):1791–1795. https://doi.org/10.1007/s10792-017-0648-6.
24. Cerda-Ibanez M, Bayo-Calduch P, Manfreda-Dominguez L, Duch-Samper A. ACUTE VISION LOSS AS THE ONLY SIGN OF LEUKEMIA RELAPSE. *Retinal cases & brief reports*. *Winter*. 2018;12(1):10–11. https://doi.org/10.1097/icb.0000000000000378.
25. Yoshida K, Hasegawa D, Takusagawa A, et al. Bullous exudative retinal detachment due to infiltration of leukemic cells in a child with acute lymphoblastic leukemia. *Int J Hematol*. Oct 2010;92(3):535–537. https://doi.org/10.1007/s12185-010-0683-9.
26. Golan S, Goldstein M. Acute lymphocytic leukemia relapsing as bilateral serous retinal detachment: a case report. *Eye*. Oct 2011;25(10):1375–1378. https://doi.org/10.1038/eye.2011.157.
27. Dambricourt L, Sampo M, Levy N, Arnould T, Ho Wang Yin G, Denis D. [Leukemic chorioretinal infiltrates with serous retinal detachment in acute pre-B lymphoblastic leukemia]. *Journal francais d'ophtalmologie*. *Jun*. 2019;42(6):e247–e249. https://doi.org/10.1016/j.jfo.2018.12.011. Infiltrats leucemiques chorioretiniens compliques d'un decollement sereux retinien dans une leucemie aigue lymphoblastique pre-B.
28. Gillette TB, Cabrera MT, Tarlock K, Murphy CE, Chisholm KM, Stacey AW. Rapidly progressive, isolated subretinal leukemic relapse: a case report. *Ocular oncology and pathology*. *Jun*. 2018;4(4):220–224. https://doi.org/10.1159/000484054.
29. Paydas S, Soylu MB, Disel U, et al. Serous retinal detachment in a case with chronic lymphocytic leukemia: no response to systemic and local treatment. *Leuk Res*. Jun 2003;27(6):557–559. https://doi.org/10.1016/s0145-2126(02)00263-1.
30. Martin-Gousset D, Lawki F, Baudu P, Moreau PG. [Syndrome of acute choriocapillaris ischemia in leukemia. Thoughts apropos of a case]. *J Fr Ophtalmol*. 1982;5(10):609–613. Syndrome d'ischemie aigue choriocapillaire au cours d'une leucose. Reflexion a propos d'une observation.
31. Azik FM, Akinci A, Sayli TR, et al. Unilateral exudative retinal detachment as the sole presentation of relapsing acute lymphoblastic leukemia. *Turk J Haematol : official journal of Turkish Society of Haematology*. Jun 2012;29(2):181–184. https://doi.org/10.5505/tjh.2012.72623.
32. Johnson JS, Lopez JS, Kavanaugh AS, Liang C, Mata DA. A 25-year-old man with exudative retinal detachments and infiltrates without hematological or neurological findings found to have relapsed precursor T-cell acute lymphoblastic leukemia. *Case reports in ophthalmology*. Sep-Dec 2015;6(3):321–327. https://doi.org/10.1159/000439375.
33. Koshy J, John MJ, Thomas S, Kaur G, Batra N, Xavier WJ. Ophthalmic manifestations of acute and chronic leukemias presenting to a tertiary care center in India. *Indian journal of ophthalmology*. *Aug*. 2015;63(8):659–664. https://doi.org/10.4103/0301-4738.169789.
34. Riss JM, Kaplanski G, Righini-Chossegros M, Harle JR, Escoffier P, Saracco JB. [Bilateral serous detachment of neuroepithelium of the posterior pole disclosing acute leukemia]. *J Fr Ophtalmol*. 1990;13(11-12):563–568. Decollement sereux bilateral du neuroepithelium du pole posterieur revelant une leucemie aigue.
35. Chen MT, Wu HJ. Acute leukemia presenting as diabetes insipidus and bilateral exudative retinal detachment–a case report. *The Kaohsiung journal of medical sciences*. *Mar*. 2001;17(3):150–155.
36. Naseripour M, Abdolalizadeh P, Abdi F, Mehrvar A, Tashvighi M. Serous retinal detachment as an initial presentation of childhood acute myeloid leukemia. *Canadian journal of ophthalmology Journal canadien d'ophtalmologie*. *Aug*. 2019;54(4):e170–e173. https://doi.org/10.1016/j.jcjo.2018.10.008.
37. Kishimoto T, Fukuda K, Nishiuchi T, Hayashi N, Fukushima A. Unilateral serous retinal detachment with choroidal thickening as a first presenting sign of acute myeloid leukemia. *American journal of ophthalmology case reports*. Jun 2019;14:51–54. https://doi.org/10.1016/j.ajoc.2019.02.005.
38. Smith AG, London NJ, Pao K, Lipkowitz J, Kurup SK, Garg SJ. Leukemia presenting as serous retinal detachment. *Retinal cases & brief reports*. *Fall*. 2014;8(4):279–282. https://doi.org/10.1097/icb.0000000000000074.
39. Caillaux V, Querques G, Ramahefasolo C, Darugar A, Souied EH. Bilateral macular serous retinal detachment revealing acute myeloblastic leukemia. *Retinal cases & brief reports*. *Winter*. 2013;7(1):62–66. https://doi.org/10.1097/ICB.0b013e318263d405.
40. Sharma H, Majumder PD, Rao C, Biswas J. A case of Acute Myeloid Leukemia masquerading as unilateral exudative detachment. *American journal of ophthalmology case reports*. Dec 2016;4:47–49. https://doi.org/10.1016/j.ajoc.2016.08.004.
41. Montero J, Cervera E, Palomares P, Amselem L, Diaz-Llopis M. Serous retinal detachment as a presenting feature of chronic myelogenous leukemia. *Retinal cases & brief reports*. *Fall*. 2010;4(4):394–396. https://doi.org/10.1097/ICB.0b013e3181b5ef71.

42. Lee CS, Shim JW, Yoon JS, Lee SC. Acute lymphoblastic leukemia presenting as bilateral serous macular detachment and lacrimal gland enlargement. *Canadian journal of ophthalmology Journal canadien d'ophtalmologie.* Oct 2012;47(5):e33–e35. https://doi.org/10.1016/j.jcjo.2012.03.013.
43. Malik R, Shah A, Greaney MJ, Dick AD. Bilateral serous macular detachment as a presenting feature of acute lymphoblastic leukemia. *Eur J Ophthalmol.* Mar-Apr 2005;15(2):284–286. https://doi.org/10.1177/112067210501500219.
44. Vieira L, Silva NA, Medeiros MD, Flores R, Maduro V. Acute lymphoblastic leukemia presenting with bilateral serous macular detachment. *Arquivos brasileiros de oftalmologia. Nov.* -Dec 2015;78(6):382–384. https://doi.org/10.5935/0004-2749.20150101.
45. Katz MS, Fingerhut DE, Jonna G. Exudative retinal detachment as a presenting sign in Philadelphia chromosome-positive acute lymphoblastic leukemia. *Retinal cases & brief reports. Fall.* 2014;8(4):340–341. https://doi.org/10.1097/icb.0000000000000064.
46. Chinta S, Rani PK, Manusani U. Bilateral exudative retinal detachment as a presenting sign of acute lymphoblastic leukemia. *Middle East Afr J Ophthalmol.* Oct 2012;19(4):410–412. https://doi.org/10.4103/0974-9233.102762.
47. Kincaid MC, Green WR, Kelley JS. Acute ocular leukemia. *American journal of ophthalmology. May.* 1979;87(5):698–702. https://doi.org/10.1016/0002-9394(79)90307-6.
48. Abdallah E, Hajji Z, Mellal Z, Belmekki M, Bencherifa F, Berraho A. [Macular serous detachment revealing acute lymphoblastic leukemia]. *Journal francais d'ophtalmologie. Jan.* 2005;28(1):39–44. https://doi.org/10.1016/s0181-5512(05)81023-x. Decollement sereux maculaire revelateur d'une leucemie aigue lymphoblastique.
49. Ortiz JM, Ruiz-Moreno JM, Pozo-Martos P, Montero JA. Visual acuity loss and OCT changes as initial signs of leukaemia. *Int J Ophthalmol.* 2010;3(3):281–282. https://doi.org/10.3980/j.issn.2222-3959.2010.03.24.
50. Fackler TK, Bearelly S, Odom T, Fekrat S, Cooney MJ. Acute lymphoblastic leukemia presenting as bilateral serous macular detachments. *Retina.* Jul-Aug 2006;26(6):710–712. https://doi.org/10.1097/01.iae.0000236484.24808.bb.
51. Gronbech KT, Rewes A, Grauslund J. [Chorioretinopathy as the first symptom of acute lymphoblastic leukaemia]. *Ugeskr Laeger.* Jan 13 2014;176(3a):V07130455 (Korioretinopati som forste symptom pa akut lymfoblastisk leukaemi).
52. Vangheluwe O, Ducasse A, Culioli B, Kwong FH, Segal A. [Macular manifestations of acute lymphoblastic leukemia. A case report]. *Bulletin des societes d'ophtalmologie de France.* Jun-Jul 1990;90(6-7):677–682. Manifestations maculaires d'une leucemie aigue lymphoblastique–a propos d'un cas.
53. Walter G, Ausserer B. [Retinopathia centralis serosa–initial symptom of acute lymphoblastic leukemia]. *Klinische Monatsblatter fur Augenheilkunde. Nov.* 1985;187(5):441–442. https://doi.org/10.1055/s-2008-1054366. Retinopathia centralis serosa–Erstsymptom einer akuten lymphoblastischen Leukamie.
54. Leonardy NJ, Rupani M, Dent G, Klintworth GK. Analysis of 135 autopsy eyes for ocular involvement in leukemia. *Am J Ophthalmol.* Apr 15 1990;109(4):436–444. https://doi.org/10.1016/s0002-9394(14)74610-0.
55. Adam MK, Pitcher JD, Shields CL, Maguire JI. Enhanced depth imaging optical coherence tomography of precursor cell leukemic choroidopathy before and after chemotherapy. *Middle East Afr J Ophthalmol.* Apr-Jun 2015;22(2):249–252. https://doi.org/10.4103/0974-9233.150630.
56. Adaniya A, Bazterrechea P, Trucco JI, Schlaen BA, Kusminsky G, Saravia MJ. Bilateral macular detachment: choroid as a sanctuary of acute lymphoblastic leukemia. *American journal of ophthalmology case reports.* Sep 2020;19:100746. https://doi.org/10.1016/j.ajoc.2020.100746.
57. Spaide RF, Goldbaum M, Wong DW, Tang KC, Iida T. Serous detachment of the retina. *Retina.* Dec 2003;23(6):820–846. https://doi.org/10.1097/00006982-200312000-00013. quiz 895-6.