

Acute lymphocytic leukemia with initial manifestation of serous retinal detachment and choroidal thickening: case report and literature review

Journal of International Medical Research

49(3) 1–7

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DOI: 10.1177/0300060520964373

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Abstract

This report describes a patient who had acute lymphocytic leukemia with exudative retinal detachment (RD), which mimicked Vogt–Koyanagi–Harada disease (VKH). A 61-year-old woman presented with painless loss of vision in the left eye. Fundus examination revealed RD in her left eye. B-scan ultrasonography confirmed localized RD and choroidal thickening. Fundus fluorescein angiography revealed stippled pinpoint hyperfluorescence in the upper macula. One week later, reduced visual acuity was noted in the right eye. B-scan ultrasonography and optical coherence tomography revealed serous RD in both eyes. A provisional diagnosis of VKH was made. However, subsequent hematologic analysis detected an extremely high leukocyte count. Elevated numbers of leukocytes and tumor cells were found in cerebrospinal fluid. Bone marrow biopsy revealed 77% primary atypical blood cells, 89% of which were immature lymphocytes. The patient was subsequently diagnosed with acute lymphocytic leukemia and transferred to the Department of Hematology. However, the patient and her family refused chemotherapy; she eventually died. Our findings suggest that exudative RD, similar to VKH, could be a sign of leukemia. Pinpoint hyperfluorescence leakage is important for differential diagnosis, particularly with respect to VKH.

Keywords

Exudative retinal detachment, Vogt–Koyanagi–Harada disease, choroidal thickening, acute lymphocytic leukemia, uveomeningoencephalitic syndrome, fluorescein angiography, optical coherence tomography, macula lutea, ultrasonography, leukocytes

Date received: 2 June 2020; accepted: 14 September 2020

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Introduction

Ocular manifestations can occur in patients with leukemia, which is a malignant neoplasm of hematopoietic stem cells.¹ Leukemic ophthalmic signs result from direct infiltration by neoplastic cells or from various indirect etiologies. Ocular tissues most frequently involved in leukemia include the retina and choroid. Common ocular signs in leukemia comprise retinal hemorrhage, Roth spots, cotton wool patches, and tortuosity and dilation of retinal vessels.²

Notably, choroidal involvement in leukemia is often caused by perivascular infiltration of leukemic cells, which manifests as choroidal thickening. This could lead to signs of exudative retinal detachment (RD), which is a relatively rare condition that mimics manifestations of Vogt–Koyanagi–Harada disease (VKH).³ VKH is a unique type of uveitis that typically presents as bilateral exudative RD. However, exudative RD may also precede the diagnosis of leukemia or occur during the course of the disease.⁴

Here, we describe a patient who had VKH-like exudative RD with choroidal thickening that constituted the initial manifestation of acute lymphocytic leukemia. Our report implies that awareness of the ophthalmic manifestations of leukemia may aid in differential diagnosis, particularly with respect to VKH.

Case report

Initial symptoms and clinical findings

A 61-year-old Asian woman was referred to our department with the complaint of painless loss of vision in the left eye. She had a history of hearing loss, headache, dizziness, nausea, and vomiting before the onset of ocular symptoms. Her ocular and medical histories were otherwise unremarkable. The

patient's initial best-corrected visual acuity values were 20/400 in the left eye and 20/20 in the right eye. Intraocular pressure values were normal in both eyes (15 mmHg in the left eye and 17 mmHg in the right eye; normal range, 10–21 mmHg). Both eyes had quiet anterior chamber, clear lens, and no cells in the anterior vitreous cavity. Light reflex was normal in the right eye, whereas it was sluggish in the left eye; the left pupil diameter was 5.5 mm. Fundus examination of the left eye revealed RD in the posterior pole, which involved the fovea. However, no retinal hole or retinal hemorrhage was found in the posterior pole or other regions of the retina. The posterior part of the right eye was normal.

Imaging examination and initial treatment

Subsequently, the patient underwent B-scan ultrasonography and fundus fluorescein angiography (FFA) examinations. B-scan ultrasonography of the left eye showed localized RD temporal to the optic nerve, which involved the macula; it also revealed choroidal thickening. The right eye exhibited normal findings (Figure 1). FFA revealed stippled pinpoint hyperfluorescence in the upper macula in the left eye, which began in the early phase and lasted into the late phase (Figure 2). Magnetic resonance angiography to exclude tumors in the brain or retina demonstrated negative results.

One week after initial presentation to our clinic, the patient experienced reduced visual acuity in the right eye (best-corrected visual acuity of 20/30). B-scan ultrasonography and optical coherence tomography examinations revealed obvious serous RD below the macula in both eyes (Figures 3 and 4). Thus, a provisional diagnosis of VKH was made, based on the patient's systemic complaints of headache, hearing loss, and the ocular sign of bilateral RD. However, the patient did not exhibit

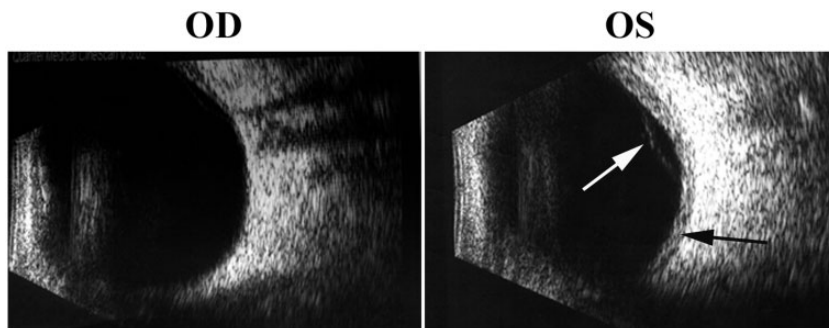


Figure 1. B-scan ultrasonography of both eyes during the patient's first visit. Localized retinal detachment (white arrow) and choroidal thickening (black arrow) were evident in the left eye, while the right eye appeared normal.

OD, right eye; OS, left eye.

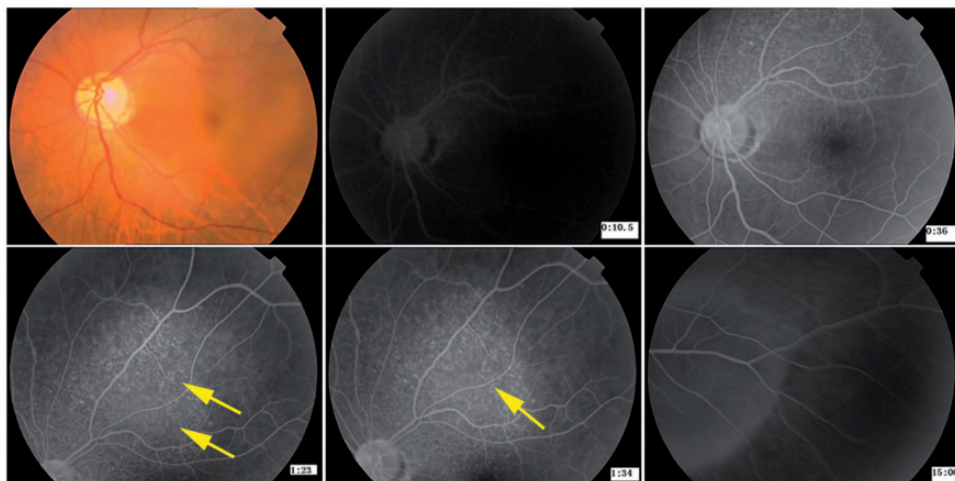


Figure 2. Fundus photography and fundus fluorescein angiography of the left eye. Fundus fluorescein angiography revealed stippled pinpoint hyperfluorescence, temporal and superior to the macula of the left retina (yellow arrows).

integument signs, such as poliosis, vitiligo, or alopecia. Notably, 1 week of steroid treatment did not attenuate the RD.

Diagnosis and outcome

Two weeks after initial presentation to our clinic, the patient had high blood pressure (166/93 mmHg) and slurred speech. Hematologic analysis then revealed an

elevated leukocyte count ($41.96 \times 10^9/L$; normal range, $4\text{--}10 \times 10^9/L$), which primarily constituted lymphocytes (64.4%; normal range, 20%–40%). Elevated numbers of leukocytes and tumor cells were found in cerebrospinal fluid. Furthermore, bone marrow biopsy revealed 77% primary atypical blood cells, 89% of which were immature lymphocytes. The patient was then diagnosed with acute lymphocytic leukemia and transferred

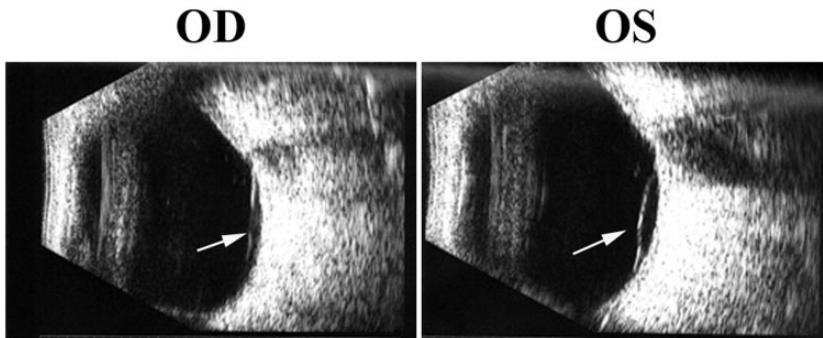


Figure 3. B-scan ultrasonography of both eyes, 1 week after the onset of ocular signs. B-scan ultrasonography revealed obvious retinal detachment in both eyes (white arrows). OD, right eye; OS, left eye.

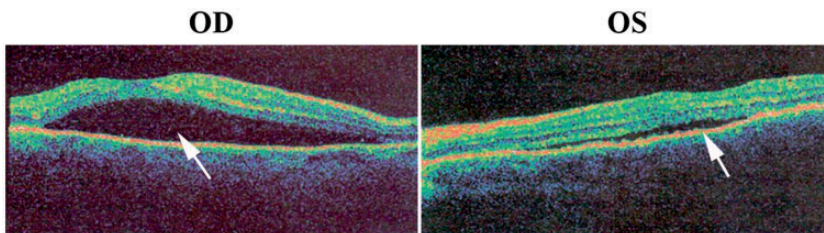


Figure 4. Optical coherence tomography images of both eyes, 1 week after the onset of ocular signs. Optical coherence tomography confirmed serous retinal detachment under the macula in both eyes (white arrows). OD, right eye; OS, left eye.

to the Department of Hematology for further treatment. However, the patient and her family refused chemotherapy; she died within 6 months.

Discussion

In this report, we described a patient who presented with VKH-like bilateral RD and was eventually diagnosed with acute lymphocytic leukemia. During the course of leukemia, ocular manifestations have been reported to occur in up to 90% of patients.² Zimmerman and Thoreson were the first to report vision loss in patients with leukemia in 1964.⁵ Ophthalmic manifestations of leukemia vary among patients; they most frequently include retinal hemorrhage and

optic disc edema.⁶ However, our patient initially presented with exudative RD.

Exudative RD is a relatively rare manifestation of leukemia and could be easily misdiagnosed as VKH, especially in patients who exhibit neurological manifestations and integument signs.^{4,7} AlZamil⁸ reported VKH-like RD in a patient who was eventually diagnosed with acute lymphocytic leukemia; prodromal symptoms might thus lead to misdiagnosis of VKH. Chawla et al.³ described chronic myelocytic leukemia during hematological remission in a patient with prodromal symptoms and other meningism signs suggestive of VKH. Our patient also presented with exudative RD, which was later attributed to acute lymphocytic leukemia.

During VKH, patients usually present with neurological complaints, including malaise, fever, and meningism (i.e., headaches and neck stiffness). Integument manifestations, such as poliosis, vitiligo, and alopecia, may also develop with typical ocular signs of serous RD.⁹ Specifically, the VKH ocular signs might be bilateral without evidence of other ocular disease, trauma, or surgery.¹⁰

As AlZamil⁸ suggested, the exudative RD in our patient, combined with the presence of prodromal symptoms (e.g., hearing loss and headache) led to misdiagnosis of VKH disease, although no integument manifestations were found. There are three types of VKH disease: complete, incomplete, and probable.¹¹ Incomplete or probable VKH disease was originally regarded as the diagnosis for our patient. Choroidal involvement in various systemic diseases can lead to exudative RD.^{12,13} Notably, the choroid is one of the most frequently involved ocular tissues in leukemia. The possible mechanism underlying bilateral serous RD during leukemia could involve choroidal ischemia and secondary retinal pigment epithelium dysfunction. These manifestations might be caused by perivascular infiltration of leukemic cells, as well as hematological disturbances.^{14,15} Furthermore, autopsies of patients with leukemia have revealed features of choroidal thickening and leukemic cell infiltration that may cause choriocapillaris occlusion and delayed choroidal circulation, leading to choroidal ischemia.^{16,17} Although we were not able to identify leukemic cells in the choroid in our patient because no biopsy was taken, B-scan ultrasonography revealed choroidal infiltration.

It is important to acknowledge that the FFA feature of stippled pinpoint hyperfluorescence in our patient is somewhat different from the findings in patients with VKH, who exhibit fluorescence pooling and bilateral disc staining.¹⁸ Choroidal metastases exhibit hyperfluorescent pinpoint leakage on FFA.¹⁹

However, magnetic resonance angiography examination did not reveal remarkable results. FFA features may vary in patients with leukemia. Sharma et al.²⁰ found the signs of early stippled pinpoint hyperfluorescence, placoid dye pooling and late disc staining on FFA in patients with leukemia. Consistent with our findings, Merle et al.²¹ also reported deep retinal infiltration characterized by the juxtaposition of hyperfluorescent points in their patients with leukemia. In addition, leukemia-related hyperfluorescent pinpoints in the posterior retina were described by Vieira et al.²² These hyperfluorescent pinpoints were presumed to be constituted of the accumulation of leukemic cells between the retinal pigment epithelium and Bruch's membrane.²¹ The underlying mechanism has been attributed to choroidal infiltration by leukemic cells, which leads to choriocapillaris ischemia and the disruption of intercellular tight junctions or necrosis of the retinal pigment epithelium.²²

Conclusions

In this report, we have described a rare instance in which a patient with acute lymphocytic leukemia presented with an initial manifestation of VKH-like exudative RD. Clinicians should consider the FFA features of pinpoint fluorescence leakage during differential diagnosis, particularly with respect to VKH.

Ethics statement

The Ethics Committee of the 900th Hospital of Joint Logistic Support Force, PLA approved the publication of this case report. The patient's family provided informed consent for publication of this case report.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This work was supported by grants from the 2018 Scientific Research Project of the 900th Hospital of Joint Logistic Support, PLA (Project numbers: 2018Q02) and the Pilot project of Fujian Province (Grant number: 2013Y5009, 2016Y0067, 2020Y0076, 2020J05282).

Author contributions

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