A Young Man with Bilateral Hemorrhages

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Introduction:

A 23-year-old man was referred for bilateral intraretinal hemorrhages. He reported moderate blurry vision and new floaters in both eyes for the past 4-5 days. He had not had an eye examination for many years and did not have any known prior ocular history or family history of eye problems. Of note, over the past 4-5 months he had been experiencing fatigue, decreased appetite, decreased energy, weight loss, and increased nosebleeds. About one week ago he noticed onset of a bilateral lower extremity rash. The patient was not diabetic but did have a family history of type 2 diabetes mellitus. He denied any personal or family history of blood dyscrasia, autoimmune disease, or malignancy but did report bleeding during dental procedures. He reported he was not sexually active and did not have reason to believe he was exposed to any infectious disease, sexually transmitted or otherwise. Several months ago, he was severely hypertensive and found to have elevated liver enzyme and iron levels. These were addressed with systemic medications to control his hypertension, and the patient believed his liver function tests and iron levels had since normalized. He was overweight, had a history of anxiety disorder, and had previously been vaccinated against Corona virus (COVID)-19.

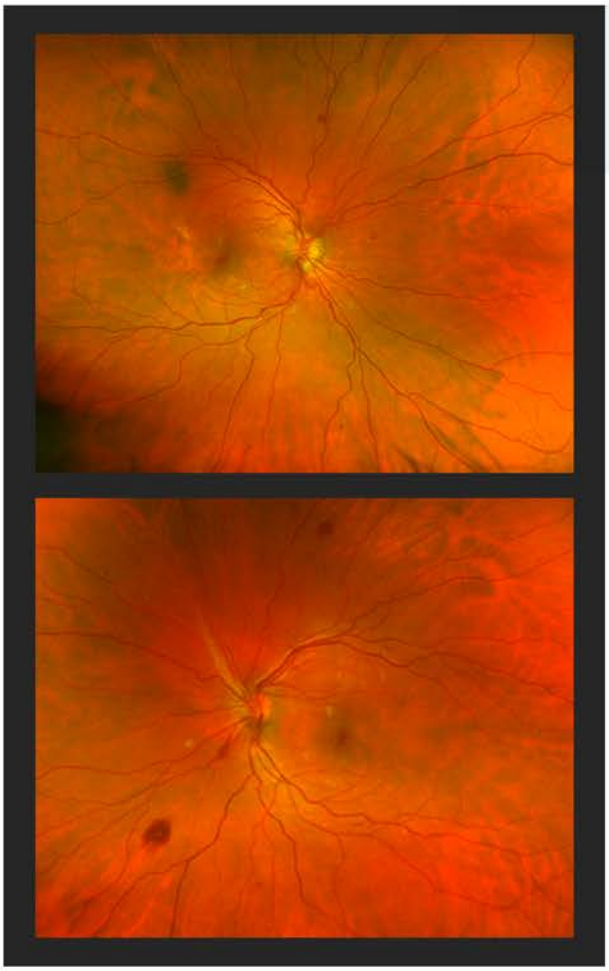

Figure 1. Bilateral color fundus images demonstrating intraretinal hemorrhages and cotton wool spots .

Exam:

Best corrected visual acuity was 20/25 in the right eye and 20/20 in the left eye. Pupillary responses were normal to light and accommodation in both eyes, there was no relative afferent pupillary defect, and visual fields were full to confrontation. Dilated funduscopic examination showed hyperemic discs bilaterally, scattered intraretinal hemorrhages throughout the posterior pole and midperiphery bilaterally, and cotton wool spots diffusely throughout the posterior pole bilaterally. The right eye also had a flat oval pigmented lesion consistent with a choroidal nevus. (See Figure 1) The anterior chamber and vitreous were clear of inflammatory cells on careful slit lamp examination.

Imaging and Further Workup:

To aid in diagnosis, spectral domain optical coherence tomography (SD-OCT) and a fluorescein angiogram were obtained. SD-OCT showed hyper-reflective lesions along the nerve fiber layer consistent with cotton wool spots and a normal appearing macula and choroid (Figure 2). Fluorescein angiography revealed blockage from intraretinal hemorrhages, normal arm-to-eye time, and absence of leakage from the vessels or optic disc bilaterally (Figure 3).

Blood pressure in the office was obtained and was 132/80 (sitting, arm). A number of laboratory tests were

ordered. Normal values/results were obtained for a basic metabolic panel, hemoglobin A1c, urinalysis, prothrombin time (PT), international normalized ratio (INR), fibrinogen, amylase, C-reactive protein (CRP), antinuclear antibody (ANA), rheumatoid factor (RF), antineutrophil cytoplasmic antibody (ANCA), human immunodeficiency virus (HIV), Lyme antibody, and rapid plasma regain (RPR). Abnormal tests included significantly elevated triglycerides, decreased high density lipoproteins (HDL), elevated ALT (alanine transaminase) and AST (glutamine transaminase), elevated erythrocyte sedimentation rate (ESR), and elevated angiotensin converting enzyme (ACE). Most notably, complete blood count revealed a profoundly elevated white blood count, along with anemia and severe thrombocytopenia. The peripheral smear revealed numerous lymphoblasts, concerning for acute leukemia.

Treatment:

The patient was admitted to a hospital, where a bone marrow biopsy was consistent with acute B-lymphocytic leukemia. A lumbar puncture was performed for a cerebrospinal fluid (CSF) sample, which was negative for malignant cells on pathology. Treatment with systemic chemotherapy was initiated.

Discussion:

Ophthalmic manifestations of leukemia are varied and affect nearly all ocular structures. Retinopathy may result from direct infiltration of leukemic cells or indirectly from hematologic abnormalities such as anemia and thrombocytopenia or infectious disease.[1] Dilated and tortuous veins and venules may be an early sign of leukemia, hemorrhages at all levels are common, and cotton wool spots are frequently seen. In the case of direct infiltration by neoplastic cells, grayish white plaques may be seen anywhere in the retina, subretinal space, choroid, and/or optic nerve. This is generally associated with high white blood cell counts.[2] Vascular occlusions are commonly seen, including simultaneous bilateral venous occlusions.[3] In cases of chronic leukemia, microaneurysms, capillary dropout, and peripheral neovascularization may occur, along with tractional retinal detachment.[3]

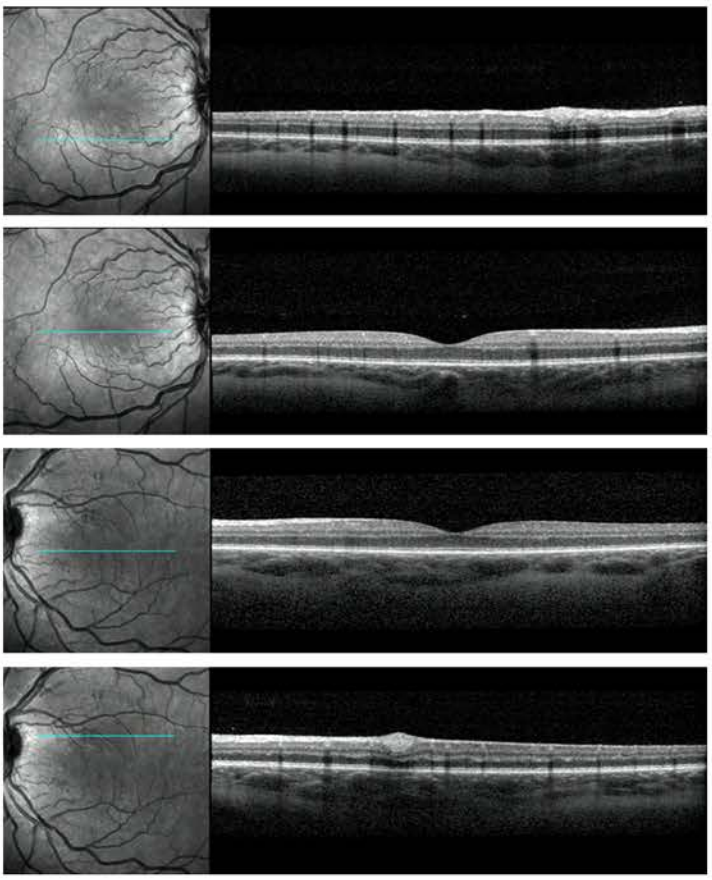

Figure 2. SD-OCT demonstrating macular cotton wool spots in both eyes.

Figure 3. Fluorescein angiogram of both eyes, at a) 54 seconds and b) 3 minutes 5 seconds, The arm-to-eye time was 17 seconds. Note no leakage present.

Treatment of systemic leukemia with chemotherapy often causes improvement or resolution of the retinopathy, however ophthalmic manifestations are often first signs in case of disease recurrence.[4]

Interestingly, the patient's rash, which

sparked additional concern and reinforced the need for systemic evaluation, is a somewhat common systemic manifestation of acute leukemia. Leukocytoclastic vasculitis presents with a bilateral purpuric rash on the lower extremities and is associated with hematologic malignancy, severe allergy, infection, or autoimmune disease.[5-7] The characteristic rash results from immune-mediated damage to small blood vessels and on histopathology shows immune complex deposition along the dermal capillaries and venules.[5] An example of such a rash can be seen in Figure 4. Such a finding, while not specific, should prompt a thorough history, examination, and laboratory testing.

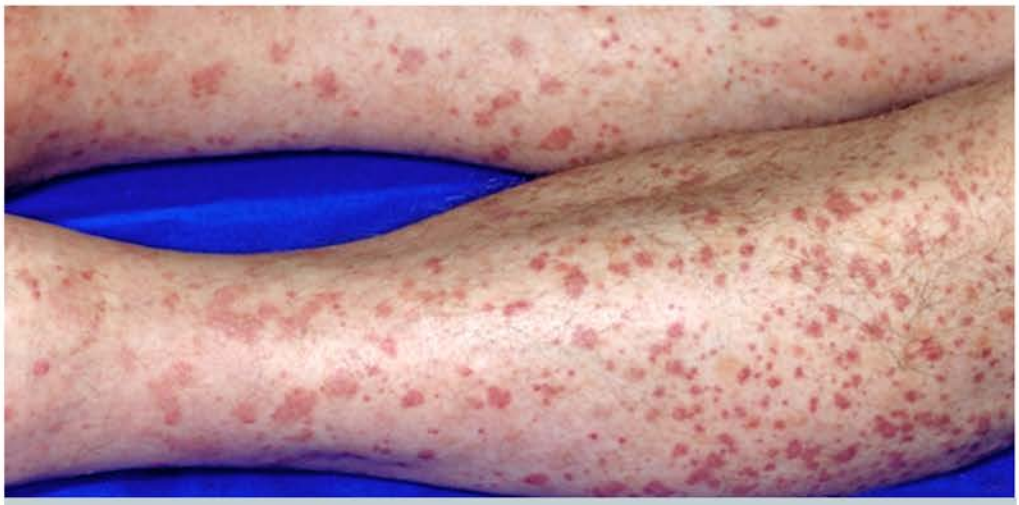

Figure 4. Leukocytoclastic vasculitis, representative photograph. (Courtesy of https://www.healthline.com/health/leukocytoclastic-vasculitis#pictures)

References:

1. Talcott, K.E., R.J. Garg, and S.J. Garg, Ophthalmic manifestations of leukemia. Curr Opin Ophthalmol, 2016. 27(6): p. 545-551.

2. Sharma, T., et al., Ophthalmic manifestations of acute leukaemias: the ophthalmologist's role. Eye (Lond), 2004. 18(7): p. 663-72.

3. Rosenthal, A.R., Ocular manifestations of leukemia. A review. Ophthalmology, 1983. 90(8): p. 899-905.

4. Lezrek, O., C. Daoudi, and M. Laghmari, Leukemic Retinopathy before and after Chemotherapy. Ophthalmol Retina, 2017. 1(6): p. 561.

5. Baigrie, D., et al., Leukocytoclastic Vasculitis, in StatPearls. 2021, StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.: Treasure Island (FL).

6. Shavit, E., A. Alavi, and R.G. Sibbald, Vasculitis-What Do We Have to Know? A Review of Literature. Int J Low Extrem Wounds, 2018. 17(4): p. 218-226.

7. Frumholtz, L., et al., Cutaneous Vasculitis: Review on Diagnosis and Clinicopathologic Correlations. Clin Rev Allergy Immunol, 2021. 61(2): p. 181-193.

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