Unique Case of Pediatric Choroidal Neovascularization in the Setting of Acute Myeloid Leukemia

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Introduction

Choroidal neovascularization (CNV) is a major cause of vision loss in the United States. It is characterized by a break in the retinal pigment epithelium (RPE) and Bruch's membrane, subsequently leading to accumulation of subretinal fluid. CNV is associated with more than 30 different ocular diseases, the most common being wet age-related macular degeneration (AMD). [1] Other common associations of CNV include ocular histoplasmosis syndrome, traumatic eye injury, and myopia. [2]

Leukemia is a systemic disease that commonly results in ocular manifestations, with some studies reporting a prevalence as high as 90%. [3] Leukemic retinopathy is the most common ocular manifestation in patients with leukemia and is characterized by multilayer hemorrhages involving all quadrants bilaterally. The most common type of hemorrhages seen are preretinal and intraretinal hemorrhages, though other manifestations such as Roth spots, cotton wool spots, and flame hemorrhages can also be seen. [4] In addition to ocular findings resulting from underlying leukemia, the chemotherapeutic agents used to treat leukemia can also be a major cause of ophthalmic findings. [5]

Leukemic retinopathy is not classically associated with CNV, however there have been three reported cases since 2018. Two cases of CNV were in the setting of acute myeloid leukemia (AML) and one in the setting of chronic myeloid leukemia (CML), however, there have been no reported cases in the pediatric population. [6] [7] [8] To our knowledge, this is the first reported case of CNV in the setting of leukemia in a pediatric patient.

Case Presentation

A five-year-old male with a history of Neurofibromatosis type 1 was seen by the ophthalmology consult service at Upstate University Hospital on December 20, 2021 for a two-day onset of decreased vision in his right eye. He had been diagnosed with AML and was receiving chemotherapy (cytarabine, venetoclax, decitabine, and azacitidine) as well as granulocyte colony-stimulating factor. Chemotherapy resulted in severe myelosuppression and pancytopenia. Treatment with cytarabine also resulted in keratopathy three weeks prior, which resolved with dexamethasone drops.

On physical exam, visual acuity in the right eye was 20/100 compared to 20/30 in the left, and dyschromatopsia was noted in the right eye. Pupils were equal and reactive to light and accommodation, with no afferent pupillary defect. Intraocular pressure, extraocular motion testing, and slit lamp exam were all unremarkable. Direct fundus exam (DFE) was performed under anesthesia three days after onset of symptoms and revealed a greyish macular hemorrhage at an undetermined level (Figure 1A). Repeat DFE under anesthesia nine days after the onset of symptoms revealed a slightly darker but similar sized hemorrhage in the same location (Figure 1B). Optical coherence tomography (OCT) obtained 12 days after onset of symptoms revealed subretinal fluid with disruption of the RPE, consistent with a diagnosis of CNV (Figure 2).

Case Presentation (continued)

Treatment options were discussed with the parents and an anti-VEGF injection was offered. The parents wanted to take a conservative approach and observe the patient's presumed CNV because of his upcoming bone marrow transplantation. Due to the immunocompromised status of the patient and the parents wanting to minimize the patient's exposure to public environments, the patient has not been seen in the clinic since December 2021.

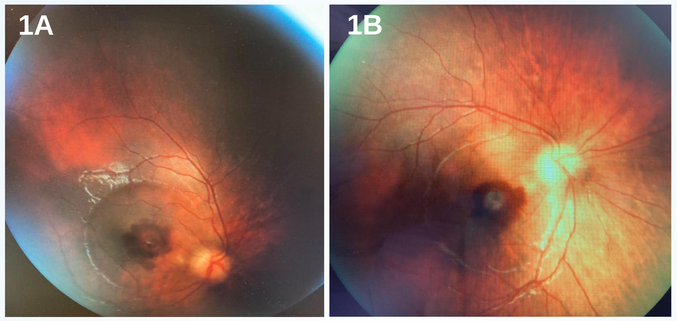

Figure 1. Fundus photos revealing greyish macular hemorrhage extending temporally.

A) Initial photo 3 days after onset of symptoms. B) Follow up photo 9 days after onset of symptoms.

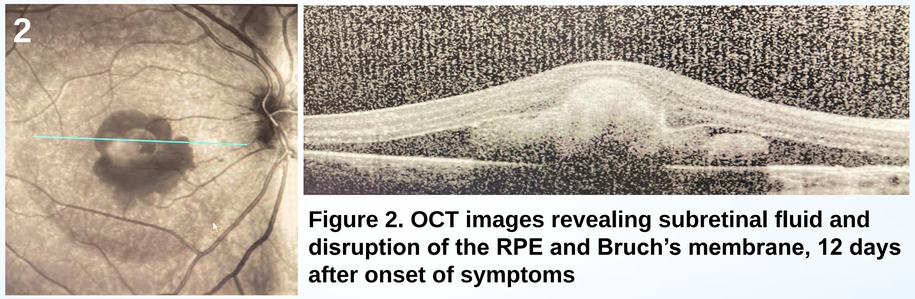

Figure 2. OCT images revealing subretinal fluid and disruption of the RPE and Bruch's membrane, 12 days after onset of symptoms

Discussion

Ophthalmic involvement in patients with leukemia is common and, in some cases, may be the only presenting symptom of leukemia. [9] When ocular involvement is present, there is an associated worse prognosis. One study showed that there was a higher five-year mortality rate in patients with leukemia that had ocular involvement compared to those that did not (45.7% vs 21.4%). [10] The fact that ocular manifestations may be the only presenting symptoms along with the associated worse prognosis of ocular involvement demonstrates the importance of close monitoring and routine eye examinations in patients with leukemia.

One must be cautious when determining the etiology of ocular findings of leukemia, however, as many chemotherapy agents used to treat leukemia can cause ocular toxicity. Discussion of all chemotherapeutic agents that cause ocular toxicity is beyond the scope of this poster but, notably, two agents (ipilimumab and cytarabine) have been associated with CNV. [11] [6] Cytarabine has also been associated with keratopathy, with a prevalence as high as 85%. [12] The patient in this case was treated with cytarabine and developed both keratopathy and CNV. This suggests that cytarabine might be a contributing factor in the development of this patient's CNV, in addition to AML.

The other three reported cases of CNV in the setting of leukemia occurred in a 22-year-old female and 51-year-old male with AML and in a 45-year-old male with CML. This case involving a five-year-old male developing CNV in the setting of AML and cytarabine treatment is the first reported case of CNV in a pediatric patient with leukemia.

Discussion (Continued)

Conclusion

- CNV is a major cause of vision loss in the United States, most commonly secondary to wet AMD.
- Ocular manifestations seen in leukemia are prevalent as a result of leukemia itself and chemotherapeutic agents.
- There have been three other reports of CNV in the setting of leukemia, with one involving treatment with cytarabine.
- This is the fourth reported case of CNV in the setting of leukemia, the second in the setting of cytarabine, and the first in the pediatric population.

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