Unilateral macular choroidal neovascularization—a rare manifestation in acute myelocytic leukemia

Case report

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Abstract
Rationale: Characteristic signs of leukemic retinopathy include bilateral intra-retinal hemorrhage, white-centred hemorrhage, macular hemorrhage and cotton-wool spots. Capillary closure, retinal microaneurysms and neovascularization following massive fundus hemorrhage could be involved in few of the above instances. However, single choroidal neovascularization (CNV) in macular has not been observed in acute myelocytic leukemia (AML).

Patient concerns: A 22-year-old woman presented with a 7-day history of vision decline in the right eye (OD). The patient was diagnosed as M3 AML one month earlier. Chemotherapy was immediately administered, which led to temporary myelosuppression. Recent examination showed that best corrected visual acuity was 20/400 OD. Fundoscopy showed petechial and patchy intra-retinal hemorrhage in both eyes and grayish-white lesion in the right macular center, which was confirmed as macular CNV by OCT and OCTA.

Diagnoses: The patient was diagnosed as macular CNV OD related to AML and chemotherapeutic regimens.

Interventions: She received intravitreal ranibizumab injection 0.5 mg (10 mg/ml) in the right eye for once on January 3, 2017.

Outcomes: CNV resolved three days after treatment with intravitreal ranibizumab injection 0.5 mg for once. No recurrence was observed after 10-month follow-up. Vision recovered to 20/40 at the last visit.

Lessons: This is the first report demonstrating that macular CNV could be an ophthalmic side-effect secondary to initiated chemotherapeutic regimens in patients with M3 AML. Intravitreal injection of ranibizumab could be beneficial and safe in treating this CNV.

Abbreviations: AML = acute myelocytic leukemia, BCVA = best corrected visual acuity, CNV = choroidal neovascularization, OCT = optical coherence tomography, OCTA = optical coherence tomography angiography, OD = right eye, OS = left eye, OU = both eyes, VEGF = vascular endothelial growth factor.

Keywords: acute myelocytic leukemia, anti-VEGF, choroidal neovascularization, optical coherence tomography angiography

1. Introduction
Leukemic retinopathy is one of the significant causes of visual disturbance in patients with acute and chronic leukemia. The ophthalmic manifestations in leukemic process include bilateral intraretinal hemorrhage, white-centred hemorrhage, macular hemorrhage, and cotton-wool spots.[1,2] In few instances, capillary closure, retinal microaneurysms, and neovascularization following massive fundus hemorrhage have been involved.[3] However, single macular choroidal neovascularization (CNV) in individuals with acute myelocytic leukemia (AML) has not been documented. Herein, we report a case with M3 AML who developed unilateral macular CNV secondary to initiated chemotherapeutic regimens.

2. Case presentation
A 22-year-old woman presented with a 7-day history of vision decline in the right eye, without ophthalmodynia and headaches, visited the ophthalmology department of the First People’s Hospital of Yunnan Province on December 12, 2016. She worked as a manicurist and hairdresser. On October 31, 2016, she was admitted to the hematology department of our hospital due to bleeding gums and large skin ecchymosis for 1 week. A diagnosis of M3 AML based on bone marrow aspiration as well as flow
cytometry examination was made, and chemotherapy (tretinoin 30mg d1–28, arsenic trioxide 10mg d1–28, DNR 60mg d1–3 and Ara-C 200mg d1–4) was given on November 1, 2016. Four days after chemotherapy, she temporarily suffered from severe myelosuppression (WBC 0.39 × 10^9/L, RBC 2.53 × 10^12/L, HBG 66g/L, PLT 10 × 10^9/L, HCT 20.4%), which was rapidly cured by metachysis and strengthen-hematopoiesis treatments.

Recent examination showed that the best corrected visual acuity (BCVA) was 20/400 in the right eye (OD) and 20/20 in the left eye (OS). Intraocular pressure in both eyes (OU) was normal. Slit lamp demonstrated anterior segment and vitreous negative. Petechial and patchy intraretinal hemorrhage was seen in the posterior pole of both eyes. A single grayish-white lesion, about 1/4 PD, was seen in the right macular center by multicolour fundus photography (Fig. 1A). Optical coherence tomography angiography (OCTA) (SPECTRALIS OCT, Heidelberg Engineering GmbH, Heidelberg, Germany) showed a barely visible small mass of capillary in the avascular area of fovea in the transverse image (Fig. 1B). Optical coherence tomography (OCT) showed circumscribed apophysis above chorioid in the central fovea (Fig. 1C). Meanwhile, dampened choroid refection under the lesion was also noted. The retinal thickness in fovea was 208 μm. OS macular examinations were normal. Pathological examination of bone marrow showed complete remission of AML.

The patient’s findings were consistent with a clinical diagnosis of macular CNV OD related to AML and chemotherapeutic regimens. She was given intrathecal dexamethasone 5mg, cytosine arabinoside 50mg, methotrexate 5mg, and chemotherapy (DNR 60mg d1–3, Ara-C 150mg d1–7) on December 13, 2016. Then, she received intravitreal ranibizumab (Novartis) injection 0.5mg (10mg/mL) in the right eye for once on January 3, 2017. Grayish-white lesion in macular center diminished on fundoscopy 3 days after intravitreal injection (Fig. 2A). Structure and continuity of retina in macular recovered more than before and retinal thickness in fovea dipped to 106 μm on OCT (Fig. 2C). Neovascularization network in avascular area obviously atrophied on OCTA (Fig. 2B). The above findings indicated that CNV had resolved. Her vision recovered to 20/200. Petechial and patchy intraretinal hemorrhage of both eyes faded after 1 month. At the last follow-up on October 6, 2017, OD BCVA was 20/40. No recurrence of CNV and AML was observed.

Collection of sample was approved by the Hospital Ethics Committee, and the patient signed an informed consent.

3. Discussion

The proportion of cases with AML manifested in retina is high (approximately 50%), while ophthalmic manifestations could be the primary and only symptoms to be detected.[4] Besides, some ophthalmic symptoms have been documented as the signs of AML relapse, for example, choroidal effusion syndrome.[5] However, retinal neovascularizations are rarely observed and only saw in those with chronic disease. To our knowledge, this is the first report of macular CNV seen in AML after initiating chemotherapy.

Leukemic retinopathy per se and ophthalmological side-effects induced by chemotherapy play a causative role in visual decline.
Reddy and Jackson\cite{6} compared 127 cases with acute leukemia, and concluded that a low platelet count was statistically related to intraretinal hemorrhages in AML patients. Van Bol et al\cite{7} conducted ophthalmologic exploration and follow-up in 2 cases with sudden bilateral visual decrease and dyschromatopsia 1 month after being treated with intravenous deferoxamine for AML, and showed a serous detachment in neuroepithelium accompanied with elongation in photoreceptor outer segment. Leukocytosis, platelet fiber aggregation, blood viscosity increase, and slow blood flow could be associated with the mechanism of retinal hemorrhage, proliferation, and hypoxia in leukemia\cite{8,9}. Anemia may also lead to hypoxia\cite{10}. Moreover, leukemia cells in AML secreted excessive vascular endothelial growth factor (VEGF), which is critical for the occurrence and development of CNV, and VEGF receptors were over-expressed in these cells\cite{11}. The patient in this report had developed erythropenia and low hemoglobin due to severe myelosuppression, which aggravated the hypoxia-ischemia in fundus that may be related to more VEGF production and macular neovascularization.

Although anti-VEGF agents are used for treating acute and choroid leukemia\cite{12}, the clinical efficacy and safety of these drugs in patients’ ocular with leukemia are not known. Sheu\cite{13} reported a woman with leukemia who developed CNV in the right macula secondary to endogenous endophthalmitis. Macular exudates rapidly resolved after single intravitreal injection of ranibizumab, and no recurrence or complications were noticed during 10-month follow-up. This case also demonstrated that ranibizumab decreases CNV in patients with leukemia.

In summary, this is the first report demonstrating that macular CNV could be an ophthalmic side-effect secondary to initial chemotherapy in patients with AML. The therapeutic regimen of intravitreal injection of ranibizumab in ocular CNV, is also beneficial and safe in AML.

4. Patient consent
Written informed consent was obtained from the patient for publication this report.

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Data curation: J. Xu, X. Yang.
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