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LETTER TO THE EDITOR

Uveal Infiltration in an Acute Myeloid Leukemia Case

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ABSTRACT

Purpose: To report a rare case of a 16-year-old girl with acute myeloid leukemia developing severe widespread ocular infiltration during chemotherapy intermission.

Methods: Case report.

Results: A 16-year-old girl diagnosed with acute myeloid leukemia (M5) developed blurred vision in both eyes 1 week after the second course of chemotherapy. Ocular examinations revealed severe iris involvement in both eyes and choroid infiltration in the right eye. Visual acuity improved and ocular infiltration resolved after the third cycle of chemotherapy and local radiation treatment, with serous retinal detachment remaining in the right eye.

Conclusion: Severe extramedullary relapse in the eye might occur during chemotherapy intermission.

Leukemia is a malignant proliferative disorder of leukopoietic bone marrow stem cells. It is characterized by over-crowding of the bone marrow by immature neoplastic leukocytes and widespread infiltration of organs, tissues, and peripheral blood with immature leukocytes. Leukemia constitutes 34.8% of the ocular metastases that the retina, choroid, optic nerve, vitreous, iris, and anterior chamber could be involved in.1 It was reported that ocular manifestations occur in about 3% of cases of acute lymphoblastic leukemia (ALL) patients, but ocular complications at presentation or relapse have rarely been reported in acute myeloid leukemia (AML).2 The retinal manifestations of leukemia metastasis include retinal hemorrhages, cotton-wool spots, Roth spots, retinal microaneurysms, and neovascularization. Leukemia metastasis can also cause vitritis, exudative retinal detachment, pseudohypopyon, hyphema, and iris heterochromia, but iris and choroid infiltration has scarcely been reported.3

Case Presentation

A 16-year-old girl visited our hospital in December 2019 with a one-week history of blurred vision. She had been diagnosed with a type of AML, acute monocytic leukemia (AML-M5), according to World Health Organization (WHO) criteria.4 The biopsy of the bone marrow revealed marked proliferations of leukemic cells, with at least 81% being of monocytic lineage (Figure 1). The patient had undergone two courses of systemic chemotherapy in the previous 2 months. After the second course of chemotherapy, bone marrow aspiration showed remission and the white blood cell count in the peripheral blood was 1.86 × 10⁹/L. However, her vision began to blur in both eyes, particularly in the right eye. Her best-corrected visual acuity (BCVA) was 0.01 (recorded in decimals) in right eye and 0.15 in the left. Slit-lamp examination showed 4+ aqueous chamber (AC) cells (according to Standardization of Uveitis Nomenclature criteria5) and pigmented and dust-like keratic precipitates (KPs) in both eyes. Multiple iris bombs were observed in both eyes and goniosynechia in the left eye (Figure 2 A1, A2). Ultrasonic biological microscope (UBM) revealed thickened irises and low, dense, dotted echoes in the anterior chamber of both eyes (Figure 2 B1, B2). Fundus examination showed 2+ (OD) and 1+ (OS) vitreous haze.6 In the right eye, tortuous, dilated retinal vasculature was faintly visible on the fundus. Panoramic fundus photography revealed a large circular uplift beneath the retina, with the optic disc and macula involved (Figure 2 C1). Retinal detachment and a subretinal space-occupying mass could be detected by optical coherence tomography (OCT; Figure 2 D1). B ultrasonic sound showed a large choroidal goiter at a posterior area of the right eye (Figure 2 E1), and color doppler image (CDI) examination presented an arterial-type spectrum in the mass of the right eye, indicating a solid lesion (Figure 2 F). Furthermore, orbit MRI revealed posterior eyeball thickening in the right eye (Figure 2 G1, G2). The fundus of the left eye was relatively normal according to fundus photography, OCT, B ultrasound, and MRI (Figure 2 C2, D2, E2, G1, G2).

In consideration of these findings, it was strongly presumed that ocular leukemia contributed to the pathology of this case, with uveal infiltration occurring while the bone marrow was still in remission. We did not take ocular samples for further histological confirmation.

From December 26 to January 15, the patient was treated with a third cycle of chemotherapy and low-dose external beam irradiation, with a total dose of 20 Gray (Gy) applied using a lens-sparing technique on both eyeballs and orbits. After that, she returned to us for an ocular assessment. The patient

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complained of poor vision recovery in her right eye. Her BCVA improved to 0.1 in right eye and 1.0 in the left. AC cells and KP's disappeared. The uveal infiltration resolved (Figure 3 B1), but exudative retinal detachment (ERD) remained in the right eye (Figure 3 A1, C1). However, unfortunately, bone marrow biopsy revealed severe relapse in the bone (with the joint involved) two weeks later. The patient chose to cease treatment and left the hospital.

Discussion

Isolated ocular relapse of leukemia has been reported previously, but the vast majority of cases are ALL rather than AML. Our AML patient was an extremely unusual case, suffering ocular involvement while the bone marrow was in remission after chemotherapy.

Studies have demonstrated a high prevalence of extramedullary relapse after allogeneic stem cell transplantation (allo-SCT) in patients with AML, as well as a close association between extramedullary relapse and graft-versus-host disease (GVHD). However, extramedullary relapse remains a rare event in patients being treated with chemotherapy. It has been reported that a 52-year-old man with AML developed leukemia hypopyon 37 days after the fourth course of chemotherapy, and a 47-year-old woman suffered anterior segment infiltration 3 months after her AML diagnosis during complete remission. Ocular relapse in both of these two cases were in the anterior segment. In ALL, migration of leukemic cells along the posterior ciliary vessels in the subarachnoid space surrounding the optic nerve has been proposed as a mechanism linking the central nervous system and the anterior segment. This supports the idea that the anterior segment of the eye is a pharmacologic "sanctuary" only marginally affected by systemic chemotherapy, resulting in suppression – but not eradication – of malignant cells by chemotherapeutic agents. In contrast to the relapse in the anterior segment seen before, our case presented a widespread ocular infiltration, especially in the iris and choroid. This may be the result of dissemination of leukemia cells from the anterior segment, or of direct uveal metastasis from bone marrow.

It has been reported that, on the basis of histopathological examination, the choroid is the most common ocular tissue to be involved in leukemia (85% of 79 cases); however, this is rarely reported clinically. An autopsy study pathologically examined 60 eyes from children who died of acute leukemia and reported that 26 patients (43%) had choroid infiltration. This feature was not apparent from clinical examination. All 26 patients with choroidal involvement had many other sites of leukemic infiltration at autopsy (liver, spleen, bone marrow, meninges, etc.), and none were considered to be in clinical remission. Choroidal involvement was not related with high terminal leukocyte counts but was associated with widespread infiltration of other organs. In addition, it has been reported in a case – which only showed symptoms of panuveitis initially – that choroidal infiltrates could be the first clinical manifestation of leukemia. In another report, a 9-year-old girl presented diffuse uveal thickening as the initial feature of ALL.

Figure 1. Bone marrow biopsy at initial diagnosis (magnified 100 times).

Figure 2. Ocular manifestations in both eyes at first visit (right eye: 1; left eye: 2).
without any signs or symptoms of systemic disease. In the subject of the present study, extensive uveal involvement occurred after the first two rounds of chemotherapy, while the bone marrow was in remission and the white blood cell count was low in the peripheral blood, suggesting that the uveal metastasis may have already existed prior to the start of chemotherapy.

AML is a rapidly progressing disease that is accompanied by angiogenesis in the bone marrow or myeloid sarcoma (MS). MS, also termed as "granulocytic sarcoma," "extra-medullary myeloid tumor," or "chloroma," is the occurrence of one or more tumor masses at an extra-medullary site, such as skin, bone or lymph node. Although MS is a rare condition, it can be the first evidence of AML or can appear as the initial manifestation of relapse in a previously treated AML in remission. Increased angiogenesis is a characteristic of MS and is believed to correlate with survival. Uveal MS is a rare complication of AML, and only two cases have been reported with iris and choroid involvement, respectively. In the present case, CDI examination revealed a vascularized solid tumor in the sub-retinal space in the right eye, and UBM examination demonstrated thickened irises. These masses resolved after another round of chemotherapy and local external beam irradiation, suggesting that they should be MSs in the ocular uvea. The current findings also indicate poor prognosis in patients.

SRD is associated with direct infiltration of the choroid, which induces choroidal ischemia and secondary retinal pigment epithelium (RPE) dysfunction. Usually, chemotherapy can completely resolve SRD and restore visual function, but irreversible changes in photoreceptors can also occur in this situation. SRDs have been reported in ALL, T cell prolymphocytic leukemia, precursor B-cell lymphoblastic leukemia, early pre B cell lymphoblastic leukemia, and AML. In this case, the SRD persisted when the tumor was resolved. This could be because the local radiotherapy and the third round of chemotherapy had just finished and the RPE function had not fully recovered, or it could be that the RPE function was further damaged by radiotherapy.

Differential diagnosis includes uveitis and other tumors such as bilateral diffuse uveal melanocytic proliferation (BDUMP). BDUMP is a very rare paraneoplastic syndrome that occurs in patients with occult carcinoma, characterized by multiple elevated pigmented and nonpigmented uveal melanocytic tumors with diffuse uveal tract thickening, exudative retinal detachments, and rapid cataract development. Giraffe patterns upon autofluorescence examination are a diagnostic characteristic of BDUMP. BDUMP is most commonly associated with
carcinomas of the ovary and lungs, followed in frequency by the gastrointestinal and genitourinary malignancies, but has not been reported in hematologic malignancies.23

In conclusion, uveal infiltration of leukemia cells can occur in AML patients, even during remission. It may, therefore, be appropriate to regularly examine the eyes’ involvement in acute leukemia patients and to make whatever possible correlations with the systemic state of the disease as applicable.

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Declaration of Interest

The authors declare that there is no conflict of interest. We are responsible for the content and writing of this paper.

References


