Ocular Granulocytic Sarcoma: A Case Report and Literature Review of Ocular Extramedullary Acute Myeloid Leukemia

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Clinical Practice Points

- Ocular granulocytic sarcoma (OGS) can occur at any point in the disease course of acute myeloid leukemia (AML)—as an initial presenting symptom, during systemic relapse, or even in the setting of a complete remission (CR).
- With nonspecific clinical presentations, pathologic diagnosis of OGS is important.
- OGS can occur without central nervous system (CNS) involvement.
- Treatment with systemic chemotherapy alone may alleviate conjunctival involvement without requiring ocular-directed radiotherapy.
- AML-M2 (acute myeloblastic leukemia with maturation), AML-M4 (acute myelomonocytic leukemia), and AML-M5 (acute monocytic leukemia) are more often associated with OGS.
- The most commonly reported cytogenetic abnormality associated with extramedullary AML—t(8;21)—has also been associated with pediatric OGS.

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Introduction

Ocular granulocytic sarcoma (OGS) is a rare complication of acute myeloid leukemia (AML).[1] Postmortem, the choroid is most commonly affected, with conjunctival involvement in only 2% to 4% of cases.[2] Only 1 case series, few adult OGS cases, and several pediatric cases have been reported.[2,3] Herein, we describe a subconjunctival relapse of acute myelomonocytic leukemia (AML-M4) and review the literature.

Case Report

A 67-year-old woman presented with fatigue, gingival hyperplasia, and leukocytosis (white blood cell count 115,000/μL). Bone marrow (BM) examination revealed AML-M4 with a diploid karyotype. With induction chemotherapy (idarubicin and cytarabine), a complete remission (CR) in the marrow was attained and 3 courses of intermediate-dose cytarabine were administered.

Left conjunctival erythema, with clear secretions, developed 7.5 months into remission. Despite topical antibiotics, symptoms progressed. Magnetic resonance imaging (MRI) revealed soft tissue enhancement of the anterior left orbit without brain abnormalities. Conjunctival biopsy results confirmed relapsed AML-M4.

Despite no neurologic deficits, cerebrospinal fluid (CSF) revealed central nervous system (CNS) leukemia. A BM aspirate revealed trisomy 8, with 0.5% leukemic blasts seem on flow cytometry.

After 1 month of weekly intrathecal (IT) liposomal cytarabine and hydrocortisone administration, the CSF cleared. Continuing with maintenance IT liposomal cytarabine, the patient received salvage chemotherapy with mitoxantrone and etoposide (ME) for 5 days, yielding clinical and radiographic resolution of conjunctival findings. A month later, the BM was hypocellular with no flow cytometric evidence of AML, but trisomy 8 persisted. A month later, repeated BM aspiration demonstrated persistent hypocellularity with 4.2% blasts on flow cytometry. At this point, bilateral conjunctival recurrence developed. Because stem cell donors were not found, she was referred to our institution.

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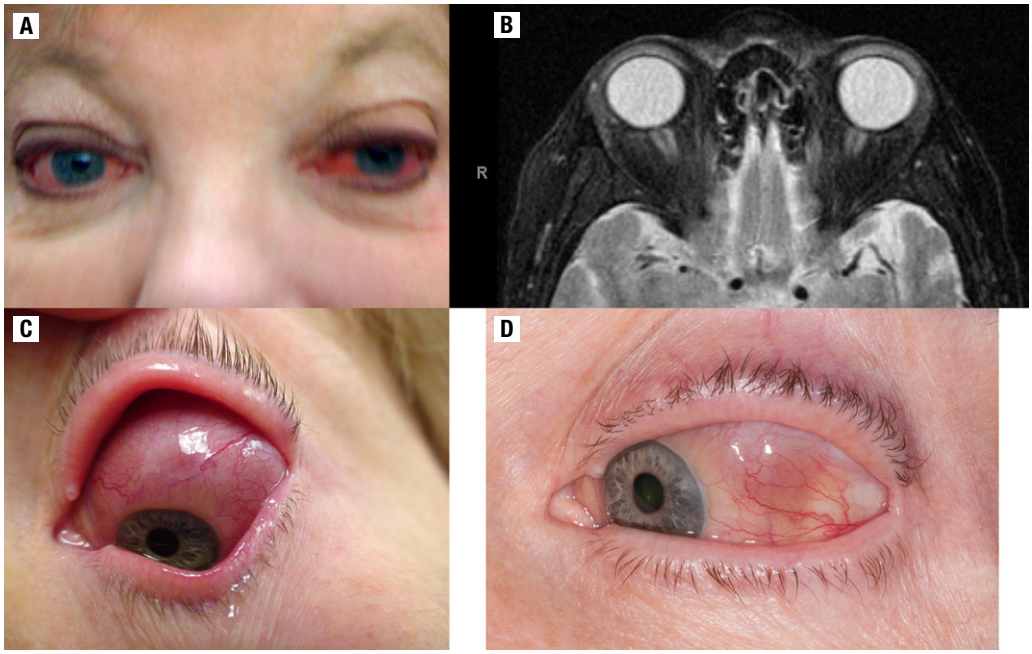
Figure 1 (A) At Initial Consultation (3 Months After Treatment With Mitoxantrone and Etoposide [ME]), Bilateral Conjunctival Erythema and Swelling Were Noted. (B) Orbital MRI Revealed Conjunctival Enhancement Bilaterally. (C) Conjunctival Erythema and Swelling Were Worse on the Left Side at Initial Consultation. (D) Two Days into Salvage Chemotherapy Ocular Secretions Decreased and Conjunctival Swelling/Erythema Regressed



At initial consultation (3 months after treatment with ME), bilateral conjunctival erythema and swelling were noted and were worse on the left side (Figure 1A and C). Orbital MRI revealed conjunctival enhancement bilaterally (Figure 1B). BM aspiration examination showed progressive AML-M4, 33% blasts, and trisomy 8. Molecular studies revealed mutant *RAS, IDH2*, and *NPM1*. Two days into salvage chemotherapy with clofarabine, idarubicin, and cytarabine, ocular secretions decreased and conjunctival swelling/erythema regressed (Figure 1D). Examination of BM aspiration on day 28 confirmed complete remission (CR). With persistent myelosuppression, the second course of treatment was delayed 66 days, and on day 29 of the second course of treatment, a BM aspirate contained 9% blasts. Conjunctival erythema/secretions gradually developed, but there was no vision loss. With a persistent *RAS* mutation, she was given an MEK inhibitor (GSK1120212, phase 1/2 protocol).

Discussion and Literature Review

Although our patient had nonspecific ocular symptoms, other patients occasionally present with proptosis, pain, chemosis, extraocular motion impairment, visual acuity defects,[4] and exophthalmos.[5]

In the largest case series to date, ocular manifestations in 53 patients with de novo AML were prospectively evaluated. None had evidence of CNS leukemia. Retinopathy, present in 53%, was associated with significantly lower platelet counts than was seen in patients without retinopathy ($P < .05$). The only symptoms were visual acuity changes in 10 patients; 3 patients with conjunctival involvement had monocytic leukemia (M-4 or M-5), the only finding linked to specific French-American-British (FAB) subtypes. Other findings included conjunctival hemorrhages and retinovascular abnormalities. Most patients received daunorubicin and cytarabine. Ocular findings resolved among induction chemotherapy survivors.[6]

Among OGS case reports, the course of disease varies. OGS occurs at any point during the course of AML, even in the context of a CR. Diffuse ocular infiltration is more common than tumor formation.[2] OGS can occur without other AML symptoms, preceding marrow involvement by years.[5] Other case reports of OGS are summarized in Table 1 and described further on.

OGS can be the initial AML manifestation without other symptoms.[2] For example, a 73-year-old woman with a myeloproliferative syndrome presented with bilateral ocular chemosis and motion impairment. Conjunctival and marrow biopsy results confirmed OGS and AML. Orbitally directed external beam radiation (30 Gy) was delivered, yielding resolution of lesions and symptoms; however, systemic leukemia ensued. Low-dose cytarabine was initiated with partial response, and the patient died of pneumonia 5 months later with no evidence of OGS.[2]

Isolated ocular relapse has been described.[1] For example, OGS was found in a 75-year-old woman during hematologic remission. When initially diagnosed with AML-M5 she had an indolent 5-month course before requiring systemic therapy. After commencing low-dose cytarabine treatment (2 weeks), she achieved a hematologic