repeated lumbar puncture showed resolution of pleocytosis. Following 8 weeks of systemic amphotericin B and 5-flucytosine, her visual acuity improved to 20/50 OS (Figure 2).

Retrospective review of the medical records showed that 2 months prior to the initial ophthalmic evaluation, the patient was treated for C albicans urosepsis with 10 days of intravenous amphotericin B. At the time, she remained afebrile, and repeated blood, urine, and catheter cultures obtained subsequently were all negative for organisms. The source of the intraocular seeding was thought to be the indwelling catheter that was placed around the time of the heart transplantation. Because of the repeated negative cultures, the catheter was presumed to be sterile and was not removed until the time of vitrectomy.

Comment. Fungal intraocular infection often results from hematogenous spread of fungal elements into the ciliary body most likely was followed by extension into the iris and body of the lens, resulting in intralenticular abscess formation.

Mild cases of fungal chorioretinitis can be successfully treated with systemic antifungal agents. Severe endogenous fungal chorioretinitis with the presence of vitritis is most often treated with pars plana vitrectomy and intravitreal injection of amphotericin B with systemic antifungal medications. In cases where fungal invasion of an avascular tissue such as the lens is suspected or proven, a thorough debulking, including lensectomy and capsulectomy, may play an important role.

Intravitreal injection of antifungal medication provides therapeutic levels, which may not be achieved by systemic administration alone. In our case, because of the extensive nature of the infection and the presumably higher vitreous clearance rate in an aphakic and vitrectomized eye, we elected to repeat the intravitreal injection of amphotericin B.

Endogenous fungal endophthalmitis may present a diagnostic challenge. Ocular signs and symptoms can be atypical, vague, and slowly progressive. A high degree of suspicion in susceptible patients along with an aggressive surgical di-agnostic and therapeutic approach can lead to preservation of life and vision.

Ramin Monshizadeh, MD
Colton, Calif
Rebecca E. Sands, MD
Wilfredo C. Lara, MD
William Driebe, MD
Gainesville, Fla

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Corresponding author: Ramin Monshizadeh, MD, Vitreoretinal Service, Inland Eye Institute, 1990 E Washington St, Colton, CA 92324 (e-mail: rmonshizadeh@inlandeye.com).


Bilateral Orbital Myeloid Sarcoma as Initial Sign of Acute Myeloid Leukemia: Case Report and Review of the Literature

Most pediatric orbital tumors are unilateral, and little is mentioned in the literature of the frequency and differential diagnosis of bilateral pediatric orbital tumors. Acute myeloid leukemia (AML) can involve the orbit as a solid tumor termed myeloid sarcoma or chloroma. We herein describe a child who was seen with bilateral orbital tumors that were the initial manifestation of AML. A literature review suggests that leukemia might be the most likely diagnosis in a child with bilateral soft tissue orbital tumors, a point that has not been widely recognized.

Report of a Case. Painless, progressive proptosis of the left eye developed in a previously healthy boy aged 25 months during the course of 2 weeks. Orbital magnetic resonance imaging (MRI) showed bilat-
eral orbital tumors, and he was referred to the Oncology Service at Wills Eye Hospital, Philadelphia, Pa, for diagnosis and management.

Examination disclosed that the child could follow and fix on small objects with each eye and had normal intraocular pressures. A 4-mm left proptosis was seen (Figure 1), and ductions and versions were normal. An ill-defined orbital mass was palpable inferior to the left eyebrow. The remainder of his ocular examination, including ophthalmoscopy, showed normal findings. Orbital computed tomography (CT) was performed.

A review of the CT (Figure 2) and MRI (Figure 3) scans disclosed a superior, irregular, homogeneous tumor in each orbit. The left orbital mass measured $38 \times 24 \times 15$ mm, and the right orbital mass measured $27 \times 18 \times 11$ mm. Both lesions showed enhancement with contrast agents. There was no bone erosion or sinus or brain involvement.

Based on the clinical findings and imaging study results, the differential diagnosis included leukemia, lymphoma, metastatic neuroblastoma, and idiopathic orbital inflammation (inflammatory pseudotumor). The initial peripheral blood cell count revealed an elevated white blood cell count of $26.9 \times 10^3/\mu L$, with a differential count of 3% segmented neutrophils, 56% lymphocytes, 17% monocytes, 6% promyelocytes, and 18% blast cells, which was strongly suggestive of leukemia. No anemia or thrombocytopenia was found. Serum chemistry studies disclosed a markedly elevated lactate dehydrogenase level of 1143 U/L.

A confirmatory left orbital biopsy was performed through an eyelid-crease incision. Diagnostic frozen sections obtained at the time of the orbital biopsy showed poorly differentiated malignant round cells. The differential diagnosis included leukemia, lymphoma, and, less likely, rhabdomyosarcoma or neuroblastoma. Given this differential diagnosis, tissue was saved for flow cytometry and possible electron microscopy in addition to routine histopathologic study. Review of the permanent sections showed a dif-

Figure 1. Facial photograph shows proptosis of the left eye.

Figure 2. Coronal computed tomographic scan of the orbits shows bilateral superior orbital masses. The mass on the left eye is larger and more clearly seen.

Figure 3. Coronal magnetic resonance scan of the orbits in a T1-weighted image with enhancement shows diffuse masses along the roof of each orbit.
fuse proliferation of poorly differentiated blast cells with somewhat irregular nuclear contours and prominent nucleoli. Occasional cells demonstrated finely granular eosinophilic cytoplasm (Figure 4).

Numerous mitoses were evident. Flow cytometry showed a blast population with a myeloid phenotype, including greater than 90% of cells that expressed CD11c and CD56 and 66% of cells that expressed CD13. Enzyme cytochemistry on cytospin preparations showed the blasts to be diffusely and strongly positive for α-naphthyl acetate esterase, an indicator of monocytic differentiation. The preparations were negative for myeloperoxidase and Sudan black B, which are indicators of granulocytic differentiation. Results of immunohistochemical stains were strongly positive for lysozyme and CD68, further indicating monocytic differentiation. They were negative for terminal deoxynucleotidyl transferase, which is present in lymphoblastic leukemia and lymphoblastic lymphoma. Approximately 20% of the cells were positive for Leder (chloroacetate or specific esterase) stain in paraffin sections (Figure 5), indicating granulocytic differentiation. The immunophenotype and the other described features of the biopsy specimen were most consistent with AML of the poorly differentiated monocytic type (M5a). By definition, however, final subtyping of AML must be performed by studying the bone marrow.

The patient subsequently underwent a diagnostic bone marrow aspiration and biopsy that showed replacement of the normal bone marrow with blasts and cells with maturing monocytic features. Auer rods were not seen. Flow cytometry findings were positive for the monocytic markers CD14, CD33, CD4, and CD15. A diagnostic lumbar puncture showed no evidence of central nervous system involvement. On the basis of these findings, a final diagnosis of M5b AML was made.

The patient was treated under the current protocol of the Children’s Oncology Group for newly diagnosed AML, which consists of 2 cycles of highly intensive chemotherapy, followed by an allogeneic bone marrow transplantation if a suitable donor can be found. The first round of chemotherapy was started and consisted of idarubicin hydrochloride, vidarabine, etoposide phosphate, thioguanine, dexamethasone, daunorubicin hydrochloride, and intrathecal vidarabine for central nervous system prophylaxis.

The patient was found to be in remission by results of bone marrow aspiration performed 6 weeks after initiation of chemotherapy. He then underwent a second round of chemotherapy, which consisted of fludarabine phosphate, idarubicin, and vidarabine. Results of a second bone marrow aspiration after the second round of chemotherapy showed that the patient remained in remission. An orbital MRI obtained 10 weeks after diagnosis demonstrated resolution of the bilateral orbital masses seen at diagnosis. The patient’s sister was found to be a 6/6 antigen match, which made her a suitable donor, and the patient underwent an allogeneic bone marrow transplant 13 weeks after diagnosis. At present, he is undergoing close follow-up as an outpatient.

Comment. It is well known that AML can be seen initially with orbital involvement, before the diagnosis of the underlying leukemia. Soft tissue accumulations of leukemic cells were previously referred to as granulocytic sarcoma or...
chloroma.7-31 As several variants of AML by definition have few or no cells of granulocytic lineage, the broader term myeloid sarcoma is currently preferred. The term chloroma “green tumor” is derived from the greenish gross coloration of this lesion, attributable to the myeloperoxidase in the cells of granulocytic lineage, which are present in varying proportions according to subtype. Myeloid sarcomas are most common in certain subtypes of AML, in particular M5a (monoblastic), M5b (monocytic), M4 (myelomonocytic), and M2 (myeloblastic with maturation).32

The French-American-British Cooperative Group defines this subtype of AML, which is also referred to as acute monocytic leukemia, as having a bone marrow biopsy specimen showing 80% or more of the nonerythroid cells demonstrating monocytic lineage (therefore, less than 20% are of granulocytic lineage). In addition, fewer than 80% of the monocytic lineage cells must be monoblasts (ie, maturing promonocytes are clearly evident). When 80% or more of the cells are monoblasts, the lesion is classified as acute monocytic leukemia (M5a).33,34

In most instances, orbital myeloid sarcoma occurs in young children. It is rare among the orbital tumors of childhood, accounting for only 1 of 250 cases in a previous report from our department.5 The disease is relatively uncommon in the western hemisphere, but is more prevalent in the Middle East, Asia, and Africa.1 Most of the larger reported series have come from Turkey53 and India.21,26

When evaluating an orbital mass in a child, the ophthalmologist must consider a variety of benign and malignant conditions, particularly inflammatory, cystic, and vascular lesions such as idiopathic orbital inflammation, dermoid cyst, capillary hemangioma, lymphangioma, and others.45 About 90% to 95% of orbital masses of childhood that come to biopsy prove to be benign on histopathologic examination.5 Of the 5% to 10% that are malignant, rhabdomyosarcoma is the most common disease.5,6

Most childhood orbital tumors are unilateral.3-5 Most benign conditions, like dermoid cyst, capillary hemangioma, lymphangioma, and optic nerve glioma, usually affect only a single orbit. Rhabdomyosarcoma, the most common malignant orbital tumor of childhood, is invariably unilateral.2-6

The main conditions that can cause bilateral orbital masses in children are idiopathic nongranulomatous orbital inflammation,33 metastatic neuroblastoma,36 and myeloid sarcoma. Pediatric idiopathic nongranulomatous orbital inflammation is initially unilateral in 10% of cases, but it can eventually show bilateral involvement in 46%.37 However, involvement of the second eye is usually sequential and not simultaneous. Orbital metastasis is the initial sign of abdominal neuroblastoma in 3% to 4% of patients and is bilateral in 50%.36,37

Our patient had bilateral orbital involvement by myeloid sarcoma. Although myeloid sarcoma is a relatively uncommon pediatric orbital tumor, it becomes a major diagnostic consideration in the setting of bilateral orbital involvement. Published reports on orbital myeloid sarcoma have not always provided complete details with regard to initial features and laterality. However, on the basis of a review of the available literature, we calculated that about 88% of cases with propostis that are seen by the ophthalmologist have no history of leukemia at the time of presentation (Table). In addition, we estimate that about 60% of orbital myeloid sarcomas are bilateral.

Orbital involvement by acute myeloid sarcoma is relatively rare among orbital tumors and pseudotumors. However, in the setting of simultaneous bilateral orbital tumors in children, myeloid sarcoma appears to be a highly likely, if not the most likely, diagnostic possibil-

### Lateality Among Some Reported Cases of Orbital Myeloid Sarcoma in Children and Young Adults With Myeloid Leukemia

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>Unilateral</th>
<th>Bilateral</th>
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<td>1/2</td>
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Total No. (% of Cases) | 89 | 36 (40) | 53 (60) | 104/121(86)|

*The large series of 33 cases reported by Zimmerman and Font‡ is not included in the tabulation of laterality here, because it was a histopathologic series of slides and tissue submitted to the Armed Forces Institute of Pathology and, in most cases, insufficient data were submitted to determine laterality. In that series, only 4 of the 33 cases were listed as having bilateral proptosis. However, the number of bilateral cases in that series would probably have been much higher had complete histories and imaging study results been available (Lorenz E. Zimmerman, MD, oral communication, December 23, 2001).†Quoted by Consul et al.‖Information was unclear from article review.
ity. Any child with an orbital mass of uncertain origin, particularly if it is bilateral, should undergo prompt evaluation for underlying AML.

Jerry A. Shields, MD
Gary A. Stopyra, MD
Brian P. Marr, MD
Carol L. Shields, MD
Philadelphia, Pa

Wilbur Pan, MD, PhD
New Brunswick, NJ

Ralph C. Eagle, Jr, MD
Philadelphia

Jay Bernstein, MD
Westfield, NJ

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Corresponding author and reprints: Jerry A. Shields, MD, Oncology Service, Wills Eye Hospital, 840 Walnut St, Philadelphia, PA 19107.


