"Doctor, My Son's Eye Is Swollen!"

Basar Cecil,* a healthy and active 4-year-old, was busy with his daily task of building things out of Lego bricks when his parents noticed swelling around his right eye. Since he also had a mild cough and intermittent ear pain, his parents took him to his pediatrician, who prescribed Keflex (cephalexin) and an over-the-counter allergy medication.

Much to his parents' dismay, Basar's orbital swelling continued to worsen over the next two weeks and even began to spread to the left eye. He was then taken to the family's eye care provider, who sent him straight to the emergency department for further workup and diagnostic testing.

Our Team Gets a Look

The presentation. The emergency department is where our team first met Basar.

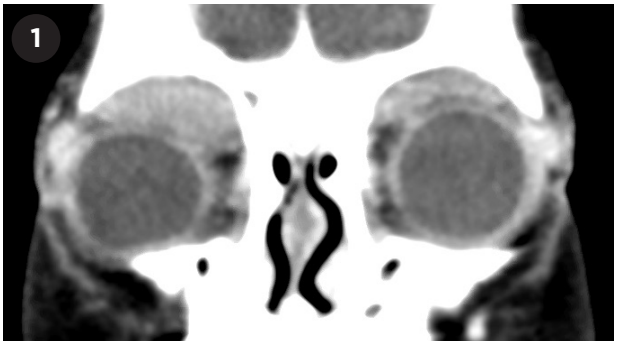
His parents described recent "eye bulging" involving the right eye that had worsened during the past two weeks and now affected the left eye. They also told us that the referring eye care provider had said that their son's vision was worse in the right eye than the left.

The review of symptoms was unremarkable, other than the cough and intermittent otalgia. Basar had no relevant past medical, surgical, family, or ocular history.

The exam. On examination, we found the following:

- Fullness of the bilateral superior orbits along with right hypoglobus.
- Fix-and-follow vision in both eyes with a symmetric red reflex. (Basar's limited knowledge of letters and numbers prohibited more detailed visual acuity [VA] assessment, given that the emergency department was not equipped with Lea symbol charts or HOTV charts. We were unable to confirm an asymmetry to his VA at this visit.)
- Equal, round, and reactive pupils with no afferent pupillary defect (APD).
- Intraocular pressure of 15 mm Hg in both eyes.
- Proptosis without periorbital ecchymosis in both eyes.
- Restricted ductions in all directions in both eyes, with greatest limitations in supraduction bilaterally.
- Unremarkable anterior segment exam—including the conjunctiva, sclera, cornea, anterior chamber, iris, and lens—in both eyes.
- Unremarkable dilated fundus exam, with no signs of vitritis, retinitis, vasculitis, or optic nerve abnormalities.

Initial workup. Computed tomography (CT) of the orbits (Fig. 1) obtained in the emergency department revealed abnormal homogeneous soft tissue mass lesions in both orbits. The mass located in the right superior orbit resulted in inferior displacement and slight flattening of the right globe with effacement of the superior aspect of the superior rectus muscle. Multicentric masses also were noted in the left orbit. There was no evidence of acute inflammatory changes in the visualized fat. There was no extension into the cavernous sinus, no fluid collections, and no bone destruction or invasion.



COMPUTED TOMOGRAPHY. *Initial imaging of the orbits revealed homogeneous soft tissue mass lesions bilaterally.*

Magnetic resonance imaging (MRI) with and without contrast demonstrated similar results as the CT, with no associated osseous destruction or invasion into the extraocular muscles.

Thinking Through the Differential

At this point, we had a 4-year-old boy, who had previously been healthy, presenting with reported worsening VA and significant right hypoglobus. He also had proptosis in both eyes, marked motility deficits in both eyes, and the imaging findings that are described

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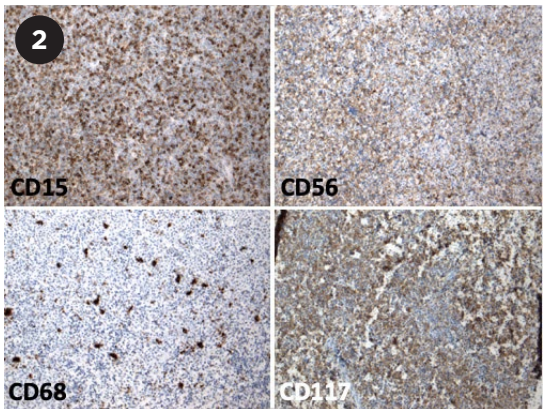
above. With this imaging completed, we began to work through the most likely neoplastic, inflammatory, and infectious etiologies:

- Neoplasms considered were rhabdomyosarcoma, neuroblastoma, leukemia, lymphoma, Langerhans cell histiocytosis (LCH), and vascular tumors.
- Inflammatory etiologies considered included granulomatosis with polyangiitis, sarcoidosis, and NSOI (nonspecific orbital inflammation).
- Infectious causes considered included orbital cellulitis or an orbital abscess.



PATHOLOGY. *Tumor cells were stained with various biomarkers.*

Naturally, we were most concerned for a neoplastic process. His presentation could fit with rhabdomyosarcoma, as it is the most common primary orbital malignant tumor of childhood, presenting acutely with similar exam and imaging findings. However, this is usually unilateral.

Neuroblastoma was considered, as it is the most frequent source of childhood orbital metastases, but Basar did not exhibit orbital ecchymosis, pupillary abnormalities, or the systemic symptoms typical of this diagnosis.

Leukemia's most common ocular manifestation is leukemic retinopathy, which includes retinal flame hemorrhages, white centered hemorrhages, or perivascular infiltrates. Although Basar exhibited none of these findings, a leukemic process was not excluded, as it can involve solely the orbit.

There were no bony lytic lesions or bone involvement on imaging; thus LCH was deemed less likely.

The contrast imaging was also inconsistent with a vascular lesion.[1]

Inflammatory processes, including orbital pseudotumor, were considered. Orbital pseudotumor is more typically a bilateral process in children, as opposed to a unilateral process in adults. It manifests with painful proptosis, orbital edema and erythema. However, it should be noted that this is a diagnosis of exclusion.[2]

Other inflammatory diagnoses in the differential included granulomatosis with polyangiitis and sarcoidosis, even though Basar was not the typical demographic. He exhibited no intraocular inflammation or systemic signs (other than mild cough) that might be consistent with these conditions.

Infectious processes were moved down our differential. Signs of infection (such as warmth, erythema, and pain) were absent. There was no concurrent significant sinus disease, no recent trauma had occurred in the periocular area, and no abscess was identified on imaging.

Continued Workup and Diagnosis

Initial blood work showed an immature granulocyte lineage of cells in circulation without any cytopenia, which raised concern for marrow disease.

At this point, the hematology/oncology service was consulted, and the consulting physician recommended CT of the chest/abdomen/pelvis to look for a primary malignancy along with an urgent orbitotomy with biopsy. The imaging yielded no primary malignancy.

The following day, Basar underwent orbitotomy and biopsy. The right superior mass was identified as a yellow-green, friable mass diffusely occupying the superior orbit. Fresh and frozen samples were sent for pathology. The tumor cells stained positively for CD15, CD56, and CD117 (Fig. 2), confirming a tumor of myeloid lineage.

We reached a definitive diagnosis of granulocytic (myeloid) sarcoma of the orbit.

About the Disease

Granulocytic sarcoma (GS) is also known as a chloroma due to its yellow-green color (chlorine is a yellow-green gas). It is an extramedullary tumor of immature granulocytic cells that is frequently accompanied by a diagnosis of acute myeloid leukemia (AML) and, more rarely, chronic myeloid leukemia or myelodysplastic syndromes.[3] Basar underwent a bone marrow biopsy and was diagnosed with AML.

A chloroma can be detected before other systemic signs or symptoms of leukemia arise, as in this case. When GS occurs in the absence of AML it is referred to as primary or nonleukemic myeloid sarcoma.[3]

GS can occur at any age and can present as uni- or multifocal lesions in several sites, including soft tissue, bone, peritoneum, lymph nodes, the gastrointestinal system, genitourinary tract, and central nervous system (CNS). Due to the vast differences in location, the presenting symptoms vary. Diagnosis of GS with a known hematologic malignancy is generally straightforward; however, primary GS may be misdiagnosed as frequently as 25%-47% of the time.[3]

CT or MRI are appropriate as initial imaging studies. Positron emission tomography (PET) scans can be useful for radiation therapy planning and assessing disease progression.[3] Even though fine needle aspiration (FNA) has been used for diagnosis, tissue biopsy is the preferred method. The specimen should be sent for immunohistochemistry, flow cytometry, fluorescence in situ hybridization (FISH), and molecular analysis.

If a hematologic disorder is suspected, a bone marrow biopsy should be pursued.

Treatment

GS secondary to AML requires immediate systemic chemotherapy. This can be combined with local radiation therapy (RT).[4] RT is not recommended without systemic treatment but should be considered when rapid relief of symptoms is necessary or in cases with CNS involvement. Local surgical excision can be considered for rapid symptom relief,

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but it should be followed by systemic chemotherapy.

There is no clear consensus as to the ideal treatment of primary GS, but case reports suggest that systemic chemotherapy with cytarabine may be successful.[4]

How's He Doing?

Basar underwent several rounds of systemic chemotherapy. At his six-week follow-up, his VA was 20/80 in his right eye and 20/40 in his left. He was orthotropic and exhibited full ocular motility. At his three-month follow-up, VA was 20/30 in both eyes.

Basar is being monitored at regular intervals by our hematology/oncology service and, as of January 2020, the disease remains in remission.

* Patient name is fictitious.

1 Rodrigues MC et al. *Int J Radiol Radiat Ther.* 2017;3(4):252-256.

2 Berger JW et al. *Int Ophthalmol Clin.* 1996; 36(1):161-177.

3 Yilmaz AF et al. *Am J Blood Res.* 2013;3(4):265-270.

4 Bakst RL et al. *Blood.* 2011;118(14):3785-3793.

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