Case Report

Bilateral Orbital Proptosis and Corneal Ulcer in a Child with Acute Myeloid Leukemia

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Keywords
Bilateral orbital proptosis · Corneal ulcer · Childhood acute myeloid leukemia

Abstract
A 5-year-old girl had a 2-week history of protruding bilateral eye with blurred vision. The patient had a history of low-grade fever. Bilateral proptosis with a markedly severe protrusion of the conjunctival palpebral and infraorbital tissues was observed. A more pronounced proptosis occurred on the left eye. Lagophthalmos and corneal defects were found in the left eye. Laboratory tests revealed anemia, hyperleukocytosis, and thrombocytopenia. A confirmed diagnosis of acute myeloid leukemia-M2 was established from bone marrow aspiration. The patient was treated with standard multiagent chemotherapy and topical antibiotic eyedrops. Proptosis had resolved in 4 months with residual corneal cicatrix in the left eye.

Introduction
Orbital and intraocular involvement of acute leukemia in children is frequent among other extramedullary locations after the meninges and testicles. Infiltration occurs as circulating leukemic cells accumulate throughout the anterior and posterior segment, including uvea, retinal nerve fibers, optic disc, and other intraocular tissues and fluids [1]. However, proptosis is considered as a rare extramedullary involvement in acute childhood myeloid leukemia (AML) (6.3–8.3%). Moreover, most cases reported are unilateral [2]. Several
studies showed a higher incidence (2.5–9.1%) of rare orbital involvement in Asian and African populations among patients with AML [3, 4]. Here, we report a case of childhood AML with bilateral proptosis and corneal ulcer on the left eye.

**Case History**

A 5-year-old girl presented to our ophthalmology department with a 2-week history of protruding bilateral eye with limitation of the lid closure and associated blurred vision over the last 2 days. The patient was referred to the ophthalmology department with the diagnosis of orbital proptosis and AML. Apart from intermittent low-grade fever, there were no systemic complaints.

The ophthalmology examination showed a bilateral proptosis with a markedly severe protrusion of the palpebral conjunctiva and infraorbital tissues, more pronounced in the left than the right eye (Fig. 1a). Visual acuity in the right eye was established as 6/60 in the right eye, and no perception of light in the left eye, and increased intraocular pressure of 22 mm Hg in both eyes. The right eye was able to fix and follow but was unable to do so using the left eye. There was a marked axial proptosis on the right eye and inferotemporal nonaxial proptosis on the left eye with gross conjunctival, ciliary injection, and chemosis. A firm, non-tender palpable mass in the superior palpebra was observed on both eyes. A 5 mm lagophthalmos on the right eye and 15 mm on the left eye was measured. The size of proptosis causing corneal exposures was 4 mm in the right eye and 10 mm in the left eye. A size of 1.5 × 1 mm and 1.2 × 1 mm of corneal defects on the left eye was confirmed in positive fluorescein staining showing infiltrate (Fig. 1b). Slit-lamp examination suggested a deep anterior chamber in both eyes. No involvement of the posterior segment was found during the fundoscopy examination.

Laboratory studies revealed anemia (hemoglobin was 9.9 g/dL), hyperleukocytosis (white blood count of 21.36 × 10³/µL), and thrombocytopenia (platelet count was 42 × 10³/µL). The bone marrow aspiration confirmed the diagnosis of AML-M2. The CT-scan image only showed pansinusitis. No posterior orbital involvement was described to support significant bilateral proptosis. This finding suggests the success of continuous chemotherapy treatment given. The ocular manifestations were treated with 0.5% levofloxacin eyedrop each hour and 0.3% gentamicin eye ointment three times daily on the left eye. Increased intraocular pressures on both eyes were managed with 0.5% timolol eyedrop twice daily and lubricating eyedrop six times daily. A lid taping was placed on the right eye

**Fig. 1.** a Ophthalmology findings at the initial visit showed bilateral proptosis, more severe in the left than the right eye. b Examination of the left eye revealed conjunctival infection, infiltrates, and corneal ulceration in the nasal area within the size of 1.5 × 1 mm and 1.2 × 1 mm.
to preserve the eye. Treatment with standard multiagent chemotherapy was given by the pediatrician and promptly went into remission.

The infection and orbital proptosis on both eyes were successfully managed by combining a multidisciplinary approach, proper antibiotics, and chemotherapy treatment. Four months after the first admission, follow-up examination showed improvement in visual acuity, 6/12 in the right eye and 0.5/60 in the left eye, with residual corneal cicatrix in the left eye. Ocular movements were good in all directions, normal intraocular pressure and proptosis had resolved.

Discussion

AML refers to a group of neoplastic disorders of the hematopoietic precursor cells of the bone marrow, resulting in unregulated replication of myeloid cells [5–7]. Leukemia cells can reach and infiltrate any extramedullary site [5]. Extramedullary infiltration may appear at various sites, including the orbit, sinuses, ovaries, testes, and breasts [6]. Presentations of orbital and ocular lesions were common in AML (66.6%) compared to acute lymphocytic leukemia (15.1%). Ocular involvement can be pathognomonic in acute leukemia or leukemic relapse [1, 2].

Orbital infiltration by malignant cells, first described as chloromas by Dock in 1893 and granulocytic sarcoma by Rappaport in 1966, manifested as proptosis [3, 5]. A rare case of bilateral proptosis was reported in 2012 with bilateral chloromata shown as a sign of AML [5]. Chefchaouni reported that 2% of children treated for leukemia suffered from proptosis [8]. Almaki et al. [9] also reported a case of unilateral proptosis in a previously healthy child as an initial sign of acute myeloid leukemia. Such conditions should be considered in the absence of systemic leukemic manifestations as the form of granulocytic sarcoma (chloroma) [9]. However, our patient showed bilateral proptosis, which is a unique case of acute myeloid leukemia. This case defined a significant contribution of anterior segment involvement that later led to the diagnosis of AML in the patient.

Orbital and ocular manifestations are classified into specific and non-specific lesions. The specific lesion occurs as direct leukemic infiltration. This includes orbital infiltration, which caused exophthalmos, and infiltration in the palpebral, conjunctival, and lacrimal gland, which are less common. The non-specific lesion appears due to secondary complications, such as anemia, thrombocytopenia, and leukostasis. Such conditions lead to ischemia and opportunistic infections [2]. As both presentations were shown in our case, a combination of direct and secondary complications may also be possible.

A study suggests that secondary ocular involvements are more frequent (40.8%) than direct infiltrations (16.9%), with symptoms only occurring in 15.49% [2]. However, a higher frequency of leukemic relapses in the bone marrow and/or central nervous system in patients with specific lesions (63.1%) are expected compared to patients with non-specific lesions (42%) and in patients without orbital or ocular lesions (29.2%) (p<0.05). Relapse in childhood with acute leukemia often leads to a lower survival rate [1].

Our patient presented an orbital mass with lagophthalmos in both eyes, exposure corneal ulcer on the left eye, and secondary glaucoma in both eyes. Lagophthalmos, due to proptosis, may in turn, jeopardize the tear film quality, changing the volume of the tear and its buffering capabilities. These conditions may subsequently decrease tear film lubrication and cause dry eyes. Lagophthalmos later affected and reduced the blinking mechanism causing severe exposure of the cornea and infection resulting from exposure keratitis [10], and in more severe, become a corneal ulcer [3]. Secondary glaucoma is generally caused by anterior chamber angle obstruction from leukemic cells floating in the anterior chamber [10]. As the
patient was also receiving chemotherapy, therapeutic management successfully improved the clinical condition as well as the visual acuity. In severe cases, irradiation may be necessary to fully eradicate the disease [11].

This case marked the possibility of intraocular involvement in AML both as mechanisms of direct specific lesion and non-specific lesion resulting in secondary complications. Presentations of intraocular lesions manifest as the form of acute or relapse in AML. Thus, ocular manifestation in patients with the known leukemic disease is considered as the cardinal sign of the disease improvement.

**Statement of Ethics**

Written informed consent was obtained from the parent/legal guardian of the patient for publication of the details of their medical case and any accompanying images. Ethics approval was not required. The study was reviewed and the need for approval was waived by the research and ethical committee of ophthalmology department, Cipto Mangunkusumo Hospital, Universitas Indonesia, Jakarta. Consent was obtained from the mother of the patient in March 2020. Permission for publication including history taking, ophthalmology examination, laboratory results, and photographs of clinical presentation was granted. Written informed consent was given by the mother following examination and publication.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

All authors contributed to designing the concepts, literature research, data analysis, and manuscript preparation including editing and reviewing the study. Made Susiyanti initiated the concepts and the designs of the study, including data acquisition and analysis, manuscript preparation, editing, and reviewing the study. Made Susiyanti is also the main author and guarantor of the study. Burhana Mawarasti contributed to designing the concepts, literature research, data analysis, and manuscript preparation including editing and reviewing the study. Sesaria Rizky Kumalasari contributed to designing the concepts, literature research, data analysis, and manuscript preparation including editing and reviewing the study.

**Data Availability Statement**

All data that support the findings of this study are included in this manuscript.
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