Case Report

Bilateral Proptosis in a Child: A Rare Presentation of Acute Lymphoblastic Leukemia

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Abstract

Purpose: Acute lymphoblastic leukemia (ALL), a common hematological malignancy observed in children, typically presents with fever, pallor, easy bruising, hepatosplenomegaly and lymphadenopathy. However, when ALL manifests with unusual signs and the blood counts and peripheral smears are normal, it causes a diagnostic dilemma.
Case Report: We report a 5-year-old boy who presented with bilateral proptosis as the initial manifestation of ALL. He presented with fever and bilateral knee pain attributed to a fall while playing. There was a history of progressive bilateral proptosis for a 3-month period not associated with any other complaints such as fever, eye pain, redness, or tearing. Thyroid function tests were normal. Blood counts acquired upon proptosis presentation were normal. When he presented to us three months later, blood counts revealed a pancytopenia but the peripheral smear showed no abnormal cells. Magnetic resonance imaging of the brain and orbits was normal. Bone marrow aspirate flow cytometry confirmed the diagnosis of B cell acute lymphoblastic lymphoma.
Conclusion: Ophthalmologists should be aware of the unusual ophthalmologic manifestations of acute leukemia, as they may precede overt leukemia and cause diagnostic dilemmas. Knowledge about the rare and isolated extramedullary manifestations of ALL facilitates early diagnosis and thereby improves prognosis.

Keywords: Acute Leukemia; Child; Proptosis

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INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common malignancy diagnosed in children, characterized by proliferation of poorly differentiated precursors of lymphoid cells. Although any organ can be infiltrated, a predominant feature of the disease is bone marrow failure due to an accumulation of blast cells. Lebreich[1] was the first to describe the ophthalmological signs in leukemia patients as leukemic retinopathy in 1863. Orbital infiltration or mass formation can result in proptosis or diplopia. In a study by Russo et al. evaluation of orbital and ocular manifestations in the recruited patients with acute childhood leukemia revealed that orbital or ocular lesions were noted more commonly in patients with acute myeloid leukemia (AML) (66.6%) than in those with ALL (15.1%).[1] We report a case of a 5-year-old boy

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who presented with fever, knee pain, bilateral proptosis, and pancytopenia; bone marrow studies confirmed the diagnosis of precursor B cell ALL.

CASE REPORT

A 5-year-old boy presented to us with fever and bilateral knee pain attributed to a fall while playing. There was a history of bilateral proptosis for a period of three months, progressively increasing, but not associated with any other complaints such as fever, eye pain, redness, tearing, visual disturbances, restriction of eye movements, or any head trauma. Initially, the child was evaluated by an ophthalmologist, and his visual acuity and fundus were normal. Thyroid function tests performed to rule out thyrotoxicosis revealed normal findings. Repeated complete blood count reports were inconclusive with normal hemoglobin (Hb) levels, differential counts, and platelets.

He was brought to us 3 months after the onset of symptoms and on examination, he exhibited bilateral proptosis [Figure 1a] and was pale with no significant lymphadenopathy or organomegaly. Imaging studies included computed tomography (CT) and magnetic resonance imaging (MRI) of the orbits, with normal magnetic resonance angiogram (MRA)/ magnetic resonance venogram (MRV) findings. Bilateral X-rays of the knees showed multiple osteolytic lesions.

Complete blood counts indicated pancytopenia with Hb levels, 5.6 gm/dl; leukocyte count, 3,100 cells/mm^3; differential count, including polymorphs, 56%, lymphocytes, 34%, and monocytes, 5.9%; and thrombocytopenia, 35,000 lakh/mm^3. A peripheral smear showed no atypical cells. A bone marrow aspiration study revealed hypercellular marrow with 40% lymphoblasts, and flow cytometry confirmed the diagnosis of CALLA-positive precursor B cell ALL. The child was initiated on chemotherapy per the children's oncology protocol. Cerebrospinal fluid (CSF) analysis did not reveal the presence of malignant cells. His proptosis improved after one month of chemotherapy [Figure 1b]. He is in remission since 9 months of diagnosis and regular chemotherapy is administered to him.

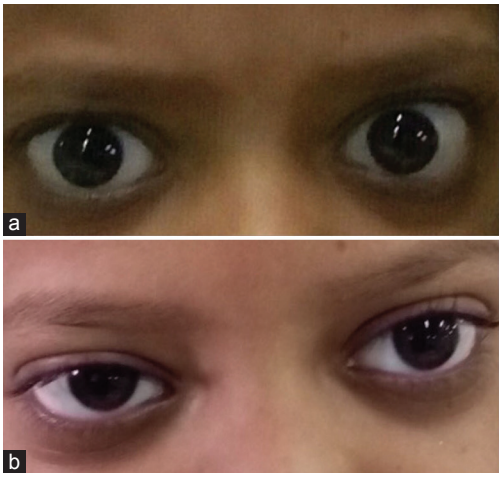

Figure 1. (a) Proptosis at presentation and (b) improvement after induction chemotherapy

DISCUSSION

ALL accounts for almost 30% of childhood malignancies, of which the most common is precursor B cell ALL. Clinical features such as fever, fatigue, and spontaneous bruising/bleeding are often present as initial symptoms.[2,3] Proptosis is a clinical sign characterized by bulging of the eye anteriorly out of the orbit, and must be differentiated from thyrotoxicosis, and microphthalmos of the contralateral and involved eyes. Proptosis is a common symptom in a wide variety of diseases involving the structure in and around the orbit. The work-up for proptosis requires careful ocular and systemic history pertaining to the particular age group. History-taking should include the duration, mode of onset, progression and associated symptoms, prior medical and surgical treatment, and family history. Etiology should be confirmed after the peripheral smear, MRI, and bone marrow assessment, and with histopathological examinations if needed.[4,5]

Ocular manifestations in leukemia are explained on the basis of anemia, hypoxia, blood viscosity, compression by masses of cells, or direct tumor infiltration. An orbital biopsy study by Shields et al revealed that 85% of proptosis occurs due to benign lesions such as cysts, inflammatory lesions or mesenchymal hamartomas, and malignant causes including rhabdomyosarcoma, retinoblastoma, leukemia, lymphoma, and lacrimal gland tumors. Malignancies as a cause for proptosis were more common, among which the majority of cases were secondary to neuroblastoma and leukemia, usually of myeloid origin.[6] The spectrum of ocular manifestations in leukemia can occur due to direct infiltration of the orbits presenting as proptosis, lid edema, and chemosis, or vascular abnormalities of the retina presenting as intra-retinal macular or sub-hyaloid hemorrhages, cotton wool spots, and neuro-ophthalmic signs, such as blurring of vision, diplopia, extra-ocular muscle palsies, and papilledema secondary to increased intracranial pressure.[7]

A prospective study by Reddy et al reported two children presenting with proptosis in a study involving 82 children and both were diagnosed with myeloid leukemia.[7] Similarly, Biswas et al studied the uncommon clinical features in childhood leukemia and reported only two cases presenting as proptosis in a study involving 75 patients and both were diagnosed with AML.[8] Ocular manifestations of leukemia often reflect the disease status of the body; they may be the initial signs of presentation or the first manifestations of relapse of the underlying illness. In leukemia, orbital infiltration

presents with proptosis, lid edema, and chemosis, and is the third most common extramedullary manifestation of acute leukemia.[9] Hematogenous masses in the orbit are commonly due to granulocytic sarcomas, which are usually associated with AML, rather than ALL, and are rare especially when they precede systemic disease.[10] Chaudry et al have reported the case of a 3-year-old child who presented with unilateral proptosis and was diagnosed with ALL.[11] Similarly, Thakker et al reported a case of precursor B cell ALL in a young 8-month-old infant who exhibited unilateral proptosis.[12]

When children present with complaints pertaining to the eye, ophthalmologists are the first points of contact, as reported in our case. Hence, awareness about childhood leukemia and its association with ophthalmological manifestations is important for prompt recognition as a sign of possible extramedullary disease, as it is crucial for early diagnosis and for appropriate referral or therapy to be initiated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest

There are no conflicts of interest.

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