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Proptosis as Initial Presentation of Acute Lymphoblastic Leukemia in a Child with no associated symptoms: A Case Report

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Abstract
Acute lymphocytic leukemia (ALL) is one of the frequent malignancies in pediatrics and involves bone marrow and extramedullary sites. Proptosis as extramedullary involvement of leukemia usually present in acute and chronic myeloid leukemia. It is extremely rare for ALL to present initially as proptosis.Here, a-21-month-old boy was presented with proptosis without any associated symptoms except lymphadenopathy. He was referred with the impression of malignancy from an ophthalmologist. After bone marrow biopsy which showed 33% blast cells, all positive for CD10, CD19, and CD79, the diagnosis of pre-B cell ALL was finally made. His symptoms were improved completely 16 days after starting standard protocol for ALL.Afterone-year follow-up, he was free of any symptoms.According to this initial presentation of ALL and no typical associated symptoms, it is important to make rapid diagnosis and start the treatment in the childhood.
Key words: Acute lymphoblastic leukemia, Proptosis, Childhood

Introduction

Acute lymphoblastic leukemia (ALL) is the most common malignancy of the childhood and it accounts for about one-quarter of all childhood cancers (1, 2). Typically, the child is presented with nonspecific symptoms, such as fever, infection, bleeding, bone pain, or lymphadenopathy (3). The most common extramedullary site of ALL after the meninges and testicles is ocular involvement which may be seen on careful ophthalmological investigation in up to one-third of the children with newly diagnosed ALL (4). However, orbital infiltration is more common in other leukemic type hematopoietic cancers and is accounted as a rare finding in ALL (5). It presents with proptosis, lid edema, chemosis, and pain (6, 7) and is usually associated with other non-specific symptoms of ALL (8, 9). This condition might be confused with other diseases involving orbit, such as myeloblastic leukemia, hypereosinophilic syndrome, myelofibrosis with myeloid metaplasia, and polycythemia vera (10). Obviously, the precise diagnosis has an important role in prompt intervention and prognosis of the disease.

Case report

The patient was a 21-month-old boy referred to hematology and oncology department of Mofid Children's Hospital in Tehran (capital of Iran) in 2016 complaining of left eye proptosis without erythema, tenderness, and tearing. His problem was started acutely and he had no other symptoms like bone pain or fever according to his parents. He was presented

to an ophthalmologist and he was treated with eye drops but the symptoms were not resolved and with the manifestations of malignancy, he was referred to this center.

His past medical history was negative for developmental delay, metabolic disorders, or other medical illnessess. No history of medical illness or malignancy was reported in his parents or other family members. On admission, his vital signs were in normal limits. General physical examination revealed a 1.5 cm left eye proptosis with no erythema or tenderness (Figure 1). He had bilateral submandibular lymphadenopathy sized 2*1.5 cm. He had no hepatosplenomegaly and all other examinations were normal. On cranial nerve examination, his pupil was reactive and other cranial nerves examination was in normal limits. His first complete blood cell count showed white blood cells of 28000, hemoglobin of 9.1, and platelet of 512000. The patient PT and PTT were 11.0 and 27.0, respectively.

Spiral brain computerized tomography scan with contrast demonstrated a 28*16*22 mm homogenous mass with mild enhancement in superolateral aspect of left orbit, and left lateral rectus was also mildly swollen. Mild preseptal thickening is noted in left side. Optic nerve, sheet, and bony structures were intact (Figure 2).

With the manifestationsof malignancy or solid tumor, he underwent bone marrow aspiration which showed 33% blast cells, all positive for CD10, CD19, and CD79, suggesting pre-B-cell ALL diagnosis. Cerebrospinalfluid examination was negative for malignancy. Standard chemotherapy protocol for ALL was started (11). His proptosis was improved 3 days after treatment initiation and finally disappeared on day 16. He was on maintenance therapy for 12 months. After one-year follow-up, he was free of any symptoms. Written informed consent was obtained from the patient for publication of this case report.

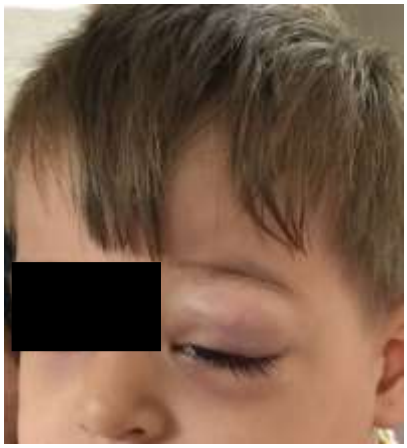

Figure 1. A large left orbital mass with impending vision compromise.

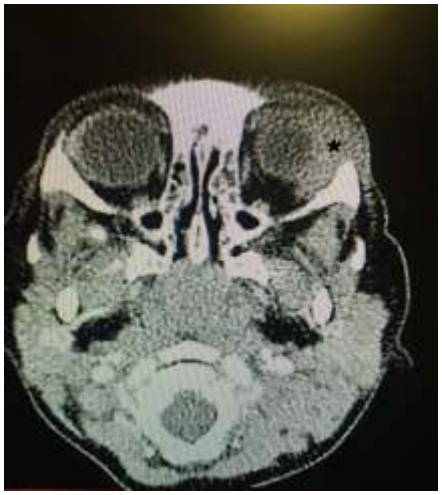

Figure 2. Contrast-enhanced computed tomography on the orbit and the brain. The star depicts a 28*16*22 mm homogenous mass with mild enhancement in superolateral aspect of left orbit. Mild preseptal thickening is noted in left side. Optic nerve, sheet and bony structures are intact.

Discussion

Neoplasms are common etiologies of pediatric proptosis. These neoplasms include retinoblastoma, optic glioma, rhabdomyosarcoma, leukemia, lymphoma, histiocytosis, Ewing sarcoma, and metastasis (12). Leukemic presentation as an orbital mass is usually observed in acute forms ofmyelogenous origin (13).

Orbital involvement in patients with ALL is exceedingly rare and can be a manifestation of a primary or relapsed disease. Presentation of proptosis in a patient which is not known for ALL, i.e. primary ALL, will be a diagnostic challenge for physicians.

In this case report, presentation of pre-B-cell ALL as proptosis in a 21-month-old boy is presented. The diagnosis of pre-B-cell ALL in this child was made based on the bone marrow aspiration. In B-lineage ALL, the most important markers for diagnosis, differential diagnosis and subclassification are CD19, CD20, CD22, CD24, and CD79; besides, the presence of CD10 antigen defines the "common" ALL subgroup (14). Bone marrow aspiration of our case showed 33% blast cells, all positive for CD10, CD19, and CD79, suggesting pre-B-cell ALL diagnosis.

Presentation of primary ALL as proptosis was reported to 9 previous case reports (8, 9, 15-21). The age group described in these cases ranged between 6 months and 16 years with no gender dominance. Bilateral involvement of the orbit was observed in only one report (18) and other cases had unilateral involvement similar to the presented case. Leukemic infiltration of orbit possibly originates from marrow cavity of the orbital wall; therefore, simultaneous ocular and orbital infiltration seems unusual. Consistently, only two studies reported simultaneous ocular and orbital involvement (20, 21). In most of these cases, proptosis is associated with other non-specific signs and symptoms of ALL, such as fever or weight loss, which help the physician to think about systemic etiologies. However, in the presented case, initial presentation of proptosis in ALL was not associated with such symptoms, potentially leading to diagnosis such as orbital cellulitis and orbital pseudo-tumor which are common etiologies of proptosis in children (12). Initial presentation of primary ALL as proptosis in a previous healthy child was only reported in two studies (16, 20). In both of these studies, a progressive proptosis was emerged during two weeks. In the presented case, the patient had a history of proptosis at the same eye about one year ago which made the diagnosis more difficult.

Although presence of orbital involvement in acute myeloid leukemia, known as granulocytic sarcoma, does not significantly alter the survival in these patients (22), the prognostic influence of orbital involvement in ALL is not known. Nevertheless, ocular involvement in ALL is associated with a poor prognosis (23). Among the previous reports who did not have an ocular involvement, all of the cases, except one case (18) survived at the end of follow up; however, length of follow-up was very short in some of these reports, precluding a conclusive interpretation. Anyway, it should be noted that the orbital manifestations of ALL regressed after chemotherapy in all of these cases similar to the presented case, addressing that a right diagnosis in these patients can completely resolve the proptosis.

Conclusion

This patient sensitized us to an unusual presentation of ALL in children. ALL should be kept in mind as a probable diagnosis in every child with acute proptosis even when the child has no past medical history and no associated symptoms in first presntation. Longer follow-up may be promising in determining the effect of orbital involvement on prognosis of the pediatric ALL.

Conflicts of interest

The authors declare no conflicts of interest for this manuscript.

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