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A Rare Ophthalmic Presentation of Acute Lymphoblastic Leukemia in an Adult Male: A Case Report

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ABSTRACT

This case report discusses a 35-year-old male patient who presented with bilateral painless proptosis as the initial manifestation of Acute Lymphoblastic Leukemia (ALL). He exhibited fever, back pain, and fatigue, leading to magnetic resonance imaging (MRI) of the brain and orbit, which suggested lymphoma. Positron Emission Tomography-Computed Tomography (PET-CT) revealed the findings suspicious of lymphoma. The diagnosis was confirmed through peripheral smear (82% blasts), bone marrow biopsy, flow cytometry indicating B-cell ALL, and a positive Philadelphia chromosome t (9:22) on FISH panel. Ocular involvement in ALL, particularly in adults, is rare, and this case demonstrates the importance of early diagnosis and multidisciplinary management. The patient responded positively to chemotherapy, with a significant reduction in proptosis. However, despite ongoing treatment for supportive care, the patient unfortunately expired six months later.

Keywords: Proptosis, Acute Lymphoblastic Leukemia, Ophthalmic manifestation, B-cell ALL, Philadelphia chromosome

INTRODUCTION

Proptosis, the anterior displacement of the eye, results from various conditions including trauma, neoplasms, autoimmune disorders, and infections[1]. Acute leukemias are diagnosed by the presence of over 20% blast cells in the blood or bone marrow. Ophthalmic manifestations in leukemia, though common in acute myeloid leukemia (AML), are rare in acute lymphoblastic leukemia (ALL), particularly in adults. This case describes an adult patient presenting with bilateral painless proptosis, eventually diagnosed with B-cell ALL, highlighting the significance of recognizing rare ophthalmic signs for timely intervention[2].

CLINICAL PRESENTATION

A 35-year-old male presented with bilateral painless proptosis for three weeks. The patient denied redness, watering, or visual disturbances and had no history of trauma or thyroid dysfunction. His visual acuity was 6/6 in both eyes, with left lateral rectus muscle restriction. Proptosis was measured at 25 mm in the right eye and 24.5 mm in the left. Intraocular pressure and fundus examination were normal (Figure 1A and B). Thyroid function tests ruled out thyrotoxicosis. MRI of the brain and orbit revealed diffuse marrow hyperintensity involving the calvarium (Figure 2), skull base, and mandible (Figure 3). T2-weighted imaging showed bilateral proptosis (Figure 4) with ill-defined soft tissue lesions in the extraconal and intraconal compartments of both orbits (Figure 5, Figure 6, Figure 7), suggestive of lymphoma. Urgent referral from Ophthalmology to Hematology was given. PET CT revealed extensive hypermetabolic activity with a few intra orbital (Figure 8) and paraspinal soft tissue components (Figure 9) and infradiaphragmatic compartment lymph nodes with mildly hypermetabolic splenomegaly (Figure 10) findings concern of neoplastic etiology lymphoma. Complete blood picture showed hemoglobin with 14 g/dl, total count was 78000/mm^3, platelet count was1.59 lakh/mm^3. The peripheral smear showed 82% blasts. Bone marrow biopsy revealed acute leukemia. Flow cytometry showed CD19, CD10, CD22, CD33, CD34, CD45, TdT and HLADR positive suggestive of B-ALL, with aberrant presentation of CD33. Lumbar puncture and CSF cytology revealed negative for malignant cells. Patient underwent chemotherapy with BFM-95 protocol and achieved a prednisone good response. However, the presence of t(9:22) Philadelphia chromosome on FISH panel, indicating ALL for which he was started on Imatinib along with BMF-95 protocol. End induction phase B, minimal residual disease analysis was less than 0.01%. The patient proptosis measured 22.5 mm in both eyes during 2 months follow up. He completed extra compartment protocol M following which BMF-95 re-induction phase A was initiated. However, the patient experienced complications such as fever, neutrophilic leukocytosis and paraplegia, ultimately leading to death from sudden cardiac arrest during reinduction phase of treatment.

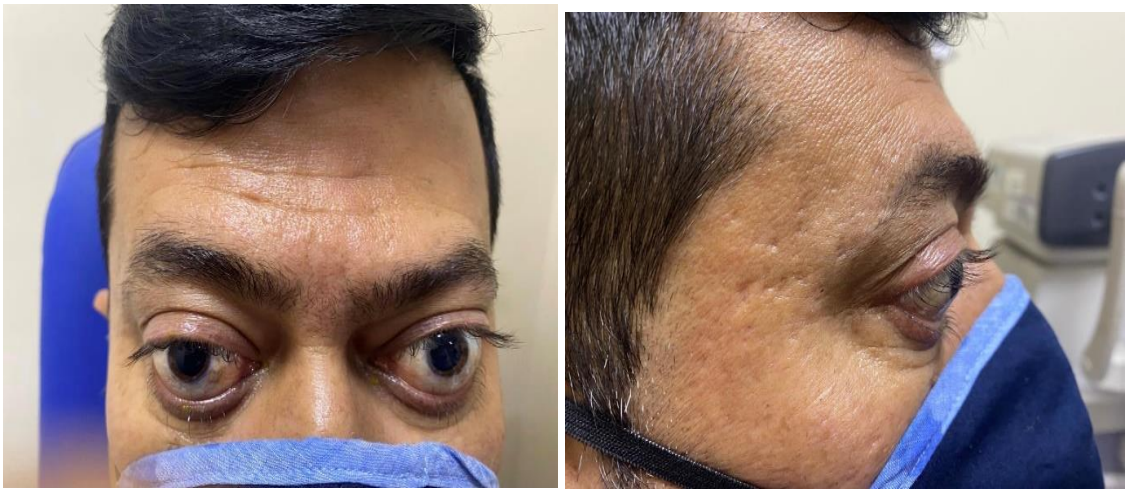

Figure 1 (A and B). Patient with bilateral proptosis.

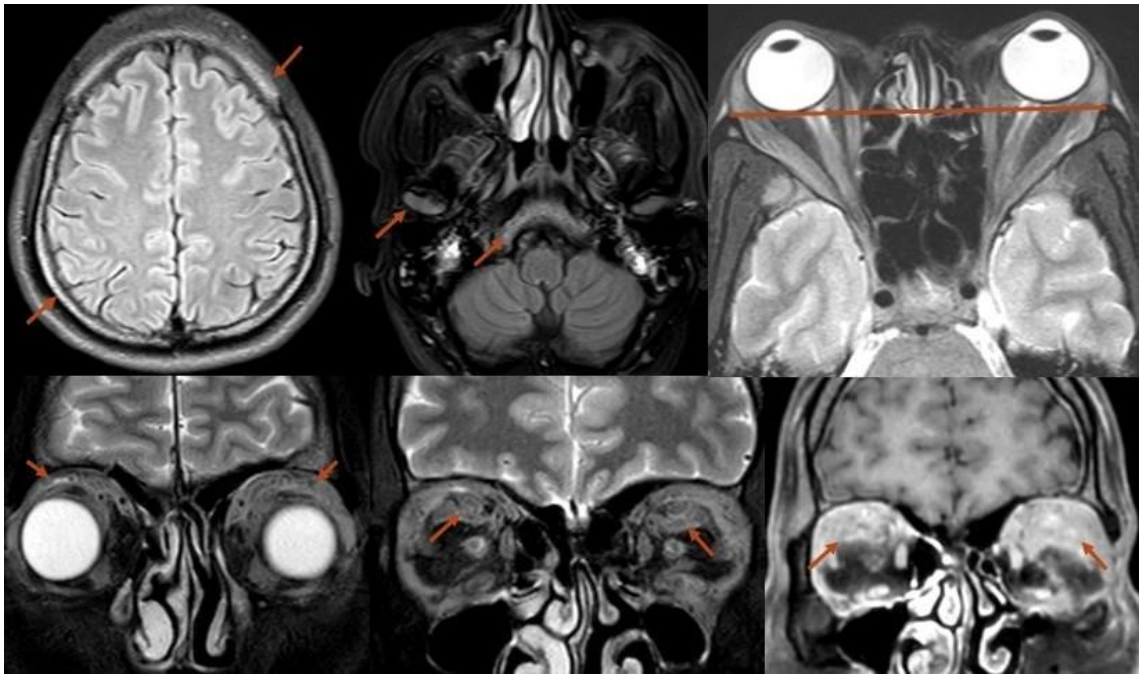

Figure 2. Diffuse FLAIR showing marrow hyperintentisty involving the calvarium and figure 3 skull base and mandible. Figure 4. T2W1 showing bilateral proptosis with globes anterior to the interzygomatic line. Figure 5.T2W1 showing ill-defined soft tissue in the extraconal compartment of bilateral orbits predominantly along the roof, lateral wall and floor abutting the extraocular muscles.Figure 6. Ill-defined soft tissue is also noted in the intraconal compartment of bilateral orbits in the superior retrobulbar region on T2W1.Figure 7. T1C+ showing homogenous enhancement of soft tissue lesion.

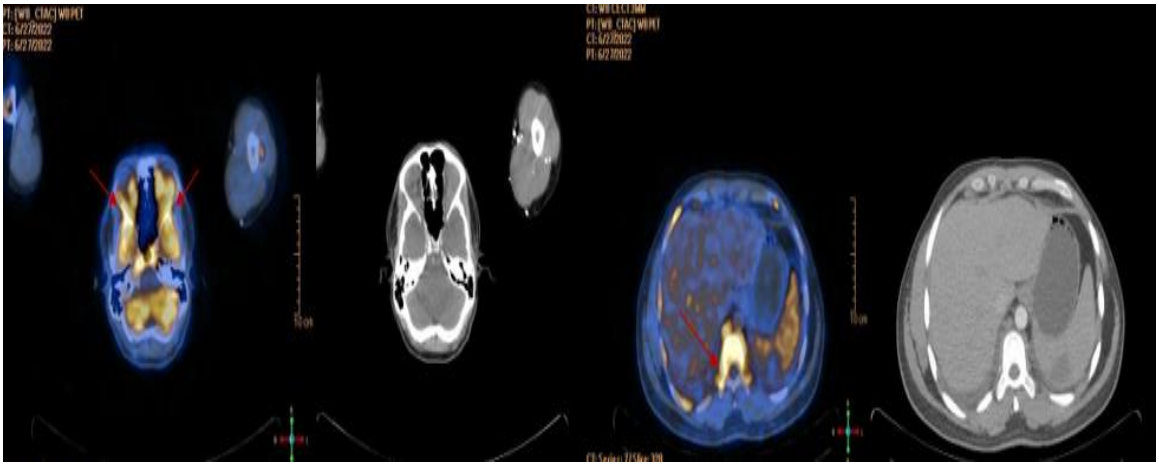

Figure 8 revealing extensive skeletal hyper metabolic activity with a intraorbital is figure 8 and paraspinal soft tissue components is figure 9 which are represented by red arrows

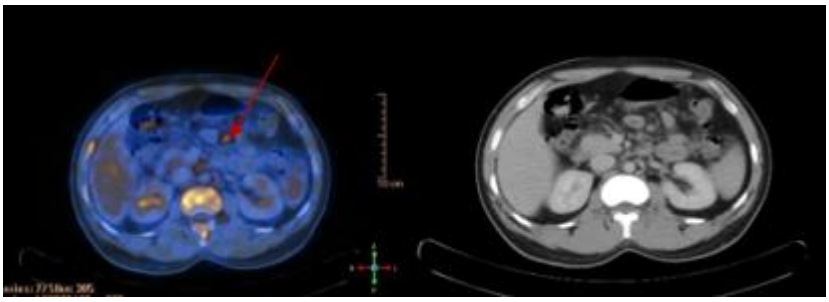

Figure 10. Multiple hypermetabolic supra and infradiaphragmatic compartment lymph nodes with mildly hypermetabolic splenomegaly.

DISCUSSION

Ophthalmic manifestations in acute leukemia, particularly ALL, are uncommon in adults. Most documented cases of ocular involvement in leukemia pertain to AML, where infiltration of the orbit may present as proptosis, lid edema, or chemosis[3]. While ocular manifestations in children with leukemia are well-documented, reports of such findings in adults with ALL are scarce. Generally, a 2mm or greater asymmetry between the protrusion of patient eye is considered abnormal [4].

The differential diagnosis of proptosis includes autoimmune, vascular, neoplastic, and infectious causes. In this case, MRI and PET-CT played crucial roles in the diagnosis, revealing ill-defined soft tissue infiltration, suggesting lymphoma [5,6,7]. Orbital masses due to ALL are rare, typically occurring later in the disease progression. Orbital lymphoma constitutes 46-47% of ocular adnexal lymphoma (OAL) and accounts for approximately 11% if all orbital masses. However, in this case, proptosis was the initial clinical manifestation, underscoring the need for comprehensive diagnostic workup in unexplained proptosis[8,9,10].

Ill-defined soft tissue is also noted in the intraconal compared to the orbits bilaterally predominantly in the superior retrobulbar region with fat stranding of the retrobulbar fat. The soft tissue appears slightly hyperintense to the extraocular muscles on T2 and isointense on T1Wt images with diffusion restriction. The lacrimal glands appear prominently bilaterally and are inseparable from the described soft tissue lesion. The above findings suggestive of likely lymphoma. The peripheral smear revealed 82% blasts and bone marrow biopsy revealed acute leukemia. Flow cytometry suggestive of B cell acute lymphoblastic lymphoma. PET-CT confirmed lymphoma. ALL FISH panel showed t(9:22).The clinical presentations of ALL are constitutional symptoms like fever, weight loss, night sweats, frequent bruising and bleeding, dizziness, dyspnea, infections, joint pains. CNS (central nervous system) involvement is higher in B-ALL. Ph-positive ALL is a prominent subtype for adults where HSCT (Hematopoietic stem cell transplantation) is only the cure. TKIs (Tyrosine kinase inhibitors) like Imatinib can produce 30% of response. The proptosis in our patient reduced after 2 months. Hematogenous masses in the orbit are commonly due to granulocytic sarcoma, which are usually associated with AML, rather than ALL, and are rare especially when they precede systemic disease [11]. Despite being the third most common site of extramedullary lesions, there have been few reports focusing on the rate of ophthalmic manifestations related to acute leukemia at the time of diagnosis[12-15.] Mirashi et al have documented that ophthalmic involvement was associated with higher rates of death on the first day after diagnosis[15].

Philadelphia chromosome-positive ALL (Ph+ ALL) is a prominent subtype in adults and is often treated with tyrosine kinase inhibitors (TKIs) alongside chemotherapy [11,12,13,14]. Early recognition and treatment are crucial, as proptosis and other extramedullary manifestations may indicate a poor prognosis[16,17,18].

Learning Points

1. Ocular manifestations: Proptosis as an initial manifestation of ALL is extremely rare in adults and requires prompt investigation.
2. Multidisciplinary approach: Collaboration between ophthalmologists, radiologists, and oncologists is critical for the timely diagnosis and treatment of ALL with ocular involvement.
3. Philadelphia chromosome (t (9:22)): The presence of this genetic abnormality in ALL suggests a more aggressive disease course and necessitates targeted therapy with TKIs.
4. Prognosis: Ocular involvement in ALL, while rare, may signify an aggressive disease course. Early intervention can significantly improve outcomes.

CONCLUSION

This case highlights the importance of recognizing proptosis as a potential early manifestation of acute lymphoblastic leukemia in adults. The use of multimodal imaging, hematological analysis, and molecular diagnostics is crucial for early diagnosis. Multidisciplinary management resulted in significant clinical improvement in this patient, emphasizing the need for awareness among ophthalmologists and oncologists of such rare presentations. Ophthalmologists should maintain a high index of suspicion for hematologic malignancies like ALL when evaluating adult patients with unexplained proptosis, as timely referral and management can dramatically alter patient outcomes.

Informed consent

The patient consent was obtained prior to case taking for confidentiality of his identity. The patient has agreed that his report and other clinical information is to be reported in the journal.

Declaration by Authors

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