

## Unilateral Proptosis, A rare Presenting Sign of Acute Myeloid Leukemia

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### Abstract

Unilateral proptosis is a rare first presenting sign of Acute Myeloid Leukemia (AML).

We report a case of unilateral proptosis in a six-years-old girl as the initial manifestation of AML. It was initially missed and was investigated as a case of hyperthyroidism.

Peripheral blood smear and bone marrow aspirate evaluation showed signs diagnostic of AML. Computed tomography scan of orbits showed infiltrative process in the right orbit, right maxillary and right ethmoidal sinuses. Unilateral proptosis as an extramedullary

first presenting feature of AML is very rare; however, it should always be remembered in the differential diagnosis of proptosis in pediatric age group.

**Keywords:** Acute myeloid leukemia; proptosis; orbit; pediatric.

### **Introduction:**

Acute myeloid leukemia (AML) is the second most common type of acute leukemia in pediatric population. It is characterized by immature myeloid cell proliferation and bone marrow failure. AML patients can develop extramedullary lesions most commonly in the meninges, testicles and the orbits. Proptosis as an initial presenting sign of AML is very rare when compared to other various signs and symptoms these patients can develop. We report a case of AML in a six-years-old girl in whom the disease primarily presented as a unilateral proptosis

### **Case Report:**

A six-years-old female child was referred from local health center to ophthalmology clinic after being investigated for hyperthyroidism, for evaluation of progressive, painless proptosis of the right eye of one-week duration. She looked pale and her parents reported easy fatigability however, no reduction in vision was noted. There was no history of recent or recurrent fever, night sweats, symptoms of upper respiratory tract infection, abdominal pain or changes in bowel habits, urinary symptoms, abnormal movements, loss of consciousness, skin rashes or bruises. No loss of appetite or recent weight change

had been noted. Past medical history was significant for eczema, allergic rhinitis and chronic otitis media with effusion causing conductive hearing impairment.

General physical examination revealed tired, pale looking child, but no organomegaly or lymphadenopathy were detected.

Ophthalmic evaluation revealed visual acuity of 6/6 in each eye. Proptosis in the right eye was noted with mild limitation of abduction (Fig. 1). There was no periocular discoloration. Both pupils react normally to light. Color vision and visual field were not assessed due to poor cooperation. Anterior segment examination was unremarkable. Ophthalmoscopy revealed hyperemic discs in both eyes. Rest of the fundus examination was normal.

The child was admitted for further evaluation. Initial blood investigation revealed hemoglobin of 6.5 g/dl (11.0 -14.5), platelet counts of  $28 \times 10^9/L$  (150-450) and white cell counts of  $21 \times 10^9/L$  (2.4-9.5). The patient received packed red blood cells and platelet transfusion to correct the significant anemia and thrombocytopenia. Peripheral blood smear showed normocytic, normochromic red cells with few elliptocytes, and numerous pleomorphic, medium to large circulating blast cells, some with bilobed nucleus, and fine granulation. Neutrophils were dysplastic and shifted to the left. Auer rods were not seen. (Fig. 3) Uric acid, renal and liver function tests, bone profile and Cerebrospinal fluid (CSF) analysis were all reported to be normal. Lactate dehydrogenase (LDH) was 500 U/L (120-500). Chromosomal analysis by florescent in-situ hybridization (FISH) showed inversion 16 which is a favorable cytogenetic abnormality.

Ultrasound abdomen as well as electrocradiogram and echocardiography were normal. Computed tomographic (CT) scan of the brain and orbits revealed features of an infiltrative process involving the right maxillary and ethmoidal sinuses with extension to the infratemporal fossa inferiorly and into the orbit with possible intraoral and intracranial extension (Fig 2). Visual evoked potential (VEP) was also done and showed normal response.

Examination of Bone marrow aspirate revealed replacement of trilineage hematopoiesis with abnormal blast population with features matching that seen in the peripheral blood smear. Residual granulocytes were dysplastic and showed hypogranulation and hypolobation. Eosinophils were prominent. Residual erythropoiesis was normoblastic. Hemophagocytic activity was noted in the background (Figure 3).

A diagnosis of acute myeloid leukemia was made based on above findings and the patient was started on the AAML 1031 standard chemotherapy arm treatment protocol on April 2019 and completed 4 cycles of the protocol on December 2019. Mutation of the FLT3-ITD gene is found in approximately 10% of pediatric AML. Poor outcome is associated with higher initial total leukocytic counts and higher induction failure rates<sup>1</sup>. Our patient has initial white blood cell count of less than  $50 \times 10^9 / l$  and she went into complete remission after course 1 of chemotherapy.

The patient has tolerated the chemotherapy cycles with no major side effects. During the courses of chemotherapy, the girl had 3 episodes of febrile neutropenia. They were managed with IV tazobactam/piperacillin. She did not have any positive blood cultures. The patient did receive antifungal prophylaxis with voriconazole during the periods of severe neutropenia.

**Discussion:**

Acute myeloid leukemia (AML) can present with ocular signs and symptoms through direct leukemic infiltration of ocular tissue. At the time of diagnosis of acute leukemia, half of children demonstrate ocular involvement most commonly those due to alterations of hematologic parameters (low hemoglobin, low platelets, and hyperviscosity states) which present as vitreous, retinal or choroidal hemorrhages <sup>2</sup>.

Ophthalmic manifestations of leukemia can be classified as extraocular manifestations and intraocular manifestation. Among the extraocular manifestations, subconjunctival hemorrhages, conjunctival chemosis, lid edema and extraocular muscle restriction were the most common presentations in descending order <sup>3</sup>.

Orbital involvement as an initial manifestation of AML is uncommon. Most cases present with unilateral proptosis, though fewer cases have been reported to have bilateral orbital involvement as an initial manifestation<sup>4</sup>. Proptosis occurs mainly because of orbital leukemic infiltrates in the orbit, orbital muscle infiltration, venous blockage or retrobulbar hemorrhage, although proptosis secondary to diffuse infiltration of the lacrimal gland and infiltration of individual extraocular muscles has also been reported <sup>5</sup>.

The proptosis might due to granulocytic sarcoma which is an extramedullary accumulation of leukemic cells infiltrates. Granulocytic sarcoma is a rare manifestation of AML and it is seen in approximately 3% of cases of AML. The suggested theory behind granulocytic sarcoma is that the cancerous cells originate in the bone marrow and then migrate through the Haversian canals to collect in the subperiosteum and form soft tissue masses most commonly in the skull, orbits, paranasal sinuses, sacrum, spine,

sternum, and ribs. However, granulocytic sarcoma presenting as an orbital mass in AML is very rare <sup>6</sup>.

In pediatric patients, the differential diagnosis of acute proptosis includes a wide range of disorders including orbital dermoids, orbital cellulitis, orbital hemangiomas, lymphangiomas, orbital varices, inflammatory causes such as thyroid eye disease or nonspecific orbital inflammation and other neoplastic tumors like retinoblastoma, rhabdomyosarcoma, metastatic neuroblastoma and Langerhans cell histiocytosis. Among these various causes, proptosis due to orbital myeloid granulocytic sarcoma appears to be such a rare entity accounting for only one of 250 cases in previous reports <sup>7</sup>.

The life expectancy of patients with acute myeloid leukemia with orbital manifestation drops to less than half compared to those with no orbital manifestation (21.4% and 45.7% respectively) <sup>8</sup>. Our case completed her chemotherapy protocol since 11 months with no major complications and on currently follow-up. Since she has favorable cytogenetics and no matched donor, she didn't have a bone marrow transplant.

In conclusion, AML should be kept in mind as differential diagnosis of a rapidly growing unilateral or bilateral proptosis in children. Radiological imaging, peripheral blood smear and subsequent bone marrow biopsy should be performed if AML is suspected.

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Figure captions

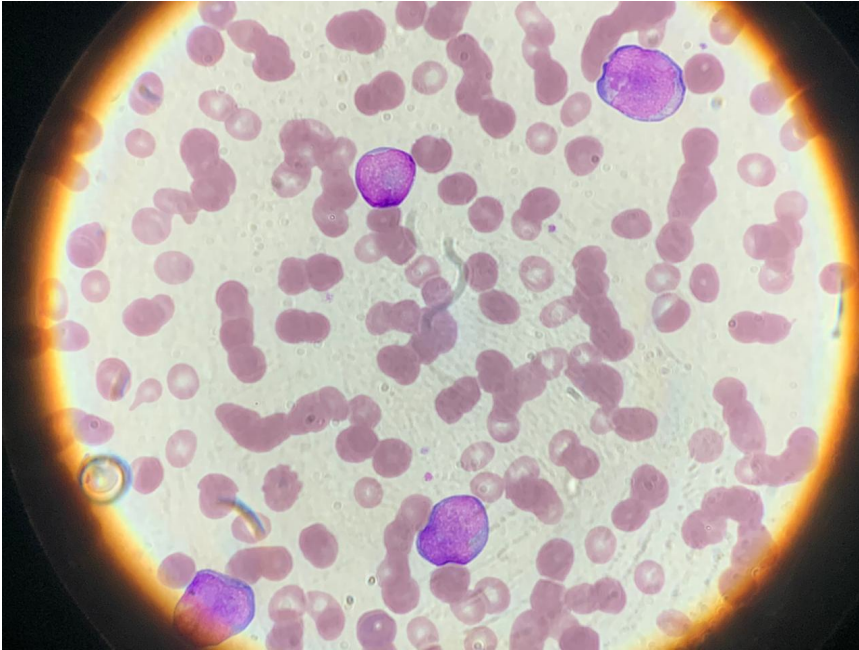




**Figure 1:** Photo of the patient showing the subtle Proptosis of the right eye



**Figure 2:** Cranial CT scan of the patient showing widening of the right pterygopalatine fossa



**Figure 3:** Bone marrow aspiration slide showing myeloblasts