Bilateral Eye Proptosis and Right Temporal Orbital Region Swelling as First Presentation in Acute Myeloid Leukemia

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Background: Acute myeloid leukemia (AML) is a cancer of the blood and bone marrow. The aim of this case is to report an unusual presentation of AML which presented with bilateral eye proptosis and swelling over the right temporal orbital region as first presentation.
Method: Case report.
Result: A 16-year-old Malay boy presented with bilateral eye proptosis and painless, progressive right temporal orbital region swelling for one month. It was associated with difficulty in passing urine and altered bowel habit. Three days prior to presentation he had lower back pain and numbness over bilateral lower limb which progressed to paraplegia two days after admission. On examination, the vision was 6/6 bilaterally with absence of relative afferent pupillary defect. There was axial proptosis in both eyes with restriction of extraocular movement in all gaze. Full blood picture showed bicytopenia with a presence of 78% blast cells. Computed tomography of brain and orbit revealed hyperdense lesions at bilateral extraconal spaces and soft tissue swelling at right temporal orbital region. Magnetic resonance imaging of thoracolumbar spine has no significant findings. Bone marrow aspiration and trephine biopsy consistent with AML type M2/M4. He received radiotherapy and was planned for chemotherapy but succumbed to his disease.
Conclusion: A child or young adult who presents with proptosis and rapidly growing orbital mass, high index of suspicion should be made against acute leukaemia as one of the differential diagnosis.
Conflict of interest: None.
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Introduction

Acute myeloid leukemia (AML) is characterized by the clonal proliferation of myeloblast in the bone marrow and blood.[1] It accounts approximately 15% of childhood leukemia and is more common among children and young adults.[2,3,4,5]

Granulocytic sarcoma is one of the extramedullary manifestations in acute leukemia. It is also known as myeloid sarcoma or chloroma. It is due to accumulation of leukemic cells infiltrating the extramedullary sites.[3] Incidence of granulocytic sarcoma among AML patients

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is reported to be between 2.5-9.1% and much lesser for central nervous system (CNS) involvement.[6]

Proptosis is the protrusion of the eyes which can clinically measure by exophthalmometer. The most common cause is due to thyroid eye disease. Other big groups of etiologies could be due to inflammatory causes (idiopathic orbital inflammation), infections (orbital cellulitis), vascular causes (carotid cavernous fistula, orbital varix), tumors(lacrimal gland tumor, glioma and meningioma of the orbit) and haematological malignancy (leukemia and lymphoma).[7]

Here we report a case of unusual presentation of AML which presented first with eye symptoms and temporal orbital region swelling followed by lower limb lower motor neuron weakness.

Case report

A 16-year-old Malay boy presented with bilateral eye proptosis and right progressive temporal orbital region swelling for one month. The proptosis was not associated with blurry vision and diplopia. There was no eye pain, eye redness or eye discharge. The proptosis was associated with swelling at the right temporal orbital region. The right temporal orbital region swelling was initially small and rapidly increased in size within a month.

One week after the presentation of proptosis and right temporal orbital region swelling, the patient developed difficulty in passing urine and altered bowel habit. His condition was getting worse with development of lower back pain and numbness over bilateral lower limbs three days prior to presentation. The lower limbs numbness progressed to bilateral paraplegia two days after admission.

The patient also had constitutional symptoms with loss of weight and loss of appetite over the period of eye symptoms. It was not associated with night sweat or fever. There was no history of subconjunctival haemorrhage, gum bleeding or any bleeding manifestation. He denied any preceding trauma or injury prior to that. The patient had no previous illnesses. He has been smoking one pack per day for the past 5 years. He has no family history of malignancy or leukemia and no history of exposure to radiation.

On examination, the visual acuity was 6/6 bilaterally with absence of relative afferent pupillary defect. There was symmetrical axial proptosis in both eyes (Figure 1) with Hertel exophthalmometer measurement at 115 mm showed 22 mm for both eyes. The patient was able to close eyes completely with Bell's phenomenon. There was restriction of extraocular movement in all gaze with no diplopia. Anterior segment examination was normal with no subconjunctival haemorrhages or hyphema. There was also no conjunctival mass. Posterior segment examination showed there was absence of optic disc oedema, cotton wool spots, Roth spots or perivascular infiltrates. There was also no pre-retinal, subretinal or intra-retinal haemorrhages.

Right temporal orbital region examination showed a soft tissue mass measured about 7×5 cm in size. The soft tissue mass was soft, non-tender, non-fluctuant, non-mobile with no overlying skin changes.

Lower limbs power bilaterally reduced to 0-1/5 with hypotonia and hyporeflexia. The plantar reflex response of both sides were equivocal. There was reduced sensation from T6 and below with absence of anal tone. Bulbocavernosus reflex was present. Both upper limbs and cranial nerves examinations were normal.

Systemically, there were no skin bruises or gums bleeding. There was also no lymphadenopathy and no organomegaly.

Blood investigation showed hemoglobin level was 11.7 g/dl with low platelet count (52×10^9/l). Full blood picture revealed bicytopenia with presence of 78% blast cells. Following blood picture findings, bone marrow aspiration and trephine biopsy was performed and showed 81% blast cells which appeared moderate to large in size, abundant cytoplasm with prominent nucleoli. Some of the blasts exhibit cytoplasmic vacuolation. There was also the presence of Auer rods.

The flow cytometry result showed positive CD45 with high side scatter (SSC)/blast window, positive CD34, HLA DR, CD117, CD13, CD33, CD16, CD56 with aberrant CD4 and Myeloperoxidase (hetero). There were negative results for CD11b, CD14, CD64, B and T markers. This result is consistent with AML whereby cell markers for myelogenous cell lines were positive and negative for white cells, T and B cells.

Computed tomography of brain and orbit revealed hyperdense lesion at bilateral lateral extraconal spaces causing displacement and stretching of lateral recti muscles (Figure 2) and soft tissue swelling at right temporal orbital region (Figure 3). Magnetic resonance imaging (MRI) of thoracolumbar spine showed no significant findings.

Based on bone marrow aspiration and trephine biopsy, the findings were consistent with AML type M2/M4. He received radiotherapy for the AML. For the proptosis, he was treated with Gutt artificial tears 6 hourly for bilateral eye lubricants. Post 5 cycles of radiotherapy, there was regression of bilateral proptosis and right temporal orbital region swelling with improvement of extraocular movement. However, his neurological symptoms remained the same with paraplegia, hypotonia and areflexia.

He was planned for chemotherapy AML 3+7 Daunorubicin and Ara-C (Cytarabine), however, the patient passed away after 5 cycles of radiotherapy due to septicemia and hypovolemic shock. He developed perforated viscus with coagulopathy and paralytic ileus secondary to sepsis with electrolyte imbalance and upper gastrointestinal bleeding.

Discussion

AML is a cancer of the bone marrow and most commonly presented with easy fatigability, infections to a variable degree and haemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis and menorrhagia.[8] All of these symptoms are related to the complications of pancytopenia that is anaemia, neutropenia and thrombocytopenia.

Its extramedullary site with leukemic cells infiltrate is an unusual presentation of AML which account between 2.5-9.1% among AML presentations.[6] Extramedullary site may involve tumorous accumulations within soft tissues, bones and rarely central nervous system.[6] The tumour affects the active haematopoiesis sites

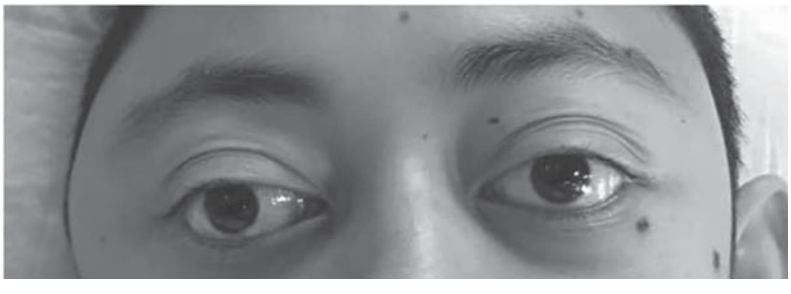

Figure 1: Bilateral proptosis with right temporal orbital region swelling.

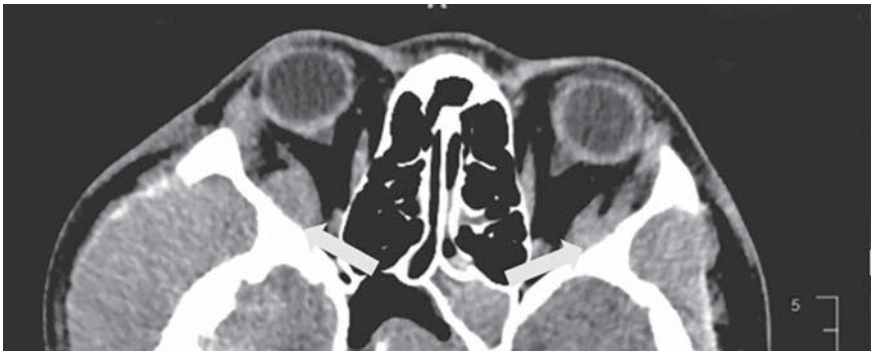

Figure 2: Computed tomography scan showing hyperdense lesion at bilateral extraconal spaces causing displacement and stretching of lateral recti muscles.

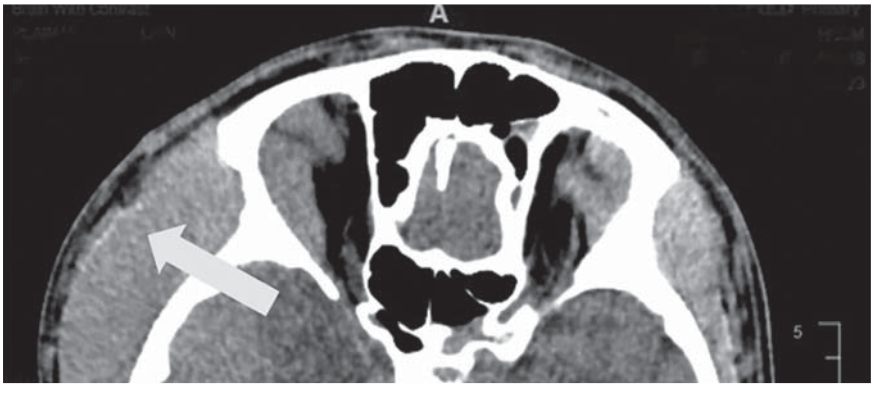

Figure 3: Computed tomography scan showing large hyperdense soft tissue swelling at right temporal orbital region.

for example the skull, orbit, paranasal sinuses, spine, ribs, sacrum and sternum.[3] Ocular manifestations is commonly observed among myeloid leukemia as compared to the lymphoid leukemia patients.[9, 10]

The incidence of the disease can occur between infancy to old age group but more commonly among children and young adult.[2, 3, 4, 5] Previous studies showed more male to female preponderance.[3, 4] The study done by Murthy et al., reported that a total of 12 patients with AML, all of them presented with proptosis; 8 patients with unilateral and 4 patients involved bilateral eyes.[3]

The diagnosis of AML can be challenging as the onset of orbital granulocytic sarcoma can precede the systemic bone marrow leukemia but is rare.[5] More commonly it can occur concomitantly or after the onset of systemic leukemia. In our case, the patient was a young adult who presented with bilateral eye proptosis and right temporal orbital region swelling. Differential diagnosis for bilateral proptosis include thyroid eye disease, orbital myositis, and cavernous sinus thrombosis that should be considered in this patient. He was diagnosed with AML type M2/M4 based on the full blood count, full blood picture and also bone marrow aspiration and trephine biopsy. In the absence of systemic leukemia, a tissue biopsy should be very helpful to obtain the diagnosis although the poorly differentiated granulocytic sarcoma could closely resemble large-cell non-Hodgkin lymphoma when the cells are myeloperoxidase-negative and weakly stained.[6]

Our patient is also presented with bilateral

lower limbs weakness with power 0-1/5, reducing sensation from T6 level and below, hyporeflexia and also bladder and bowel dysfunction. His anal tone was absence and bulbocavernosus reflex was present. Paraplegia is not a usual presentation of AML. It was reported that the prevalence of spinal extramedullary presentation among myeloid leukemia to be 1.0%.[11] In the present case, initially it was thought that the bilateral lower limb presentation with bowel and bladder presentation were due to leukemic infiltrations to the spine. However, MRI thoracolumbar did not show any significant findings pointing towards our patient problem. Most probable explanation for this could be due to paraneoplastic syndrome related to AML presented with cord compression. MRI could be used to detect granulocytic sarcoma with CNS involvement. The usage of Fluorodeoxyglucose (FDG)-positron emission tomography (PET) rather than MRI is best to detect spinal granulocytic sarcoma as FDG-PET is more sensitive in detecting the malignant tumours with increased glucose metabolism which commonly used in the treatment of radiotherapy to see the course of the treatment.[11]

With the advent of technology and improvement in medicine, there are prognostic genetic markers namely the molecular mutations and genetic aberrations to evaluate acute leukemia and assessing its prognosis. However, for granulocytic sarcoma per se, there is still limited information regarding the role of genetic mutations. Nucleophosmin gene mutation in normal karyotype carries a favourable prognosis while Feline McDonough Sarcoma (FMS)-like tyrosine kinase 3 (FLT3) gene mutations carry an unfavourable prognosis.[6] The prognostic significance of whether the occurrence of AML with extramedullary involvement confer a worse prognosis is still limited in data. The 5-year survival rates for patients with granulocytic sarcoma range between 20-30%, which are similar to AML in general.[6]

Based on the study done by Ouyang et al., CD56 is regarded as a worse prognostic factor which was positive in our patient and most probably the reason for worsening of his condition. But generally, AML is prognostically classified based on cytogenetics and molecular study.[12] For our patient, the cytogenetic features were inconclusive, and the molecular study was not performed.

Treatment approach for granulocytic sarcoma depends on whether the granulocytic sarcoma develops at initial diagnosis or relapse and depends on the extent of granulocytic sarcoma involvement. The treatment includes intensive or reinduction chemotherapy with consideration of radiotherapy and haematopoietic cell transplantation.[6]

Conclusion

The role of an ophthalmologist is vital when dealing with this type of patient because they might present first in an ophthalmology clinic due to orbital symptoms. Ocular or orbital symptoms, for instance, proptosis are usually more apparent than any other systemic manifestation which may be trivial to certain patients. High index of suspicion should be made to rule out acute leukemia as one of the differential diagnosis and non-invasive diagnostic tests such as venipuncture could be done first and should be complemented with bone marrow aspiration and trephination rather than biopsy first of the granulocytic sarcoma tissue.

Conflict of interest

We declare that we have no conflict of interest.

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