Acute unilateral third nerve palsy as an early manifestation of central nervous system relapse in a patient with acute myeloid leukemia

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ABSTRACT

تتراوح النسبة المسجلة لنظام الأعصاب المركزية (CNS) على سرطان النخاع الشوكي (AML) مابين أقل من 10 إلى 30%. يعتبر الشلل للعصب الثالث الجانب الحاد بداية غير طبيعيه لظهور تلك الحاله. يصف الباحثون ظهور أعراض نادرة في العين للانتكاس في نظام الاعصاب المركزية (CNS) عند مريض يبلغ من العمر 25 عام والذي يعاني من سرطان النخاع الشوكي (AML) وقد خضع لزراعة الخلايا الجذ عيه ويبرهنون على فعالية التصوير بالرنين المغناطيسي MRI للتشخيص المبكر.

The reported incidence of central nervous system (CNS) involvement by acute myeloid leukemia (AML) ranges widely from less than 10-30%. Acute unilateral third nerve palsy is an unusual first manifestation of such an event. We describe a rare ophthalmologic manifestation of CNS relapse in a 25-year-old patient with AML who had undergone allogeneic stem cell transplant, and demonstrate the value of MRI in the early diagnosis.

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Isolated central nervous system (CNS) relapse following allogeneic stem cell transplant (allo-SCT) is rare, and poses a major therapeutic obstacle to cure acute myeloid leukemia (AML).[1,2] We hereby present a case of acute unilateral third nerve palsy as an early and isolated manifestation of CNS relapse in AML and demonstrate the value of magnetic resonance imaging (MRI) in the early diagnosis.

Case Reports. A 25-year-old male patient with a diagnosis of AML presented to the eye clinic with a 5 day history of inability to move his left eye, and diplopia in right lateral gaze. Seven months prior to presentation, the patient had undergone allo-SCT, and since then the patient was in remission. Ophthalmic examination of the right eye was unremarkable. Examination of the left eye showed absent adduction of the eyeball (**Figure 1a**), partial ptosis of the upper eyelid in the primary position (**Figure 1b**), and normal abduction (**Figure 1c**). Elevation of the eyeball was absent (**Figure 1d**), and depression was moderately reduced (**Figure 1e**). The pupil was spared with normal size, and normal reaction to light. The patient maintained an intact corneal reflex, and normal looking optic disc. Neurological examination revealed no neurological deficits apart from the above-mentioned features of left third cranial nerve palsy. Laboratory studies including serum glucose, electrolytes, liver, and renal function tests were normal. Blood film showed blast cells compatible with AML. Bone marrow examination was carried out and reported as normal. The MRI examination with intravenous gadolinium-diethylenetriamine pentaacetic acid of the orbit and brain at the level of the prepontine cistern (**Figure 2a**), and cavernous sinus (**Figure 2b**), showed enlargement and enhancement of the cisternal, and the cavernous portion of the left third cranial nerve. There was no meningeal enhancement or parenchymal brain lesion. Diagnostic lumbar puncture showed invasion of cerebrospinal fluid with a large number of myeloid precursors. A diagnosis of CNS relapse was made, and treatment with intrathecal methotrexate was initiated.

Discussion. Extramedullary relapse without involvement of the bone marrow in patients with AML within one year of allo-SCT is rare when compared to medullary relapse,[2] and is known to be a very poor prognostic factor. Leukemic infiltration of the CNS may produce a wide variety of signs and symptoms that include cranial nerve deficits, symptoms of CNS

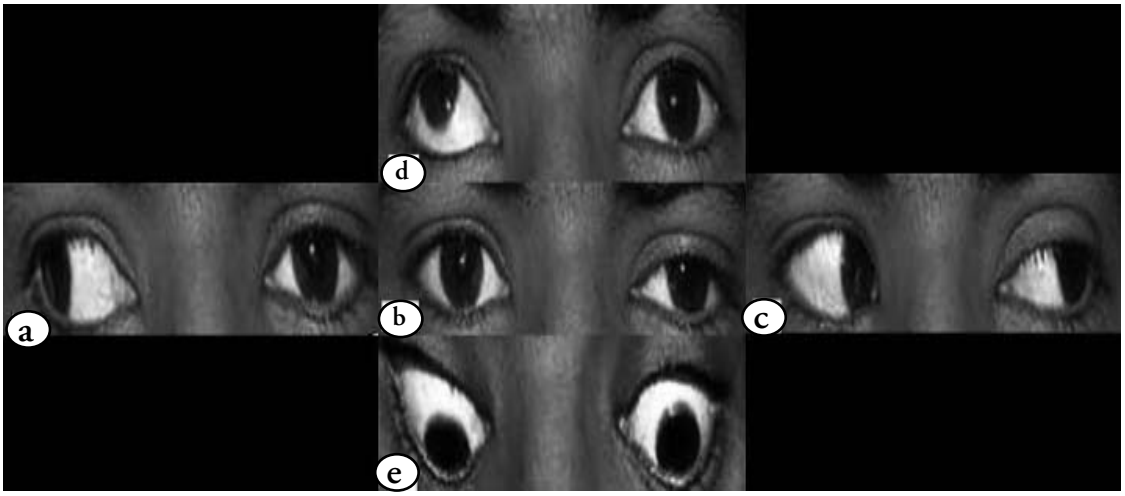

Figure 1 - Photos of both eyes on presentation showing the left eye **a)** absent adduction, **b)** moderate ptosis, **c)** normal abduction, **d)** absent elevation, and **e)** restricted depression.

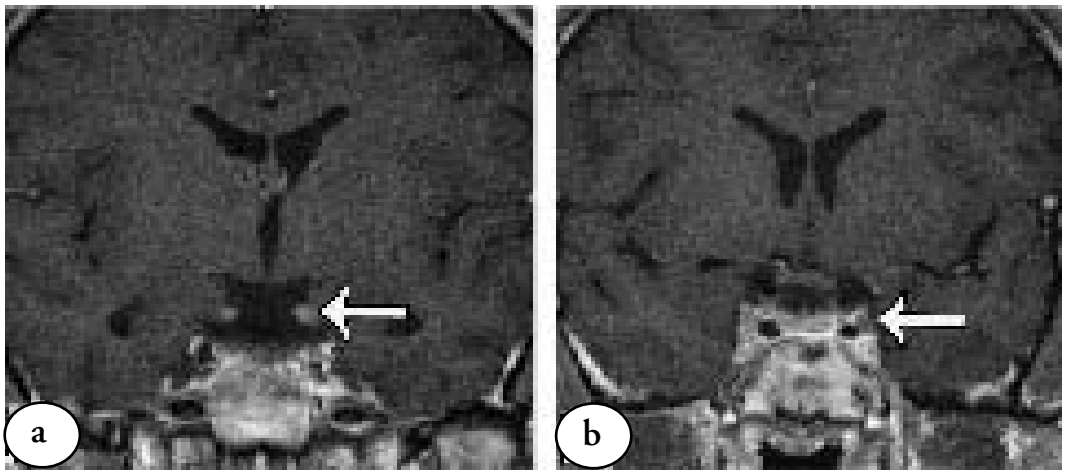

Figure 2 - Coronal enhanced T1 weighted images at level of **a)** prepontine cistern and **b)** cavernous sinus show thickening and enhancement of the prepontine, and the cavernous parts of the left oculomotor nerve (white arrow). The optic nerves are normal. The internal carotid arteries have normal diameter and flow void.

hemorrhage (seizure, altered mental status, headache, and neurological deficits), and symptoms of raised intracranial pressure (severe headache, nausea, and vomiting). Some patients with CNS leukemia have no clinical manifestations with CNS involvement being discovered at the time of the diagnostic lumbar puncture. The most common cranial nerves affected by leukemia are the facial nerves, and those controlling the eye muscles. Oculomotor nerve palsy (ONP) can be consequent to a number of different conditions, the most common of which is ischemic vasculopathy. Another important cause is a compression of the nerve by an expanding aneurysm of the posterior communicating, or basilar artery. Aneurysm should be ruled out in any patient with third nerve palsy involving the pupil, regardless of the patient's past medical history.[3] Magnetic resonance angiography provides information on vascular flow patterns, but might be inadequate to rule out aneurysm. Cerebral angiography is the definite test for intracranial aneurysms impinging on the oculomotor cranial nerve. Infectious, inflammatory, neoplastic, and metastatic lesions should also be kept in mind, as a possible cause

of ONP.[3,4] Isolated leukemic infiltration of the third cranial nerve as a first manifestation of extra medullary relapse of AML is rare. The ONP in a patient with leukemia can be due to infiltration of the cranial nerve by leukemic cells, or involvement of the brain stem. It has also been rarely reported to occur due to subarachnoid hemorrhage, and hemorrhage into the nerve.[5]

The MRI is the imaging method of choice in patients with cranial nerve palsies, particularly in patients with extra cranial solid, and hematological malignancies. Although most cranial nerves may be difficult to visualize with MRI scanning due to their small diameters, and complex anatomic course, the oculomotor cranial nerves can be visualized, and reliably assessed by standard MRI sequences, not only in the subarachnoid space, and cavernous sinus, but also in the orbit.[6] Rapid developments in the MRI have enabled evaluation of the entire course of normal, as well as abnormality in the cranial nerves. Indeed, imaging has been dramatically improved with the use of high resolution MRI.[7] This case highlights the value of MRI in the early detection, and accurate evaluation of cranial nerve lesions, thereby aiding in the clinical diagnosis, treatment, and prognosis assessment of patients with CNS relapse in leukemia.

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