Case Report

Cranial Nerve Palsies as Initial Presentation of Acute Lymphoblastic Leukemia – A Case Report

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ABSTRACT

The clinical manifestations of acute leukemia are diverse and can range from asymptomatic to life-threatening Complications.[1] Cranial nerve palsies as a presenting feature of this disease is relatively rare. It can be attributed to leukemic infiltration of cranial nerves or the development of cranial nerve palsies secondary to intracranial complications such as subdural hematoma. Our patient presented with 4-month history of progressively worsening eye and visual disturbances. On examination, there was bilateral ptosis and proptosis. The right pupil was dilated and non-responsive to light with complete blindness. Left pupil had a sluggish response to light and had decreased visual acuity. There was 6th nerve palsy on left side and bilateral sensorineural hearing loss. Bone marrow biopsy showed Acute Lymphoblastic Leukemia. He was diagnosed with Acute Lymphoblastic Leukemia with brain (CNS) infiltration causing 2nd, 3rd, 6th and 8th cranial nerve palsies.

Key Words: Acute Lymphoblastic Leukemia, Cranial Nerve Palsy, Bone Marrow Biopsy.

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INTRODUCTION

Acute leukemia is a hematological malignancy characterized by the proliferation of immature blood cells in bone marrow.[1] Clinical manifestations of acute leukemia are diverse and can range from asymptomatic to life-threatening complications.[2] CNS complications of Leukemia may be due to leukemic cell infiltration of brain parenchyma, meninges or cranial vasculature.[3] Infections, vascular disorders, leukoencephalopathy, inflammatory demyelinating polyradiculo-neuropathy and secondary tumors may occur as a result of treatment complications.[3,4] Diagnosis of CNS lesions is challenging because the clinical presentation is variable depending on the site involved and mechanism of involvement as there is no pathognomonic sign of CNS leukemia on imaging.[5,6] Gold standard of diagnosis remains brain biopsy and histo-pathological confirmation which is clinically difficult in routine practice.[6]

Cranial nerve palsies as a presenting feature are relatively rare in acute leukemia and their occurrence can be attributed to leukemic infiltration, infiltration of cranial nerves or the development of cranial nerve palsies secondary to intracranial complications such as subdural hematoma. A case of acute Lymphoblastic leukemia is presented here with initial presentation in the form of cranial nerve palsies.

CASE PRESENTATION

A 16-year-old previously healthy young male presented with 4-month history of progressively worsening eye and visual disturbances characterized by protrusion of both eyeballs bilateral drooping of upper eyelids and diminished vision. He had consulted various local general physicians and had undergone non-conclusive work-up. On exploration, there was

history of low-grade intermittent fever for the last 6 months, generalized malaise, fatigue and body aches. There was no history of weight loss, night sweats, altered bowel habits, joint pains or any palpable lumps. He was a student of 10^{th} grade and denied sexual contact. He did not smoke or use illicit drugs.

On examination, there was bilateral ptosis and proptosis with a small left-sided sub-conjunctival hemorrhage as shown in Figure 1. Right pupil was dilated and non-responsive to light. The vision in right eye was no perception of light. Left pupil had a sluggish response to light and had reduced visual acuity. On fundoscopy, there was bilateral papilledema and retinal hemorrhages. There was 6^{th} nerve palsy on left side and bilateral sensorineural hearing loss. The patient was conscious, followed commands and had normal gait. There was no focal sensory, motor or cerebellar deficit. His respiratory and cardiac examination was normal. No viscera were palpable on abdominal examination. No lymph nodes were palpable in cervical, axillary or inguinal regions.

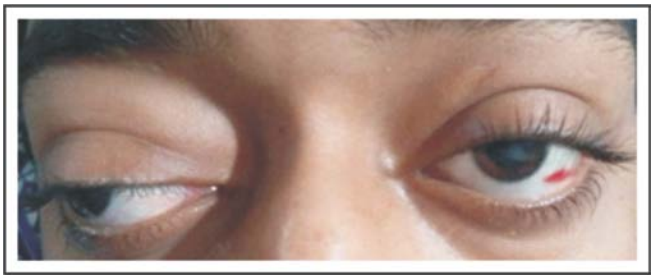

Figure 1: Bilateral ptosis and proptosis.

On investigation, Hemoglobin was 10.2 g/dL, total leucocyte count was 18.6×10^9/L and platelets were 128×10^9/L. ESR was raised (90 mm/hour). Urine analysis, liver function tests and renal function tests were normal. Serology for Treponema, Hepatitis B, C and HIV were negative. Blood and urine cultures were negative and chest X-ray was normal. Non-contrast MRI scan of brain showed left subdural hematoma in temporo-parietal region as shown in Figure 2. Lumbar puncture was done after taking high-risk consent. CSF analysis showed glucose 45 mg/dl, protein 33.8 mg/dl, WBC 100 per HPF with 75% neutrophils.

The patient was started empirically on intravenous Ceftriaxone 2g and Vancomycin 1g twice daily, Dexamethasone 8mg intravenous three times a day, on lines of bacterial meningitis. Anti-Tuberculous Therapy was also added on clinical suspicion of CNS tuberculosis. However, Giemsa staining, Acid-fast bacillus staining, malignant cell cytology, Gene Xpert-PCR for MTB and Pyogenic culture were negative on CSF.

During the hospital stay, he started to develop multiple petechiae and ecchymosis as shown in Figure 3. His serial CBC demonstrated a fall in hemoglobin and platelet count with a rise in TLC. A peripheral smear demonstrated 45% blast cells. Repeat blood and urine cultures were negative and normal PT/APTT. There was no evidence of hemolysis. A bone marrow biopsy was done which showed Acute Lymphoblastic Leukemia. Echocardiography and CT scan of chest, abdomen and pelvis were within normal limits. He was diagnosed was Acute Lymphoblastic Leukemia with CNS infiltration causing 2^{nd}, 3^{rd}, 6^{th} and 8^{th} cranial nerve palsies.

Oncologist was consulted who planned to start Vincristine-based chemotherapy regimen. Unfortunately, patient's condition deteriorated. Multiple Packed cell volume and platelet infusions were given to stabilize the patient. Imipenem 1 gm intravenous twice daily was added to cover for

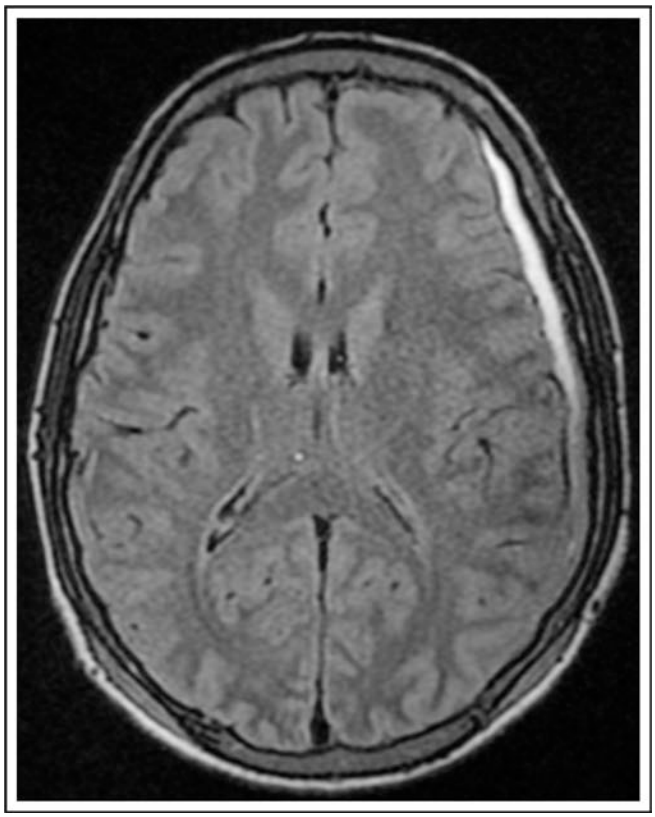

Figure 2: FLAIR sequence image of MRI scan showing subdural hematoma in the left temporoparietal region.

Neutropenia. However, he succumbed to his illness before chemotherapy could be initiated.

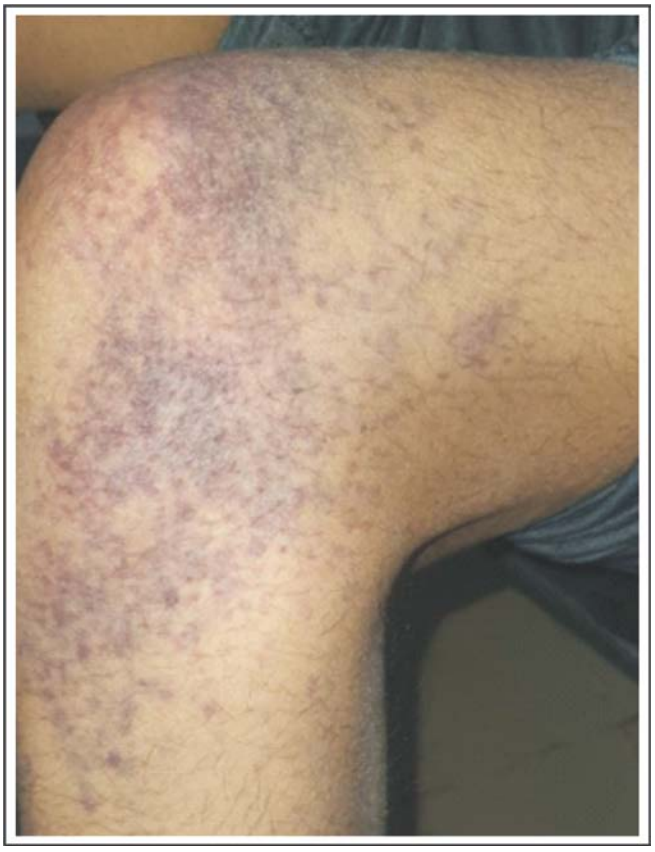

Figure 3: Petechiae and Ecchymosis over the legs.

DISCUSSION

Clinical manifestations of acute leukemia are diverse and its outcome has improved in recent years due to advancements in new therapies and better supportive care.[3]However, a major cause of disability and mortality in leukemia is CNS involvement which is a marker of poor prognosis.[7] Treatment directed specifically for CNS infiltration helps to improve outcome in leukemic patients. Differential diagnosis considered in a patient with CNS leukemia include CNS infections due to immunosuppression, meningitis, cerebral infarction, intra-cranial hemorrhage and treatment associated neuro-degeneration and demyelination.[8] It is a diagnostic challenge to identify the precise nature of CNS in leukemic patients as there is no pathognomonic sign on imaging. CNS involvement in leukemia may therefore be misdiagnosed in up to 75% patients, which leads to delay in treatment.[9] Gold standard of diagnosis remains brain biopsy and histo-pathological confirmation which is clinically difficult in routine practice.[6] Thus obtaining detailed medical history and examination followed by appropriate blood and bone marrow testing, CSF analysis and brain imaging can aid to reach at a correct diagnosis timely so that unnecessary treatment of misdiagnosis may be avoided.[10]

Our patient had 2nd, 3rd, 6th and 8th cranial nerve palsies without overt signs of leukemia at presentation. He was initially being worked-up for a neurologic cause but during the hospital stay he developed anemia, thrombocytopenia and raised TLC with 45% blast cells which ultimately lead to confirmation of diagnosis of Acute Lymphoblastic Leukemia on bone marrow biopsy.

In conclusion, Acute Lymphoblastic Leukemia presenting with multiple cranial nerve palsies as an initial manifestation is rare. CNS involvement is a poor prognostic sign in leukemia. Therefore, early recognition and treatment of acute lymphoblastic leukemia are crucial to improve prognosis and reduce mortality.

Conflict of Interest: Authors declared no conflict of interest.

Consent: Detailed informed consent was taken from the patient's attendants.

REFERENCES

1. **Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS, et al.** CONCORD Working Group. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet, 2015;**385(9972):**977-1010. Doi: 10.1016/S0140-6736(14)62038-9.
2. **Sabir K, Butt NI, Akram N, Ashfaq F, Sajid J, Bano K.** Prevalence of FLT-3 mutation in acute myeloid leukaemia. J Ayub Med Coll. 2021;**33(3):**399–402. PMID: 34487645.
3. **Walker RW.** Neurologic complications of leukemia. Neurol Clin. 1991;**9(4):**989-999.
4. **Faraci M, Lanino E, Dini G, Fondelli MP, Morreale G, Dallorso S, et al.** Severe neurologic complications after hematopoietic stem cell transplantation in children. Neurology, 2002;**59(12):**1895-1904. Doi: 10.1212/01.wnl.0000036608.42104.b9.

5. **Liu J, Wang Y, Sun X, Liu S, Yu Z, Ji N, et al.** Lesions of the central nervous system in leukemia: Pathological and magnetic resonance imaging features at presentation in 14 patients. Oncol Lett. 2017;**14(6):**8162-8170. Doi: 10.3892/ol.2017.7192.
6. **Pui CH, Thiel E.** Central nervous system disease in hematologic malignancies: historical perspective and practical applications. Semin Oncol. 2009;**36(4 Suppl 2):**S2-S16. Doi: 10.1053/j.seminoncol.2009.05.002.
7. **Sung SH, Jang IS.** Isolated central nervous system relapse of acute lymphoblastic leukemia. Brain Tumor Res Treat. 2014;**2(2):**114-118. Doi: 10.14791/btrt.2014.2.2.114.
8. **Ball WS Jr, Prenger EC, Ballard ET.** Neurotoxicity of radio/chemotherapy in children: pathologic and MR correlation. Am J Neuroradiol. 1992;**13(2):**761-776.
9. **Kumar R, Nijalingappa S, Grainger J, Ismayl O.** Acute disseminated encephalomyelitis mimicking late CNS relapse of acute lymphoblastic leukaemia: case report. J Med Case Rep. 2007;**1:**4. Doi: 10.1186/1752-1947-1-4.
10. **Göçmen S, Kutlay M, Erikçi A, Atabey C, Sayan O, Haholu A.** Central nervous system involvement of T-cell prolymphocytic leukemia diagnosed with stereotactic brain biopsy: case report. Turk J Haematol. 2014;**31(1):**75-78. Doi: 10.4274/Tjh.2012.0028.

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