

# Unusual Presentation of Childhood Acute Lymphocytic Leukemia Initially Presented As a Frontal Headache: Case Report

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## ABSTRACT

A 3-year-old female patient was presented to Ain Shams University Pediatric Hospital (Egypt) with persistent frontal headache. There were no localizing symptoms and virology studies were negative. The child's visual acuity decreased gradually. After extensive medical workup to exclude the common causes of childhood headaches, the patient was diagnosed with acute lymphoblastic leukemia (ALL) depending on the flowcytometric analysis of the Cerebrospinal fluid (CSF) sample; as the blast cell count in both complete blood count (CBC) and bone marrow (BM) samples were < 20% being decreased due to corticosteroid therapy patient already received initially in an attempt to lower her intracranial tension before her definite diagnosis. The patient received induction, consolidation chemotherapy, and central nervous system (CNS) treatment with intrathecal methotrexate and cranial irradiation. She developed ALL relapse after her first remission, she presented with intracranial hypertension and optic nerve infiltration by leukemic cells followed by systemic relapse. Subsequent surgical intervention, salvage chemoradiotherapy, and further allogeneic stem cell transplantation did not induce disease remission or restore her visual acuity. The delayed initial diagnosis due to the atypical initial presentation of the case, was associated with poor outcome, and the patient died almost one year after her initial diagnosis.

**Keywords:** Headache, Intracranial hypertension, Acute lymphocytic leukemia, Papilledema

## INTRODUCTION

Acute lymphoblastic leukemia (ALL) is primarily a disease in children <sup>[1]</sup>. Less than 10% of patients have CNS involvement at the time of their initial ALL diagnosis, but 30–60% of patients who achieve complete remission later experience a CNS recurrence if they do not get CNS prophylaxis <sup>[2]</sup>.

Over 80% of cases of ALL, the most common childhood cancer, are treated with current chemotherapy <sup>[3]</sup>. The advancements in CNS-directed systemic and intrathecal therapy are associated with a remarkable decline in CNS relapse in children diagnosed with ALL <sup>[4,5]</sup>. Even though rapid and aggressive chemotherapy, radiation therapy, and supportive care are started right once, isolated optic nerve involvement is even more uncommon and typically associated with a poor outcome <sup>[6-11]</sup>.

## CASE PRESENTATION

3-year-old female child, presented with a frontal headache. The headache was persistent and progressive for more than one month without improvement. Extensive workup was done for her diagnosis but the results were not remarkable for definite cause. Vomiting, blurring of vision, and facial palsy on the left side were the following complaints.

Fundal examination was done and it was positive for papilledema, lumbar puncture for CSF tapping was conducted to relieve the increased intracranial tension. The child hasn't had a fever since she began her first symptoms.

Magnetic resonance imaging (MRI), Magnetic resonance angiography (MRA), and Magnetic resonance venography (MRV) brain; were all ordered to exclude local CNS pathology. They revealed intracranial venous thrombosis, which became the suspected cause for her increasing progressive intracranial hypertension (ICT) and the papilledema worsen (grade four on the left side and grade one on the right-side).

The hematology profile; HB electrophoresis, iron profile, protein C and S, factor V Leiden, and prothrombin mutation all were ordered, and all were negative. Family history for thrombosis was also negative. Inflammatory reaction to an unknown cause was suspected, so corticosteroids were started, which resulted in obvious improvement of the child's facial palsy and her general condition, but the intracranial tension was still increasing evident by worsening of the child's vision.

The investigations were done to reach the definite cause. Ten times lumbar punctures under general anesthesia were performed on the patient during her first month from the primary complaint, almost every three days, and each time the CSF cell count was high (around 2000 cells/cmm<sup>3</sup> with repeated negative culture results). Cell type was mixed Polymorphonuclear neutrophils (PMN) and lymphocytes (lymphocytes were predominant).

CBC showed an absolute total leukocyte count (TLC) of 18000, absolute neutrophil count (ANC) of 6000, absolute lymphocyte count (ALC) of 10000, absolute monocyte count (AMC) of 2000/mm<sup>3</sup>, moderate anemia

(Hb 8 g/100 ml), and normal platelet count (266/mm<sup>3</sup>). Viral infection was suspected due to an increase in the ALC, especially herpes simplex (HSV), so HSV polymerase chain reaction (PCR) was ordered but its result was negative too. Her visual acuity dropped, and loss of vision was the awaiting result if she was not treated rapidly and if there was no definite cause could be reached.

At the microbiology lab, the resident doctor examined the Lishman-stained film of her CSF sample meticulously, large cells with sandy open chromatin were evident and it was confirmed with the hematology staff member. Immature cells were reported and notified immediately to the pediatric team (Figures 1 and 2). Peripheral blood smear and bone marrow examination were recommended which revealed 12% blast cells only.

Lymphoma was suspected due to the unequal presentation of the papilledema and blast cells < 20% in BM. Acute leukemia was also suspected but the unequal CNS presentation, and focal infiltration of the left optic nerve (Figure 3), which was evident in MRI brain and blast cells < 20% in BM was going against the diagnosis. Juvenile Chronic myelogenous leukemia (CML) was excluded due to the absence of splenomegaly (one of its major criteria for the diagnosis).

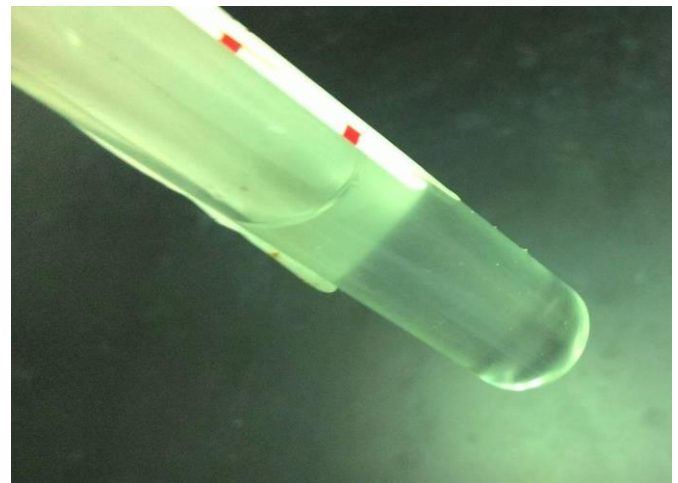
CSF Lishman-stained film was full of immature cells than the peripheral blood and the bone marrow, so the decision was taken to perform flowcytometry and cytogenetic study including T cell rearrangement on the fresh CSF sample rather than BM samples for better assessment and definite diagnosis. T-cell ALL was documented upon ensuing immunophenotypic studies (positive staining for CD3, CD45 and negative staining for CD19, CD20, TdT, CD1a, and CD30) and cytogenetic studies revealed a chromosomal abnormality supporting ALL diagnosis.

The diagnosis was documented as acute lymphocytic leukemia that was masked by corticosteroid therapy. the child began her chemotherapy cycles and was referred to the Child Cancer Hospital of Egypt (CCH 57357) to complete her medical anticancer regimen.

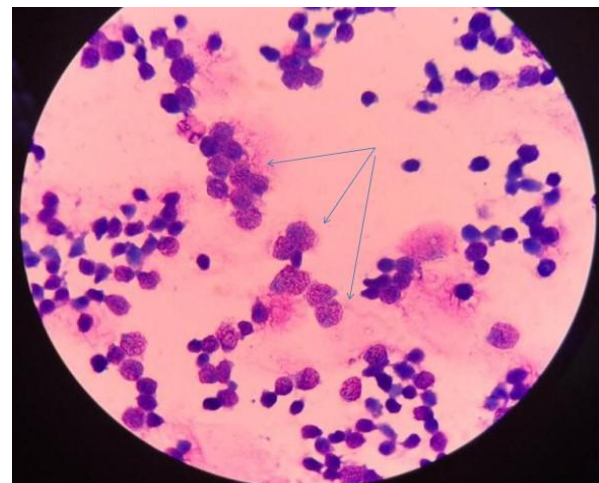
Induction chemotherapy with the conventional protocol (vincristine 1.4 mg/m<sup>2</sup>, daunomycin 60 mg/m<sup>2</sup>, prednisone 70 mg/m<sup>2</sup>, and L-asparaginase 10,000 U/m<sup>2</sup>) was instituted. Subsequent peripheral blood smears and examination of her bone marrow (BM) documented the achievement of complete remission seven weeks after induction chemotherapy. Intrathecal chemotherapy with

methotrexate and cranial irradiation was then administered.

The patient developed a relapse of ALL seven months after remission. At that time, the child presented with ipsilateral vision loss due to isolated optic nerve infiltration by leukemic cells prior to systemic relapse. Subsequent surgical intervention, salvage chemoradiotherapy, and further allogeneic stem cell transplantation did not induce disease remission or restore her visual acuity. The patient died almost one year after her initial diagnosis.

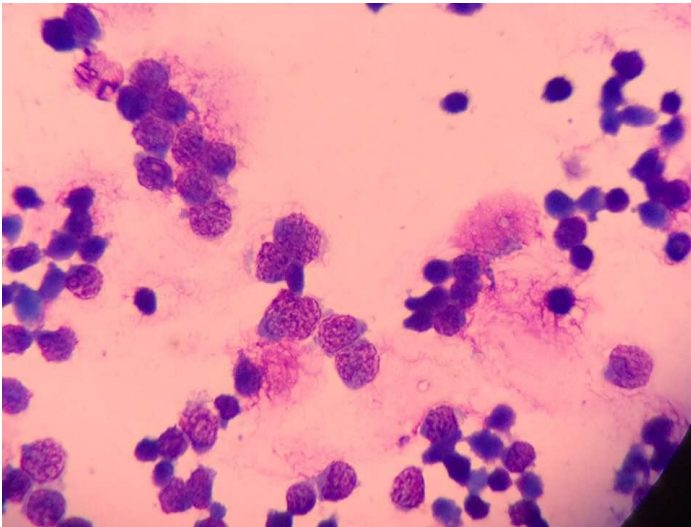


(A)



(B)

**Figure 1:** (A) CSF sample after intrathecal tapping, the sample was colorless with very slight turbidity. (B) Lishman-stained smear from the sample was performed to specify the cell type, it showed mixed cell types.



**Figure 2:** Higher magnification of the cells examined in the CSF sample. the Lishman-stained smear done in the microbiology lab showed large immature cells with open sandy chromatin characterizing acute lymphocytic leukemia in the background of lymphocytes with normal morphology.



**Figure 3:** Axial T2 MRI showing optic nerve infiltration of the left side.

## DISCUSSION

Headache is one of the unusual presentations of leukemias in the pediatric age group, which should be considered and investigated. In practical life, there are many causes of headaches in childhood, and the usual causes are commonly presented but the rare cause, like our presented case (leukemias), should be considered among the differential diagnosis [12].

We described a female child with ALL who presented for the first time with malignant intracranial hypertension being manifested as frontal headache. Her CBC result was misleading as the remarkable increase of

TLC was masked due to corticosteroid therapy that the patient had already received in an initial trial to control the disease. The flow cytometric analysis and immunophenotyping were done on the CSF sample.

Although 70-80 % of children with ALL are cured with modern chemotherapy protocols, 20- 30 % suffer disease relapse, particularly in the CNS after the achievement of disease remission [13]. Thus, to achieve complete remission and avoid recurrence of ALL following conventional induction chemotherapy, intrathecal chemotherapy and cranial irradiation are necessary. However, due to their shielding properties during brain irradiation, the orbital cavity and optic nerve represent possible havens for leukemic relapse following conventional CNS prophylaxis [14]. Furthermore, it is exceedingly uncommon for ocular structures to relapse without systemic or bone marrow involvement [1].

## CONCLUSION

Leukemias generally presents with nonspecific symptoms and signs such as fatigue, bone and muscle pains, malaise, easy bruising, weight loss, and anorexia. Intracranial hypertension can be a part of the initial presentation of leukemia. Treating clinician should be aware of leukemias as a cause of initially presented headache and/or blurred vision to be considered and investigated.

In a patient presented with intracranial hypertension with no identifiable cause, it is reasonable and warranted to perform a complete blood count and advanced hematological workup to investigate for leukemia. Delayed diagnosis in such cases, is associated with optic nerve atrophy, metastasis, and poor prognosis.

In the microbiology labs, the examining microbiologist shouldn't mind only of the microorganisms and infections as the cause of the pathology, many cancer types can be diagnosed for the first time while examining microbiology samples, especially body fluid and pus samples. The resident doctors should be well-trained to differentiate between the normal morphology of the cells and the different abnormal morphologies of the malignant cancer cells to be diagnosed.

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