

Acute Lymphoblastic Leukemia Presenting with Macrocephaly

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Abstract

Background: An eight-month old boy with the history of several admissions due to flu like symptoms was referred to our hospital with bicytopenia and significant growth in his head circumference.

Observation: After several diagnostic measures the biopsy of the bone marrow was taken for the flowcytometry with the suspicion of hematologic malignancy which lead to the diagnosis of T-cell Acute lymphoblastic leukemia (ALL). The patient responded dramatically to the chemotherapeutic regimen.

Conclusion: Although it is rare but macrocephaly can be a presenting symptom of T-cell ALL and this should be considered in differential diagnosis.

Keywords: Macrocephaly; T-cell acute lymphoblastic leukemia; Bicytopenia

Introduction

T-cell ALL is the most prevalent cancer in childhood [1,2]. It can potentially involve various organs of the body such as central nervous system. Cranial nerve abnormalities and rising of the intracranial pressure had been known as a sign of nervous system involvement but reports of macrocephaly are extremely rare especially as an initial manifestation of the T-cell ALL [3-5]. Here we describe an eight-month old boy referred to our clinic with bicytopenia and macrocephaly that was subsequently diagnosed with T-cell ALL and was successfully treated.

Case Presentation

An eight month old boy was referred to our hospital presenting with Bicytopenia and Macrocephaly. He his weight was 9 kg and his height was 68 cm at the time of admission (his birth weight and height were 3 kg and 51 cm, respectively). He had no previous history of admission prior to his referral and had no underlying disease. In a month earlier to his referral he was admitted several times because of diarrhea, vomiting and flu like symptom (tachypnea, stuffy nose, fever and shivering) which lasted for a month and was treated symptomatically. In a period of a month, his head circumference (HC) showed noticeable growth of 4 cm (34.5 cm at the birth; 47 cm at his first visit in his hometown; 51 cm at his admission in Tehran) that was associated with Hydrocephaly, Brain Atrophy and ventricular enlargement without periventricular edema in the CT scan. He was able to hold his head steadily from 3 months old and was able to sit with support from 6 months old but has lost these abilities in the past two months. Lab testing recorded thrombocytopenia (Platelet (PLT)=39000) and anaemia (Hemoglobin (Hb)=7.4). He was referred to our hospital for further evaluation (Figure 1).



Figure 1: An eight month old boy suffering from bicytopenia and macrocephaly.

Vital signs were stable on admission (temperature=36.7°C, Pulse rate=100/min, Respiratory rate=50/min). He had bone tenderness and poor feeding and was so irritable. Anterior fontanelle had an area of 3*5 cm and was not bulged. No lymphadenopathy was palpable. Borders of liver and spleen were detectable 5 cm and 2 cm below the costal margin respectively and Abdominal Ultrasonogram showed liver span of 93 mm and plenic span of 83 mm. He has edema of lower extremities. In neurological examination he was hypotonic with decreased deep tendon reflexes. Ophthalmic evaluation showed no sign consistent with metabolic diseases. Laboratory tests were as following:

White blood cells (WBC)=15.2/mm³, (Lymphocytes=84.4%), Red blood cells (RBC)=2.57/mm³, Hb=7.4 g/dl, mean corpuscular volume=91.8, PLT=72/mm³, Lactate dehydrogenase (LDH)=3390 (U/L), liver function tests (LFT) was within the normal range.

Peripheral blood smear showed 20% of highly atypical cells.

Chest X-ray showed bilateral pleural effusion and increasing interstitial and prebronchial marking.

He underwent a bone marrow aspiration from iliac bone which was a dry tap but it showed many blast congruent with ALL (Acute lymphoblastic leukaemia). Bone marrow biopsy was sent for flow cytometry analysis which showed CD3=68%, CD7=61%, blast=52% compatible with the diagnosis of T-cell ALL. Karyotype analysis for chromosomal shift (t (9,22), t (4,11), t (12,21), t (1,19) was negative).

On microscopic examination bone marrow was mildly hypocellular. Erythroid to myeloid ratio was equal to 1 to 3. Decrease in megacaryocytes was noticeable and more than 80% lymphoblasts were observed.

The cerebrospinal fluid analysis result was as following: WBC=16/mm³, Neutrophil=85%, RBC=12/mm³, Glucose=85 mg/dl, protein=43 mg/dl, LDH=40 u/ml.

With the diagnosis of T-cell ALL, the induction chemotherapeutic regimen started. He received 3 session of intrathecal chemotherapy with (5 mg Methotaxate, 25 mg Cytosar, 10 mg Hydrocortisone) along with IV injection of 6 mg Adriamycin and 0.3 mg vincristine. He also received systemic Dexamethasone which was changed to oral prednisolone (5 mg TDS) afterward.

2 weeks after his admission his HC subsided back to 48 cm. The hepatosplenomegaly was not detectable. And his general condition was back to normal. He was discharged from the hospital and the chemotherapy sessions were continued afterward.

Discussion

ALL is the most prevalent cancer in childhood and it is considered as the leading cause of death due to cancer before age twenty [1,2,6]. There is an increment in the incidence rate of ALL between years 1975 and 2010 with annual percent changes equal to 0.7% [6]. Accelerated fetal growth, high birth weight, Down syndrome, certain genetic syndromes, congenital immunodeficiency diseases and few environmental factors such as parental smoking and maternal exposure to paint were found to be associated ALL and childhood leukemia [6,7]. Surprisingly, early life exposure to infection showed to be protective against ALL [8] which may rationalize why ALL is more common in industrialized countries [9].

Introduction of new therapeutic methods have led to improvement in the survival rate up to 90% [1,2]. Mortality rate due to ALL has the greatest decline compared to other childhood cancers (average annual percent change was -3.1% during 1988 to 2010) [6]. But still ALL remains as a main cause of death due to cancer in young individuals especially in low income countries where survival rate for ALL is about 50% [2].

Symptoms are either related to decrease in blood components or leukemic infiltration of body organs such as liver and spleen. Central nervous system involvement is not a common manifestation of ALL (2-5%) and comparing to B-cell ALL, it is more frequently seen in T-cell ALL [10]. It may manifest with increased intracranial pressure or rarely with cranial nerve abnormalities [3-5,11]. Rocha et al. [12] reviewed 28 cases of different subtypes of lymphoma presented with cranial and skull involvement which were mostly older than 60 years old. As far as we reviewed the literature, macrocephaly was rarely

reported to be the presenting symptom of T-cell ALL at the onset of the disease. Jaing et al. [13] reported a 2 years old girl presenting with anemia and macrocephaly due to epidural mass, who eventually confirmed to be T-cell ALL. Mondal et al. [14] described a 3 years old boy with macrocephaly and prolonged fever who was subsequently diagnosed with acute promyelocytic leukemia.

Our case was presented with prolonged nonspecific flu like symptoms and gradual rise in head circumference during the course of the disease. No sign of mass lesion was observed in the brain CT scan prior to the admission. After the diagnosis of T-cell ALL he responded dramatically to chemotherapeutic protocol.

Conclusion

Although macrocephaly is rare among leukemic patients but when it accompanies with systemic manifestation like anemia and fever it merits further evaluation regarding underlying hematologic malignancies. Since ALL may manifest only with nonspecific features; a high index of suspicion is required to detect those cases of T-cell ALL which present with rare symptoms like macrocephaly.

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