

Infant Acute Lymphoblastic Leukemia with Atypical Presentation

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ABSTRACT

Infant leukemia is a very rare disease and consists of 5% of all childhood leukemias. Infant leukemia usually presents with high leukocyte counts and numerous extra-hematological features including central nervous system and skin involvement. Herein, we report a 1-month-old girl presented with high phenylalanine level in national newborn screening program for phenylketonuria; and subsequently diagnosed to have acute lymphoblastic leukemia.

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INTRODUCTION

Acute leukemia is the most frequent cancer in childhood (33%) and less than 5% of cases occur in infancy period [1]. Infant leukemia differs from the rest of the childhood leukemias because it usually presents with aggressive features, including high leukocyte counts, hepatosplenomegaly, central nervous system (CNS) involvement, and higher rates of leukemia cutis development [2]. Physical examination is very important because most of the infants are asymptomatic.

Herein, we report a 1-month-old girl presented with high phenylalanine level detected in national newborn screening program for phenylketonuria (PKU); diagnosed as infant acute lymphoblastic leukemia (ALL) after admission to our hospital for PKU evaluation.

CASE PRESENTATION

A 1-month-old girl was admitted to our hospital because of a high phenylalanine level detected in

national screening program for PKU. The medical history revealed that she was born as the first child of a healthy couple after 38 week of gestation. The parents have been called and referred to a hospital for the high phenylalanine level detected in the national screening program. Phenylalanine levels were found to be 2,1 mg/dL and 2,5 mg/dL (upper reference range: 2 mg/dL) in the two heel-prick blood samples; respectively. At presentation, her blood phenylalanine level was measured as 1,2 mg/dl (normal). This was consistent with resolved transient hyperphenylalaninemia of the newborn and PKU was excluded. When she admitted to our hospital since the physical examination revealed hepatosplenomegaly and pallor, complete blood count was ordered. Complete blood count revealed that hemoglobin (Hb) level was 8.8 gr/dL, white blood cell count (WBC) 523900/ mm³, and platelet (PLT) count 8000/mm³. Patient was referred to hematology department and peripheral blood smear revealed abundant lymphoblasts. Flow cytometric analysis was compatible with CALLA (-) pre-B cell ALL. Alkaline hydration and rasburicase treatment were started. Leucopheresis has been performed for once. Interfant 2006 chemotherapy protocol was initiated. Cytogenetic studies revealed that t(9;22), t(4;11), t(12;21), and t(1;19) were negative. At the 8th day of prednisolone treatment, the patient was diagnosed as prednisolone poor responder (PPR). At the 15th day of induction chemotherapy; bone marrow aspiration smear showed 17% blasts. At the 33rd day of induction chemotherapy; bone marrow revealed remission morphologically. The patient is currently ongoing Interfant 2006 protocol and in remission.

DISCUSSION

Infant ALL is a rare type of leukemia. Despite improved survival rates are achieved in the treatment of childhood ALL, infants with ALL still have poor prognosis. The 4-year event free survival (EFS) rate has been reported as 47% in Interfant-99 protocol [3]; while long-term EFS rates have been reported to be 85% in recent trials for childhood ALL [4,5].

Phenylketonuria is an inborn error of metabolism usually caused by deficiency of phenylalanine hydroxylase enzyme, which results in increased levels of phenylalanine. The occurrence of increased levels of blood phenylalanine after therapeutic

administration of folate analogues has been occasionally reported and attributed to the inhibition of dihydropteridine reductase, an enzyme maintaining the cofactor of phenylalanine hydroxylase in its active tetrahydrogenated form (tetrahydrobiopterin) [6]. Wang et al. reported unexpectedly elevated phenylalanine levels in a PKU patient when he was diagnosed as ALL and Patiroglu et al. reported elevated phenylalanine levels in a PKU patient when he was diagnosed to have AML [7,8]. In the English literature; these are the only two cases with the diagnosis of PKU who have high phenylalanine levels when they diagnosed as acute leukemia. However, these two patients had been followed up with the diagnosis of PKU while they were diagnosed as acute leukemia.

Transient hyperphenylalaninemia of the newborn is a common cause of abnormal newborn screening results. Low birth weight or premature infants or infants who received parenteral feedings are at increased risk for developing transient hyperphenylalaninemia. Transient hyperphenylalaninemia may also be the presenting feature of other significant disorders, such as classical galactosemia, tyrosinemia type I or citrin deficiency, among others [9]. The transient increase in phenylalanine in our patient may be attributed to increased protein turnover due to ALL.

In referral centers, individuals with normal post-screening confirmatory test results are usually sent home with no history taking or physical examination, since the abnormal screening results were either transient or false positive. However, it was her lucky for our patient to have a transiently elevated phenylalanine level that brought her to doctors' attention. When the physical examination revealed hepatosplenomegaly further evaluation made and she was diagnosed as infant ALL. This case illustrates the importance of physical examination in asymptomatic ALL patients and in all infants with abnormal newborn phenylketonuria screening results, even if confirmatory testing reveals no abnormalities.

CONFLICT of INTEREST STATEMENT

There are no conflicts of interest.

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