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Levetiracetam as Monotherapy for Seizures in a Neonate with Acute Lymphoblastic Leukemia

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Introduction

Congenital acute lymphoblastic leukemia (ALL) is a relatively rare neonatal disorder that is characterized by unique biological features (1) and challenging treatment considerations (2). Extreme leukocytosis and leukemic infiltration of the central nervous system are commonly encountered (1) and may increase the risk for neonatal seizures. Appropriate choice of anticonvulsant therapy with respect to ongoing oncologic treatment is not established. Phenobarbital (often considered first line therapy in neonatal epilepsy) is an inducer of hepatic P450 enzymes, and, thus, may negatively impact chemotherapy efficacy (3), increase the risk for poor neurocognitive outcome, and increase disease mortality. Levetiracetam is a relatively new anticonvulsant agent that is approved as adjunctive therapy for partial-onset seizures in children over 4 years of age. This agent has no known drug interactions and a reduced concern for neurocognitive sequelae (4). Unfortunately, there is limited experience utilizing levetiracetam in neonates (5). We report a neonate with acute lymphoblastic leukemia and seizures who was treated successfully on levetiracetam monotherapy.

Case Study

A male infant was born to a primigravida female at 40 5/7 weeks gestation after an uncomplicated pregnancy. Labor was induced with misoprostol and oxytocin and a cesarean section was performed due to failure to progress. Birth weight was 2544 grams. Mother was Group B streptococcus positive, and pretreated with Ampicillin. APGARs were eight and nine at one and five minutes respectively. He was doing well until the third day of life when he had an episode of left arm and left leg jerking. An electroencephalogram (EEG) was obtained and intermittent, sometimes repetitive sharp wave activity was seen over the left temporal-occipital area and independently over the right occipital area. The infant was loaded with phenobarbital (20mg/kg), and no maintenance antiepileptic medication was initiated. Work-up at that time included an ultrasound of the head that was negative for hemorrhage and a complete blood count that demonstrated a leukocyte count of $78 \times 10^9/L$.

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with approximately 90% blasts. The patient was then transferred to our institution for further evaluation and treatment. Analysis of the peripheral blood revealed a diagnosis of precursor B-cell acute lymphoblastic leukemia (ALL) with a DNA index of 1.0 and an *MLL* gene rearrangement. Methylprednisolone was initiated as chemotherapy treatment. On the day of admission, computed tomography (CT) of the head demonstrated extensive multifocal intraparenchymal hemorrhages in the right posterior frontal, parietal, temporal and left parietal head regions, and significant vasogenic edema with mass effect. A second generalized convulsive seizure was reported that afternoon. The patient was again given phenobarbital 20mg/kg and maintenance phenobarbital was started at 4mg/kg/day. A follow up CT that evening was unchanged from the CT earlier in the day. Subsequent magnetic resonance imaging (MRI) of the brain confirmed extensive multifocal intraparenchymal hemorrhages within the cerebral hemispheres (Figure 1A). An EEG on the eighth day of life was abnormal due to focal voltage attenuation over the right centro-temporal head region and sharp waves seen over the right central and left parietal head regions. Although no clinical seizures were noted, continuation of anticonvulsant therapy was recommended. Phenobarbital was discontinued given the potential interactions with the anticipated chemotherapy regimen (vincristine, daunorubicin, L-asparaginase,) and levetiracetam was initiated orally at 40mg/kg/day, given in two divided doses, and continued as maintenance. Over time the patient's overall clinical status improved and no additional seizures were noted. Currently, the patient is eight months of age, is seizure free, and developmentally appropriate for age while maintained on levetiracetam monotherapy.

Discussion

The use of levetiracetam monotherapy in neonates has not been formally evaluated and experience is limited. We report the successful use of levetiracetam monotherapy after an initial phenobarbital load in a neonate with leukemia and localization-related epilepsy. While this child has remained seizure free on a consistent dose of levetiracetam without the guidance of serum drug levels, we will proactively perform these in future cases secondary to the increased glomerular filtration rate and immaturity of the tubular secretion of the kidneys in this age group. As levetiracetam is primarily excreted by the renal system, the rapid developmental changes in neonates necessitate close observation of serum drug levels and appropriate dose adjustments.

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Figure 1A.
MRI of Brain on 4th Day of Life