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ORIGINAL ARTICLE

Neurometabolic Disorders-Related Early Childhood Epilepsy: A Single-Center Experience in Saudi Arabia

Sarar Mohamed [a,b,*,†], Ebtessam M. El Melegy [b,†], Iman Talaat [b,†], Amany Hosny [b], Khaled K. Abu-Amero [c]

[a] Department of Pediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[b] Department of Pediatrics, Saad Specialist Hospital, Al Khobar, Saudi Arabia
[c] Ophthalmic Genetics Laboratory, Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Saudi Arabia

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Key Words
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Background: Data on the pattern of epilepsy caused by metabolic disorders in the first 2 years of life are limited in developing countries. We aimed to identify the metabolic causes of epilepsy presented in the first 2 years of life and to describe their clinical, radiological, molecular, and electroencephalographic characteristics.
Methods: This retrospective study was conducted between January 2010 and December 2011 at Saad Specialist Hospital (Al Khobar, Saudi Arabia). All patients younger than 2 years at the onset of epilepsy caused by metabolic disorders were reviewed. The International League Against Epilepsy definition was used, and febrile convulsion was excluded.
Results: Of 221 children diagnosed with epilepsy in the first 2 years of life at our hospital, 24 had metabolic diseases. The characteristics of these 24 children included the following: consanguinity in 18 patients (75%), developmental delay in 13 (54%), generalized tonic–clonic seizures in 10 (42%), infantile spasms in four (17%), myoclonic in seven (29%), and focal seizures in three. The diagnosis was confirmed by DNA studies in 17 patients (71%) and enzyme assay in seven (29%). The main diagnoses were peroxisomal disorders ($n = 3$), nonketotic hyperglycinemia ($n = 3$), Menkes disease ($n = 2$), neuronal ceroid lipofuscinosis ($n = 2$), biotinidase deficiency ($n = 2$), and mitochondrial disorder ($n = 2$). The remaining patients had lysosomal storage disease, aminoacidopathy, fatty acid oxidation defects, and organic aciduria. Seizure freedom was achieved in one third of patients in this cohort.

* Corresponding author. Department of Pediatrics, College of Medicine, King Saud University, P.O. Box 2925, Riyadh 11461, Saudi Arabia.
E-mail address: sararmohamed@hotmail.com (S. Mohamed).
† These authors contributed equally.

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Conclusion: Different metabolic disorders were identified in this cohort, which caused different types of epilepsy, especially myoclonic seizures and infantile spasms.

1. Introduction

The burden of epilepsy on children and their families is heavy. This situation becomes worse when devastating disorders such as metabolic diseases cause epilepsy. Epilepsy secondary to metabolic diseases was previously classified as symptomatic epilepsy and is currently part of the structural/metabolic group according to the recent International League Against Epilepsy (ILAE) classification.[1] Metabolic disorders are essentially caused by deficiency of an enzyme or a cofactor. Occasionally, these disorders are caused by a transport defect in which enzymes and cofactors are intact.[2,3] This metabolic derangement results in toxic accumulation of substrates before the enzyme block, defects in energy production, deficiency of products after the block, or a combination of all these metabolic deviations.[4] The biochemical composition of brain is distinct from that of other organs, and there is a complex relationship between the concentration of metabolites and neural function.[5,6] Thus, the brain is often affected by metabolic abnormalities, leading to epilepsy and other neurologic manifestations.[7,8] Some of these inborn errors of metabolism affect the brain cells directly, causing mitochondrial, lysosomal, and peroxisomal disorders. Others affect the brain indirectly by causing hypoglycemia, as in fatty acid oxidation defects.[9,10] During early life, the immature and developing brain often exhibits a greater sensitivity to these disorders compared with other age groups.[11,12] Epileptic seizures that are caused by inborn errors of metabolism may be nonspecific or can often take a typical clinical course.[13,14] Occasionally, specific electroencephalography (EEG) features may point toward the diagnosis early in the course of the disease.[15,16] Epileptic syndromes characterized by distinct seizure semiology and a characteristic EEG pattern may be caused by metabolic disorders, especially when presenting early in infancy.[15,16]

Although epilepsy is one of the leading chronic disorders in children, its metabolic etiology is often difficult to confirm and easy to miss. Therefore, we conducted this study to identify the metabolic causes of epilepsy presented in the first 2 years of life and to describe their clinical, radiological, molecular, and electroencephalographic characteristics.

2. Methods

This was a retrospective study conducted at Saad Specialist Hospital (Al Khobar, Saudi Arabia) from January 2010 to December 2011. This is a large private institute with 600 beds, 100 of which are allocated to children. All pediatric specialized services were available in this institute including services for neurologic and metabolic diseases. We reviewed all patients younger than 2 years who came to our institute with newly diagnosed epilepsy secondary to metabolic disorders. These patients were identified from the medical records of pediatric neurologic and metabolic clinics, pediatric wards, and neonatal and pediatric intensive care units. Data were extracted from medical records using a case report form. The clinical characteristics recorded in this form included the following: demographic information, consanguinity, age at first seizure, seizure type, developmental milestones, abnormal clinical findings, results of laboratory and radiological tests, EEG reports, and final diagnosis. The results of the following tests were also reviewed from the electronic laboratory records: serum glucose, lactate, ammonia, and amino acids; blood gas; acylcarnitine profile; urinary organic acids, ketones, and reducing substances; enzyme assays; and DNA studies. The following tests were reviewed as indicated by clinical features: transferrin isofocusing; lactate-to-pyruvate ratio; and skin and muscle biopsy for functional, biochemical, enzyme, DNA, and histopathological analysis, including electronic microscopy.

In this study, epilepsy was classified according to the ILAE.[1] The diagnosis of metabolic disorder was based on biochemical, enzymatic, and molecular studies according to the clinical profile of each patient. The response to antiepileptic drugs (AEDs) was categorized into three groups according to the presence or absence of seizure freedom. The first group included seizure-free patients who became and remained seizure free within 6 months of starting AED. The AED regimen was defined as a monotherapy or a combination of two or more AEDs. The second group included patients who fluctuated between a period of seizure-free status and relapse within 6 months of starting AED. The third group includes patients who were never seizure free within 6 months of starting AED.

2.1. Statistical analysis

The data were analyzed using SPSS version 17 (SPSS Inc., Chicago, IL, USA). Mean, median, and standard deviations were used for descriptive data.

3. Results

Of the 221 children diagnosed with epilepsy presenting in the first 2 years of life at our hospital, 24 had metabolic diseases. The clinical characteristics (Table 1) of these 24 patients were as follows: 13 (54%) male patients, positive family history of similar metabolic disease in a first-degree relative in eight (34%), and consanguinity in 18 (75%). The