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Original article

Misdiagnosis of gastroesophageal reflux disease as epileptic seizures in children

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Abstract

Background: Gastroesophageal reflux disease (GERD) can mimic epileptic seizure, and may be misdiagnosed as epilepsy. On the other hand, GERD can be more commonly seen in children with neurological disorders such as cerebral palsy (CP); this co-incidence may complicate the management of patients by mimicking refractory seizures.

Objective: The purpose of our study was to evaluate the clinical features, definite diagnoses and treatment approaches of the patients with clinically suspected GERD who were referred to the division of pediatric neurology with a suspected diagnosis of epileptic seizure. We also aimed to investigate the occurrence of GERD in children with epilepsy and/or CP.

Methods: Fifty-seven children who had a final diagnosis of GERD but were initially suspected of having epileptic seizures were assessed prospectively.

Results: All patients were assigned to 3 groups according to definite diagnoses as follows: patients with only GERD who were misdiagnosed as having epileptic seizure (group 1: $n = 16$; 28.1%), those with comorbidity of epilepsy and GERD (group 2: $n = 21$; 36.8%), and those with the coexistence of GERD with epilepsy and CP (group 3: $n = 20$; 35.1%). Five patients (8.8%) did not respond to anti-reflux treatment and laparoscopic reflux surgery was performed. The positive effect of GERD therapy on paroxysmal nonepileptic events was observed in 51/57 (89.5%) patients.

Conclusions: GERD is one of the important causes of paroxysmal nonepileptic events. In addition, GERD must be kept in mind at the initial diagnosis and also in the long-term management of patients with neurological disorders such as epilepsy and CP.

Keywords: Children; Epileptic seizure; Gastroesophageal reflux disease; Misdiagnosis; Paroxysmal nonepileptic events

1. Introduction

Paroxysmal nonepileptic events (PNEs) are characterized by seizure like behaviors without concomitant ictal EEG changes. They may occur at all ages in childhood. Clinical experience and a detailed history of the patients usually lead to a correct diagnosis, and which is confirmed by diagnostic tests [1,2]. However, the accu-

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rate diagnosis of PNEs in children is one of the most common clinical problems faced by pediatricians. Misdiagnosis of epilepsy and unnecessary treatment with antiepileptic drugs are common in these patients. The frequencies of PNEs in pediatric patients are reported to range from 3.5% to 39% at epilepsy referral centers [2–4].

Gastroesophageal reflux disease (GERD) is a digestive disorder that can cause many different symptoms, and some symptoms of GERD may be associated with PNEs. GERD can cause laryngospasm, bradycardia, and apneic episodes in infants, which might be mistaken as epileptic seizures [4–7]. The diagnosis of GERD is based on clinical history, symptoms and physical examination. The application of further diagnostic tests including barium contrast radiography, 24-h ambulatory esophageal manometry, gastroesophageal scintigraphy, upper gastrointestinal endoscopy, and empiric trial of acid suppression are conducted to confirm the diagnosis [8,9]. The purposes of GERD therapy in children are relief of symptoms, the healing of tissue injuries and the prevention of growth retardation. The main treatment options are lifestyle changes including postural and nutritional suggestions, drug therapy such as proton pump inhibitors and histamine H_2-receptor antagonists, and reflux surgery [7–10].

In this study, we evaluated the clinical features, definite diagnoses and treatment approaches of the children with clinically suspected GERD who were referred to our division of pediatric neurology with a suspected diagnosis of epileptic seizure. We also aimed to evaluate the impact of GERD in children with epilepsy, whether with or without cerebral palsy.

2. Methods

The study protocol was approved by Erciyes University Local Ethics Committee (protocol # 96681246/195). Informed consent was obtained before the study from the parents or legal guardians of the all patients. All children with a final diagnosis of GERD who were initially referred with a suspected diagnosis of epileptic seizure were included to study. All enrolled children were prospectively evaluated over a three-year period. Patients with typical GERD symptoms without nonepileptic events, those with previously diagnosed GERD, and patients referred with a diagnosis of other neurological diseases except for a suspected diagnosis of epileptic seizure were excluded. All patients were assessed by two experienced pediatric neurologists in terms of detailed medical history, clinical symptoms, physical examination, neurologic evaluation, EEG, biochemical tests, and radiologic studies. Video-EEG monitoring and brain MRI were performed in patients if considered medically necessary. After the patients were neurologically assessed, they underwent investigation for GERD. GERD was diagnosed on the basis of clinical history and symptoms; it was also confirmed by at least one diagnostic test. The diagnostic tests for GERD included barium radiography, 24-h ambulatory esophageal manometry, gastroesophageal scintigraphy, and upper gastrointestinal endoscopy. The diagnostic procedures were evaluated by the pediatric gastroenterologists. Acid reflux episode was defined as a pH <4 in the esophagus. Abnormal parameters of esophageal pH monitoring included the number of reflux episodes lasting >5 min, and the percent total time when the pH in the distal esophagus is <4.0. The test was considered positive when the percent total time of the pH in the distal esophagus was greater than 6.3%, 1.2% and 4.2% on upright position, recumbent position, and total score, respectively. Gastroesophageal scintigraphy was performed in patients with clinically or radiologically suspected delayed gastric emptying.

Patients were assigned to one of the following three groups according to definite diagnoses: patients with a final diagnosis of GERD who were initially referred with a suspected diagnosis of epilepsy were categorized as group I; children with comorbidity of epilepsy and GERD were defined as group II; and those with the coexistence of GERD, epilepsy, and cerebral palsy were defined as group III.

2.1. Statistical analysis

All statistical analyses were performed by using SPSS for Windows version 22.0 software (SPSS, Inc, Chicago, IL, USA). Continuous variables were presented as mean $\pm$ standard deviation. Pearson's chi-square test was used to evaluate qualitative variables. Nonparametric statistical data were assessed by using the Kruskal–Wallis test. When a significant result was obtained, the Mann–Whitney U test with Bonferroni's correction was used for post hoc comparisons. A p value <0.05 was considered as statistically significant.

3. Results

The study population included 57 patients (27 boys and 30 girls). The mean age at diagnosis of GERD was 40.9 ± 44.0 months (age range: 3 months–17 years). Average follow-up duration was 18.2 ± 7.7 months. The distributions of patients according to definite diagnosis were as follows 16 patients (28.1%) in group I, 21 patients (36.8%) in group II, and 20 patients (35.1%) in group III.

The medical history of the study population revealed premature birth in 9 patients (15.8%), hypoxic ischemic encephalopathy in 28 patients (49.1%), and febrile seizures in 8 patients (14.0%). The clinical presentations of PNEs at admission were head and neck extension in 40 patients (70.2%), irritability in 30 patients (52.6%),