



Pediatric cardiology consultation at long-term video EEG monitoring

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Abstract

Aim: In children, a broad range of paroxysmal events, including syncope and arrhythmias, may mimic true epileptic seizures. When a definitive diagnosis could not be established, long-term video electroencephalogram monitoring (LTVEM) should be taken into consideration. Furthermore, epilepsy patients have a higher rate of cardiac comorbidities. The purpose of this study is to evaluate the rationale and results of the pediatric cardiology consultations in patients admitted to the LTVEM unit.

Materials and Methods: We retrospectively analyzed the files of children who were admitted to LTVEM unit and consulted with the pediatric cardiology department between January 2006 and May 2014. The patients who had both echocardiography and 24-hour ambulatory electrocardiogram monitoring were included.

Results: Among 70 children, 74.3% (n: 52) were classified as having epilepsy, 21.4% (n: 15) with nonepileptic events, and 4.3% (n: 3) could not be classified. In epilepsy group, 21 children (40.4%) were consulted with pediatric cardiology due to rhythm disturbances detected during LTVEM, the remaining consultations (59.6%) were due to history of known cardiac diagnosis (arrhythmias n: 2, structural/congenital heart disease n: 5), tuberous sclerosis (n: 6), drop attacks (n: 5), murmur (n: 5), and other reasons. The cardiac evaluation revealed previously undetected arrhythmia (n:3) and mitral valve prolapse (n:1) in four patients with epilepsy. In addition to the pre-existing long QT syndrome, one child experienced his typical attack, subsequently he was diagnosed as epilepsy. The remaining group consisted of 18 children, with syncope being the most common diagnosis for consultation (n: 10, 55.5%).

Conclusion: Our study revealed that a subgroup of children with epilepsy had cardiovascular comorbidities. Additionally, epilepsy was confirmed in some patients who already had cardiac problems. Pediatricians should be aware of potential mimickers of epilepsy and note that epilepsy and cardiac problems may also co-exist. Correct diagnosis and appropriate treatment are crucial in this patient group.



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Introduction

Long-term video electroencephalogram (EEG) monitoring (LTVEM) refers to the recording of EEG with simultaneous video over prolonged time periods [1]. Long-term video EEG monitoring is mainly used for detection, characterization, and quantification of seizures in epileptic patients, and evaluation for epilepsy surgery as well as establishing the differential diagnosis between epileptic seizures and epilepsy mimickers [2]. Epilepsy mimickers include a wide

range of conditions such as parasomnias, movement disorders, psychological movements, staring spells, arrhythmias and syncope, LTVEM should be considered when a definite diagnosis could not be made [3, 4]. Beyond these mimickers cardiogenic problems may be misdiagnosed as epilepsy and at times it is critical to differentiate these two entities to avoid life-threatening consequences [5, 6]. Epilepsy patients have more cardiac comorbidities than healthy population [7, 8]. Most importantly, ictal and postictal arrhythmias often occur in epilepsy patients who have the risk of cardiac autonomic dysfunction which may have a potential role in pathophysiology of Sudden Unexpected Death in Epilepsy (SUDEP) [7, 9-11]. Therefore, epilepsy patients should be carefully evaluated for cardiac rhythm

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problems.

The goal of this study was to analyze the indications and outcomes of the pediatric cardiology consultation requested for patients admitted to the LTVEM unit.

Materials and Methods

We retrospectively analyzed the files of children who were admitted to the LTVEM unit at Hacettepe University Children's Hospital between January 2006 and May 2014. In each patient, medical history was taken, and a neurological examination was performed before LTVEM was started. Home videos provided by parents were also reviewed. For inclusion into this study, a minimum continuous monitoring period of 24 hours was required; EEG recordings were performed using surface electrodes placed according to the international 10–20 system. Single-channel recording was used to record the cardiac rhythm. Seizures and etiologies in epilepsy patients were classified in the light of current classification after reviewing video EEG reports [12, 13].

After retrospectively analyzing the reports of all children admitted to our video EEG monitoring unit who had a minimum continuous monitoring time of 24 hours, we identified a total of 75 patients required pediatric cardiology consultation. Among these 75 patients who were consulted to pediatric cardiology; cardiologic work-up results either echocardiography (ECHO) or 24-hour ambulatory electrocardiogram (ECG) monitoring were not available in 5 patients. As a result, 70 patients with ECHO and 24-hour ambulatory ECG monitoring were included in this study.

This retrospective study was approved by Hacettepe University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (acceptance number: GO 16/686-09).

Statistical analysis

Descriptive statistics were used in this study, frequencies (sample size and percentages) and medians with minimum and maximum values were reported. Descriptive statistics were performed using statistical package for the social sciences program for windows (version 21).

Results

Among 70 patients, 74.3% (n: 52) were classified as having epilepsy, 21.4% (n: 15) with nonepileptic events, and 4.3% (n: 3) could not be classified with available data. The epilepsy group consisted of 52 patients (30 male and 22 female). At LTVEM admission, the median age of patients was 8 years (3,5 months-17 years). Median age at seizure onset was 7.5 years (5 days- 14 years). Among 52 patients, 29 patients had focal motor, ten patients had generalized motor, six patients had focal to bilateral tonic-clonic and seven patients had focal non motor seizures. Thirty-two (61.5%) patients had daily, ten (19.2%) patients had weekly, and four (7.7%) patients had monthly seizures, six children (11.5%) had a few seizures per year. They were on median two anti-seizure medications [1-4].

The leading underlying etiology was malformations of cortical development (n:12), following tuberous sclerosis (n: 7), metabolic disorder (n: 5), sequela (n:5), genetic disease

(n: 4), hippocampal sclerosis (n: 3), low-grade developmental and epilepsy associated brain tumors (n: 3), autoimmune encephalitis (n:2). The underlying etiology was unknown in 11 patients. Twenty-one children (40.4%) were consulted to pediatric cardiology due to rhythm disturbances during LTVEM, ten had interictal arrhythmias, four had interictal bradycardia, four had ictal tachycardia, two had ictal bradycardia and one experienced ictal atrio-ventricular (AV) block. The remaining consultations (59.6%) were due to history of known cardiac diagnosis (arrhythmias n: 2, structural/congenital heart disease: 5), tuberous sclerosis (n: 6), drop attacks (n: 5), murmur (n: 5), history of ictal arrest (n: 2), ictal cyanosis (n: 2), interictal palpitation (n:1), post-ictal hypotension (n:1) (Figure 1). One patient who previously developed arrhythmia with an anti-seizure medication drug was consulted before starting a new drug and one for cardiac involvement of his metabolic disease (mitochondrial disease).

Forty-two 24-hour ambulatory ECG monitoring (80.8%) studies were within normal limits. Abnormal 24-hour ambulatory ECG monitoring results were observed in ten patients (19.2%), these were rare ventricular or supraventricular extrasystoles in three patients; frequent monomorphic ventricular extrasystoles in three patients (one of them had non-sustained VT); frequent supraventricular and ventricular extrasystoles; frequent supraventricular extrasystoles with nonsustained supraventricular tachycardia with aberrancy; first degree AV block and long QT syndrome in each one patient.

Forty ECHO studies (76.9%) were normal, the rest of the results (n: 12, 23.1%) as follows: mitral valve prolapse (MVP) with mild regurgitation (n: 4), secundum atrial septal defect (ASD) (n: 3), increased left ventricular trabeculation (n: 2), and dilated cardiomyopathy; transposition of the great arteries (TGA) with a ventricular septal defect and pulmonary stenosis; operated cardiac rhabdomyoma with persistent left superior vena cava (each one patient). During LTVEM, after the cardiac examinations, previously unrecognized arrhythmia and MVP were detected in three and one epilepsy patient, respectively. One patient with long QT syndrome experienced his typical attack during sleep which was considered epileptic seizure and diagnosed as frontal lobe epilepsy, in addition to existing cardiac rhythm abnormality.

The remaining group consisted of 18 children (7 male and 11 female). At LTVEM admission, the median age of patients was 13 years (2-16 years). Three had history of known cardiac diagnosis (arrhythmias n: 1, structural heart disease n: 2) and one child had been followed-up with genetics department due to Cornelia de Lange syndrome. Ten children (55.5%) were consulted to pediatric cardiology due to syncope. Three had rhythm problems detected during LTVEM, two had intermittent bradycardia and one had arrhythmias. The remaining consultations were due to murmur (n: 2) and apnea (n: 3) (Figure 1). Fourteen 24-hour ambulatory ECG monitoring studies (77.8%) were within normal limits. Abnormal 24-hour ambulatory ECG monitoring results (n: 4, 22.2%) showed atrioventricular re-entry tachycardia; rare monomorphic ventricular extrasystoles; rare supraventricular extrasystoles; right bundle branch block each in one patient. Fifteen ECHOs

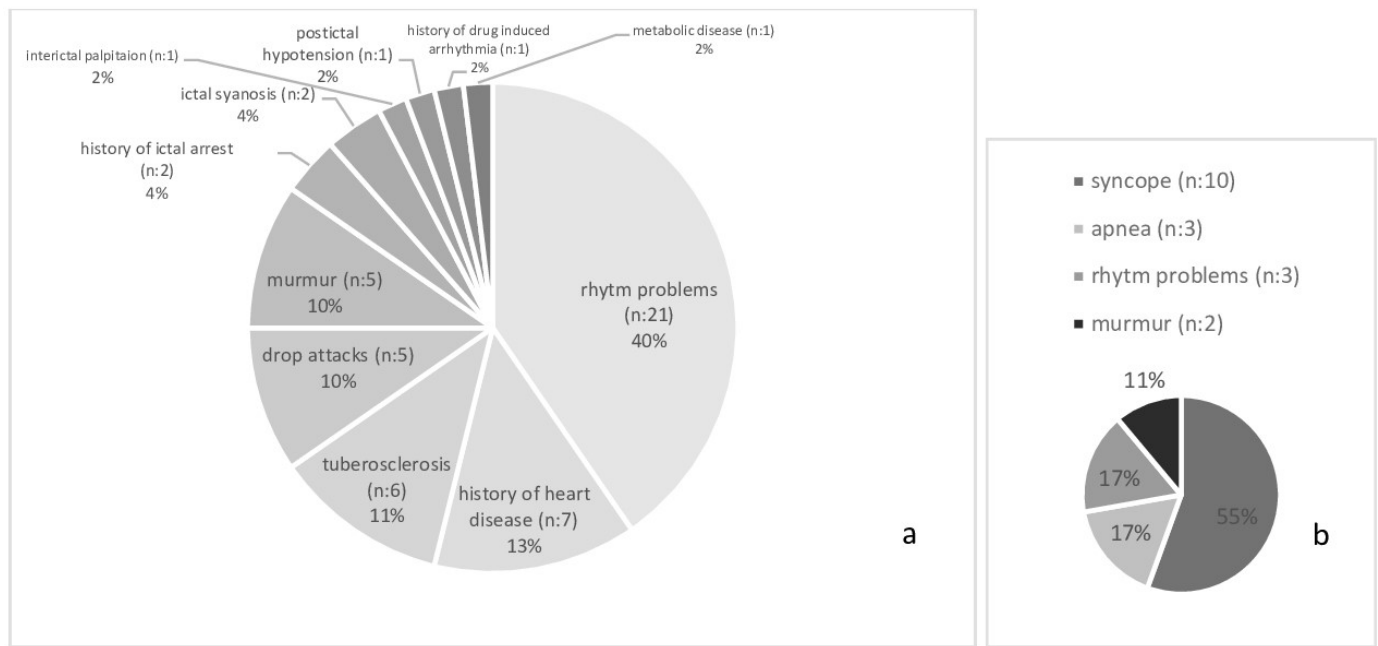


Figure 1. Distribution of the pediatric cardiology consultation in the epilepsy group (a) and the rest of the cohort (b).

(83.3%) were normal, the rest of the results (n: 3, 16.7%) were operated ventricular septal defect (VSD) with persistent left superior vena cava (n: 1), mild mitral regurgitation (n: 1) and pulmoner stenosis with mild tricuspid insufficiency (n:1).

Discussion

In the current study, around half of the children were consulted to pediatric cardiology due to arrhythmias that were detected during LTVEM. Among them, three patients were subsequently referred for follow-up in pediatric cardiology after previously unrecognized arrhythmia was detected during 24-hour ambulatory ECG monitoring. People with epilepsy more frequently have cardiovascular comorbidities. Among these comorbidities, seizure induced cardiac arrhythmias require particular attention, and ictal tachycardia is frequently observed in both adults and children [14, 15]. Both generalized and focal seizures, especially seizures originating from temporal lobe, may cause tachycardia [16, 17]. Less frequently, clinically more significant ictal arrhythmias such as ictal bradycardia, ictal asystole, ictal cardiac arrest as well as other ictal and postictal rhythm problems are also reported in epilepsy patients [9, 18-21]. Impairment in central autonomic pathways is reported in epilepsy patients and alterations in sympathetic and parasympathetic systems are suggested to play a pivotal role in arrhythmias and ictal arrest [22, 23]. In addition, the shared genetic background of cardiac disease and epilepsy, particularly channelopathies as well as the impact of anti-seizure medications on heart may facilitate dysthymias in epilepsy patients [24-26].

Four patients with congenital heart disease (n: 3 secundum ASD, n:1 TGA with a VSD and pulmonary stenosis) with epilepsy were admitted observing the seizure burden and to revise anti-seizure medication treatment. Population-based researches have shown that patients with congenital heart disease are at increased risk of developing epilepsy

[27, 28]. Beside chronic seizures, children and neonates are also under the risk of acute clinical seizures as well as electrographic seizures especially after surgery [29, 30]. Type of congenital heart disease, type, and duration of surgery, whether the patients undergo extracorporeal membrane oxygenation or not, systemic comorbidities, postoperative metabolic/infectious problems influence on risk of acute seizures in operated patients [31, 32]. On the other hand, acute seizures will not always result in epilepsy [31, 33]. Besides, patients with congenital heart disease who were not operated may also experience epilepsy in long-term follow-up [27]. The main pathophysiological factors that may lead seizures in this population are global hypoxic brain injury as well as focal cerebro-vascular events (embolic and/or hemorrhagic) and metabolic disturbances [27, 31].

In our study, one patient who had long QT syndrome was also diagnosed with concomitant epilepsy since he experienced his typical episode while LTVEM that was categorized as an epileptic seizure and diagnosed as frontal lobe epilepsy. Long QT syndrome is an arrhythmia syndrome caused by mutations in genes encoding cardiac ion channels, resulting in prolonged QT-interval on ECG which may cause syncope, potentially fatal rhythm problems, and even, sudden death in children and adults who do not have structural heart disease [34]. Patients with long QT syndrome may be misdiagnosed as having epilepsy because they exhibit seizure-like behavior; additionally, long QT syndrome-related syncopal events can be potentially misidentified as neurogenic syncope or epileptic seizure [35, 36]. Albeit, limited number of patients have been diagnosed with the coexistence of epilepsy and long QT syndrome [37]. Of note, a large multicenter study has reported that 7% of SUDEP patients have mutation in the genes causing long QT syndrome [38].

Most patients in the non-epileptic group were consulted due to syncope in this study. Syncope is a relatively

frequent symptom in clinical practice, defined as temporary loss of consciousness and postural tone brought on by global cerebral hypoperfusion, typically characterized by a quick onset, brief duration, and subsequent full recovery [39]. Vasovagal syncope is the leading subtype, less frequently followed by other subtypes such as cardiovascular-mediated, neurologic and psychogenic syncope in children [40]. A comprehensive medical exam, a complete personal and familial history, ECG, and in selected cases ECHO and head-up tilt testing are all important for accurate diagnosis [39, 41]. If cardiogenic syncope is strongly suspected, additional cardiac investigations such as exercise tests, Holter ECGs, cardiac magnetic resonance imaging, and electrophysiological studies are obtained on an individual basis. Differentiating syncope from epileptic seizures can also be difficult at times. Thus, after a detailed history, physical examination and basic tests, a subgroup of patients should be carefully considered for evaluation by pediatric neurology and cardiology.

This study has several limitations because of the retrospective nature and relatively small sample size. One of the major limitations of this study was inadequate data regarding 12 lead ECGs. None of the 24-hour ambulatory ECG monitoring studies were revised currently, all results presented in this study were obtained from previous reports. Despite the above-mentioned constraints, our study offers a remarkable data from a single center regarding cardiac problems overlapping with epileptic seizures in childhood.

Conclusion

The current study presented the reasons for cardiology consultation as well as the results of cardiologic examinations performed on patients with epileptic seizures and non-epileptic events at the LTVEM unit. A subgroup of epilepsy patients was shown to have cardiovascular comorbidities, in addition, epilepsy was observed in some patients with existing cardiac problems. Pediatricians should be aware of this association, and collaboration between pediatric neurology and cardiology is critical in the management and follow-up of this patient group.

Disclosure

This study was presented as platform presentation at the 17th Turkish National Pediatric Neurology Congress.

Conflicts of interest

The authors declared that they have no conflict of interest.

Ethics approval

This retrospective study was approved by Hacettepe University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (acceptance number: GO 16/686-09).

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