Original Article

Cyclical vomiting syndrome in children: potential role of electroencephalogram in the diagnostic evaluation

Tan LN Michelle, Quak Seng Hock, Ong Hian Tat and Aw Marion M

ABSTRACT

Aim: Cyclical Vomiting Syndrome (CVS) is a functional disorder in childhood which is increasingly being recognized. The pathogenesis of CVS remains unknown but there appears to be a link between CVS and migraine, suggestive of a central aetiology. We aimed to determine the utility of electroencephalograms (EEG) in the diagnostic algorithm of a child suspected to have CVS.

Methods: We conducted a retrospective review of children who have been diagnosed with CVS in our unit since 1999 when EEGs were performed as part of the diagnostic evaluation.

Results: There were 48 children with recurrent vomiting in whom the clinical diagnosis of CVS was entertained. Median age of onset was 4 years (6 months-12 years). Of the 48 patients, 27 received a final diagnosis of CVS/abdominal migraine, following normal investigations which included abdominal x-ray, barium study, abdominal ultrasound and screen for inborn errors of metabolism (IEM); 21 received other diagnosis which included, non-specific abdominal colic (12), hiatal hernia (1), epilepsy (3) and IEM (1). Of the 27 with CVS/abdominal migraine, 21 had EEG features consistent with mild encephalopathy during an acute attack. Twelve of them had a repeat EEG when clinically well, and all but 1 showed normalization.

Conclusions: In our series, 78% demonstrated transient electrographic changes of acute encephalopathy during the acute attacks. The use of EEG in the appropriate clinical context may provide additional evidence to support the diagnosis of CVS in patients without other aetiologies for mild acute encephalopathy.

Key words: children, recurrent vomiting, cyclical vomiting syndrome, electroencephalogram, encephalopathy

INTRODUCTION

Cyclical Vomiting Syndrome (CVS) is a functional disorder of childhood which is increasingly being recognised. It is characterized by episodes of recurrent profuse vomiting which are self-limiting and with periods of well-being between attacks.1 If left undiagnosed, it is a debilitating condition affecting schooling and social life of the patients. Unfortunately, the diagnosis of CVS remains an exclusionary one posing a clinical challenge. In a child with recurrent vomiting, it may be pertinent to screen for gastro-intestinal (GI) structural anomalies, brain tumours, and inborn errors of metabolism. Hence, initial investigations often include imaging of the GI tract, central nervous system (CNS) as well as screening for metabolic conditions.2-4 There appears to be a link between CVS and migraine, suggestive of a central aetiology.5,6 There are similarities in the symptoms for both conditions (e.g. nausea, photophobia, headache) as well as similarities in triggers (e.g. stress, lack of sleep). Interestingly, there is often co-existing personal or family history of migraine in individuals with CVS. CVS is commonly considered as precursor of migraine or migraine equivalent. Although the slowing of posterior mean frequency of EEG pattern is reported in migraine patients7, the role of electro-encephalogram (EEG) in the diagnostic evaluation of CVS remains controversial. The aim of our audit was to determine the utility of EEG in the diagnostic algorithm of a child suspected to have CVS.
MATERIALS AND METHODS

**Ethics:** The study was approved by the appropriate National Healthcare Group Domain Specific Review Board (DSRB).

**Study design and Setting:** This is a retrospective data review study of children suspected to have CVS who presented to the KhooTeckPuat-National University Children’s Medical Institute, National University Health System over a 12-year period from 1999-2011.

**Participants:** The case records of children below 18 years old with the clinical suspicion of CVS presenting to our unit were reviewed. All patients with suspected CVS underwent routine EEG, which included a sleep and wake phase, during an acute attack. The EEG was read by the paediatric neurologists in our unit. Whilst the intention was to repeat the EEG during a “well phase” on patients with abnormal EEGs during the acute attack, this may not have been logistically possible in all instances.

**Variables:** The chart review included patient demographics, clinical symptoms as well as investigations performed. The final diagnosis of CVS was made based on clinical presentation, physical examination, exclusion of any structural GI or CNS abnormalities and metabolic disorders. Investigations to rule out structural GI abnormalities included abdominal X-ray, barium study and abdominal ultrasound. Oesophago-gastro-duodenoscopy (OGD) was also performed in the majority of patients. Brain imaging was done in some cases, with either a Computed Tomography scan or Magnetic Resonance Imaging. Investigations to rule out inborn errors of metabolism (IEM) included serum electrolytes, acid-base balance, serum ammonia, lactate and occasionally, amino acid and acyl carnitine profiles and urine organic acids.

**Statistical analysis:** The final diagnosis of patients were classified as “CVS” and “non-CVS” for the purpose of analysis. Statistical analysis was performed using SPSS version 16.0. Proportion of EEG with mild encephalopathy in the “CVS” and “non-CVS” groups was compared using Fisher’s exact test, with p<0.05 being statistically significant.

**RESULTS**

We reviewed 48 children with recurrent vomiting in whom the clinical diagnosis of CVS was suspected. Twenty-seven (56%) were eventually diagnosed with CVS/abdominal migraine. Those with abdominal migraine are included in the analysis of the “CVS” group as it is being increasingly recognized as part of the spectrum of CVS. Among the non-CVS group, the diagnoses included IEM (1), gut vasculitis (1), gastro-oesophageal reflux disease (1), hiatus hernia (1), esophagitis/gastritis (2), epilepsy (3), and non-specific abdominal colic (12). Out of the 48 suspected cases, 22 (46%) showed features of slowing on EEG consistent with mild encephalopathy. Of these 22, 21 (95%) had a final clinical diagnosis of CVS/abdominal migraine. The demographics and baseline characteristics of the patients are shown in Table I. Among those diagnosed with CVS/abdominal migraine, there were 13 boys and the median (range) age of symptom onset was 5 (0.5 – 12) years. During the vomiting episodes, abdominal pain was a commonly associated symptom (52%), followed by headache (19%). In these 27 children with CVS/abdominal migraine, investigations including abdominal X-ray, barium study, abdominal ultrasound, and IEM screen were normal. OGD was performed in 12 with 7 being normal and mild gastritis seen in 5. Twenty-one had EEG features consistent with mild encephalopathy during an acute attack (Figure 1).

Two EEG patterns were identified – intermittent or excessive posterior slowing (65%), and generalized slowing with or without slowing of posterior background (35%). Twelve children had repeat EEG when clinically well. All but one patient with underlying Nager syndrome showed normalization of their EEG changes. In the non-CVS group (n=21), there were 13 boys and the median age of onset was 6 (0.3 to 13) years. In addition to vomiting, the patients had predominant abdominal pain (57%) and/or lethargy (33%). One patient had EEG findings of mild encephalopathy. This child was eventually diagnosed with an IEM. There was statistically significant association between CVS and EEG with features of mild encephalopathy (P<0.0001) (Table II).

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<tr>
<th>Table I: Demographics and Characteristics of suspected CVS cases</th>
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<td><strong>CVS cases, n = 27</strong></td>
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<td><strong>Median (range) age at symptom onset</strong></td>
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<td><strong>Gender</strong></td>
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<td><strong>Most common 3 symptoms at presentation</strong></td>
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<th>Table II: EEG in patients with and without CVS</th>
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<td><strong>CVS/Abdominal migraine</strong></td>
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<td><strong>EEG with encephalopathy</strong></td>
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<td><strong>EEG without encephalopathy</strong></td>
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DISCUSSION

Although CVS remains an idiopathic condition, it has been linked to migraine headaches as early as 1904. It has been suggested by Li et al that migraine may present with different clinical patterns in childhood -- CVS in toddlers and early elementary school-aged children; abdominal migraine in later elementary school-age children; and migraine headaches in preteens and adolescents. Notably, amongst those diagnosed with CVS in our cohort, there was a higher proportion of females, possibly linking this to maternal inheritance as has been proposed in previous studies of the role of mitochondrial DNA in CVS and migraine. Previous studies have reported abnormal EEG findings in CVS but the role of EEG remains controversial.

Our review showed that significantly higher number of children (78%) with CVS/abdominal migraine demonstrated transient electrographic changes of acute encephalopathy during the acute vomiting episodes. These EEG abnormalities support a central non-epileptic aetiology that may underlie CVS and abdominal migraine. A high incidence of slow EEG activity in 16 out of 33 CVS cases was also demonstrated in a study by Lin et al in 2011.

CVS remains a difficult diagnosis to make. Nonetheless, the use of EEG, performed at the time of an acute attack, may allow clinicians to have greater confidence to “rule-in” the diagnosis of CVS in patients who present with clinical features of CVS but without other aetiologies for mild acute encephalopathy. The main limitation to this would be access to EEG monitoring capability within 24-48 hours of onset of symptoms, as well as the opportunity to repeat another EEG at a later date when the child is well. The retrospective nature of this observational study resulted in a number of patients not having a follow-up EEG performed (i.e. no paired EEG recordings in patients who had the final diagnosis of CVS). Further work in this clinical arena could include prospective multi-centre collaborative studies evaluating paired EEG recordings, both during an acute attack as well as during the well phase in children with suspected CVS.

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REFERENCES


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