รายงานผู้ป่วย

Childhood absence epilepsy: an epileptic syndrome with excellent prognosis

Chaichon Locharernkul*

Alisa Wacharasindhu**

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Childhood Absence Epilepsy (CAE) is an uncommon epileptic syndrome occurring in neurologically and intellectually normal children at the age of 4-8 years. It has excellent prognosis with 80-90% remission rates using sodium valproate (VPA) therapy. However, absence seizures in CAE are frequently neglected, resulting in unawareness of the syndrome. We report a case of CAE from the Epilepsy Clinic of Chulalongkorn Hospital. Careful history, as well as EEG recording during hyperventilation, established the diagnosis of typical absence seizures. The video/EEG recording demonstrated brief episodes of attacks characterized by vacant stares along with generalized 3 Hz spike-wave discharges starting and ending simultaneously with the events. VPA monotherapy completely controlled his absences and clearly showed the dose response relationship. Accurate seizure counts and complete seizure records provided a reliable assessment of the treatment outcome. Since GTCs will develop in 40% of CAE cases during adolescence, continuation of VPA to puberty is recommended. The child's associated attention deficit was successfully treated with methylphenidate and showed no correlations with the seizure numbers or VPA dosage. Recognition of CAE as a distinct epileptic syndrome provides correct prognostic determination as well as appropriate type, dose and duration of antiepileptic drug therapy.

Key words: *Typical absence seizure, Childhood absence epilepsy, Pyknolepsy, Video/EEG, Generalized spike-waves, Attention deficit, Valproate.*

Reprint request: Locharernkul C, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

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*Department of Medicine, Faculty of Medicine, Chulalongkorn University.

**Department of Psychiatry, Faculty of Medicine, Chulalongkorn University.

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Childhood Absence Epilepsy (CAE) เป็นกลุ่มโรคลมชักที่พบได้น้อย มักเกิดในเด็กที่ไม่มีความผิดปกติของสมอง เริ่มตั้งแต่อายุ 4-8 ปี ผู้ป่วย 80-90% ของโรคนี้จะหายจากการชักด้วย sodium valproate (VPA) แต่อาการชักแบบ absence มีอาการน้อยและสังเกตได้ยาก จึงมักไม่ได้รับการวินิจฉัยและทำให้ผู้ป่วยไม่มีโอกาสได้รับยาที่ถูกต้อง รายงานนี้นำเสนอผู้ป่วย CAE 1 ราย วินิจฉัยจากคลินิคโรคลมชัก โรงพยาบาลจุฬาลงกรณ์ โดยอาศัยประวัติเกี่ยวกับอาการชักอย่างละเอียดร่วมกับการตรวจคลื่นสมอง การทำ Video/EEG recording ขณะผู้ป่วยหายใจหอบแรง พบคลื่นไฟฟ้าขณะชักเป็น generalized spilke-waves ความถี่ 3 Hz สม่ำเสมอ เกิดขึ้นและสิ้นสุดพร้อมกับอาการเหม่อตาค้าง และไม่รู้สึกตัวนาน 10-15 วินาที ซึ่งเป็นลักษณะของ typical absence seizure อาการชักของผู้ป่วยหายไปหมดเมื่อได้รับ VPA ในขนาด 1,000 มก.ต่อวัน พบว่ามีความสัมพันธ์ของขนาดยา VPA กับจำนวน absence ที่ตอบสนองต่อยา การบันทึกอาการชักอย่างถูกต้องและครบถ้วน มีความสำคัญมากต่อการประเมินผลการรักษา ผู้ป่วย CAE จำเป็นต้องได้รับ VPA ในขนาดที่สูงพอเพื่อคุมอาการชักให้หายหมด และจำเป็นต้องรับยาต่อไปจนเข้าสู่วัยรุ่น เนื่องจากกว่าหนึ่งในสามของผู้ป่วย จะเกิด generalized tonic clonic seizures ตามมาเมื่อถึงวัยดังกล่าว อาการ attention deficit ที่เกิดร่วมในผู้ป่วยรายนี้ ตอบสนองดีต่อ methylphenidate และพบว่าไม่มีความสัมพันธ์กับจำนวนครั้งของการชักและขนาดยา VPA ที่ให้ การวินิจฉัยกลุ่มโรคลมชัก CAE มีประโยชน์ในการพิจารณาชนิด ขนาด และระยะเวลาของยากันชักที่เหมาะสม ตลอดจนบอกการพยากรณ์โรคที่ถูกต้องแก่ผู้ป่วย

Childhood Absence Epilepsy (CAE), formerly called pyknolepsy, is an epileptic syndrome comprised of typical absence seizures starting in early childhood in an intellectually normal individual.[1] Although CAE can be easily diagnosed from its typical ictal EEG findings, the subtle clinical manifestations during seizure attacks are frequently neglected by parents or physicians, leading to unawareness or misdiagnosis of the syndrome. Absence seizures in CAE have excellent response to appropriate antiepileptic drugs (AEDs). However, as many as 40% of the cases will develop additional generalized tonic clonic seizures (GTCs) during puberty.[2] There are also significantly more patients with irregular treatment evolving to GTCs than those with regular medications.[3] Recognition of the syndrome is therefore important in determining the choice and duration of AED therapy. CAE is an uncommon syndrome with an annual incidence of 6.3 to 8:100,000 of children under 15 years age.[3] It accounts for 10-15% of all childhood epilepsy.[4] There has been no data on the incidence in the Thai populations so far. This article describes a typical case of CAE diagnosed at the Epilepsy Clinic of Chulalongkorn University Hospital. The differential diagnosis, role of electroencephalography (EEG), prognosis and line of management are discussed.

Case report

A 6-year old boy (SS-30887/38), as noticed by his mother, had frequent episodes of blank stare since the age of 4.5 years. Careful history revealed brief attacks during which he became motionless and was unaware the environment. During some attacks, he would rock his body and roll up his eyes or blink frequently. Mild side-to-side clonic head jerks or chewing were sometimes noted. Urinary incontinence occurred with some episodes. There was no limb movement or falling. The attacks usually lasted 10-15 seconds before abruptly ending. He would then return to his normal activity without apparent memory of the events. The seizures were brought upon by excessive playing, stress and hyperventilation. Despite daily occurrence, these episodes were not brought to any physicians' attention until the age of 6.

The patient is the only child of the family. There is no familial history of seizures or epilepsy. He has short attention spans and has displayed hyperactive behavior since very early childhood. His school performance were usually below average. Birth and developmental history were normal. Except for some wheezing attacks during respiratory infections up to age 4, there was no past medical illness. Physical examination revealed a 20-kg hyperkinetic boy with normal general and neurologic findings.

The routine scalp EEG as well as the video/EEG recording demonstrated several stereotypic attacks precipitated by hyperventilation. Clinically, the child suddenly became motionless, his eyes rolled upward with eyelid fluttering and mild head jerks (Figure 1). The

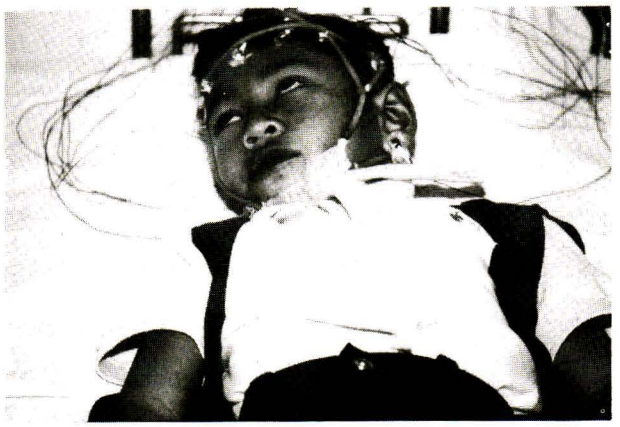

Figure 1. The child during a typical absence attack. Note a vacant upward stare without major motor component.

attacks lasted about 10 seconds and had a tendency to become shorter with repeated episodes. During one seizure, he was asked to remember a few test words but afterwards he was not able to recall any of them.

Bursts of symmetrical and synchronous generalized spike-and-slow-wave complexes were elicited at a frequency of 3 cycles per second in regular rhythm, beginning and ending abruptly with the clinical events (Figure 2). Interictally, few brief bursts of similar generalized spike-wave complexes appeared in the normal background EEG.

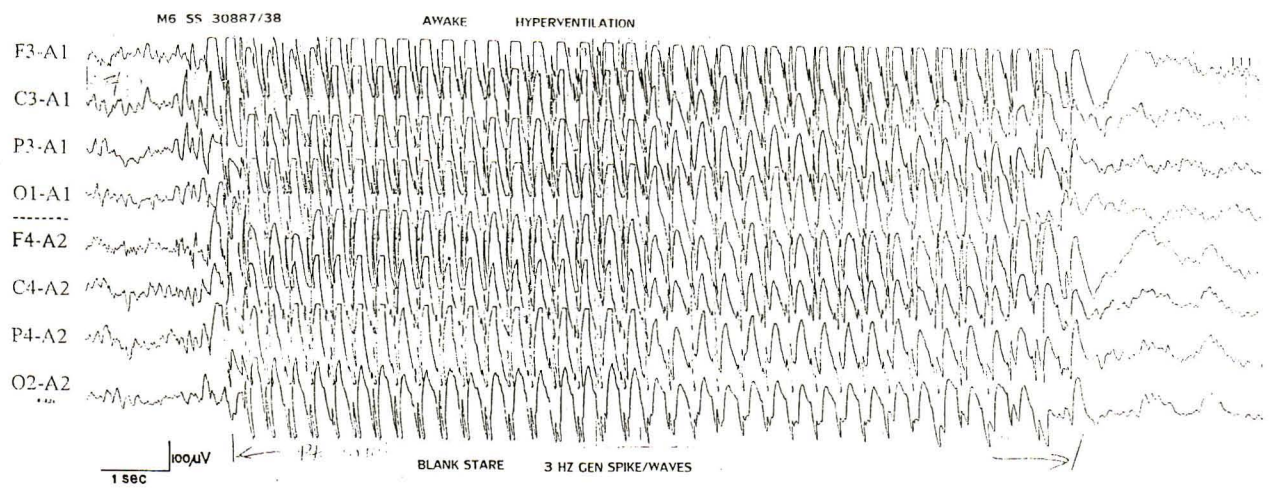

Figure 2. The ictal EEG of the child during hyperventilation showing bursts of symmetrical generalized 3 Hz spike-and-slow-wave complexes accompanying the clinical absence. The ictal discharges then abruptly return to the previous normal background.

All absence seizures were recorded in the seizure calendar by his parents before and after starting medication. Sodium valproate (VPA), given in gradually increased doses up to 1,000 mg per day eventually lowered his seizures from a baseline of 96 attacks per month (average of 2-3 attacks per day) to a seizure-free state. At 43 weeks, he has no seizures nor drug side effects and remains seizure free for more than one year. Table 1 shows the dose response relationship of the VPA given and the number of seizures controlled. There was no significant changes in complete blood count and liver enzymes during VPA therapy.

Our subject's hyperactive behavior persisted with the same intensity even though he was seizure free. A pediatric psychiatrist was consulted and 10 mg per day of methylphenidate was prescribed. His attention span then improved, as refleced in better scores on the Wechler Intelligence Scale for Children (WISC) (pretreatment: VIQ=87, PIQ=89, FIQ=87 vs post treament: VIQ=96, PIQ=86, FIQ=91). The psychological tension of his parents was obviously relieved after his seizures and behavioral problems became controlled.

Table 1. Dose response relationship of the VPA and the number of seizures controlled.

VPA dose	Duration	Average seizure frequency
Baseline	2 weeks	96/month
400 mg/d	2 weeks	14/month
600 mg/d	7 weeks	1.7/month
800 mg/d	32 weeks	0.5/month
1,000 mg/d	62 weeks	0/month

Discussion

According to the International Classification of Epileptic Seizures, our case fits the definition of typical absenses in both clinical and EEG criteria.[5] Despite frequent daily attacks, perhaps dozens to hundreds of seizures in a day,[6] the subtle clinical manifestations of absence seizures are easily overlooked. Moreover, the episodes are usually not perceived by the patients themselves.[7] In our patient, the attacks were unrecognized by medical practitioners for more than a year before the correct diagnosis was made. Simple absences can be as trivial as a few seconds of unawareness to surroundings. However, it would be easier to detect them if automatisms or some motor components coexist, as in complex absences.[8] Differential diagnosis of absence seizures include complex partial seizures,

daydreaming, fainting and psychological reactions.[9,10] The most important clue to proper diagnosis is a thorough history from reliable observers. Routine as well as video-EEG recordings play a crucial role in confirming an absence attack as well as in making differential diagnosis in difficult cases. Hyperventilation is the most powerful activating factor in absence attacks, as demonstrated in our case. Photic stimulation can induce absences in only 10-25% of patients.[11] EEG also helps in separating typical from atypical absences which usually occur in mental deficit and developmental delay patients.[12] In an atypical absence, an EEG will show generalized spike-waves of lower frequency (less than 2.5 Hz). Fast rhythm of small amplitude or high voltage 10 Hz rhythmic activity can also be found.[5]

Diagnosis of Childhood Absence Epilepsy is considered when typical absence seizures with classical 3-Hz generalized spike-wave discharges occur in an intellectually normal child at the age of 4-8 years.[1,13] Our patient fulfills all these features except for a subnormal IQ on the initial WICS score. However, he was shown later to have an average intellectual function on the follow-up test after his attention deficit was treated. Attention Deficit Disorder (ADD) and other behavioral problems can occur in one third of CAE cases[2] but are not considered cardinal features of the syndrome.[7]

Juvenile Absence Epilepsy (JAE) has a slightly higher age of onset (12-14 years) and a higher tendency than CAE[8] to develop GTCs and myoclonic seizures. The spike-wave discharges in JAE usually have a faster frequency of 4 or even 5 Hz.[14] Other epileptic syndromes having absence attacks include Juvenile Myoclonic Epilepsy (JME), Epilepsy with Grand Mal on Awakening (GMA) and Myoclonic Absences. JME and GMA usually start around puberty. Different seizure and EEG characters were helpful in differentiating these two syndromes in our case. Myoclonic absences also have 3-Hz generalized discharges as CAE, but bilateral clonic arm jerks usually accompany absence attacks. Most children with Myoclonic Absences have prominent learning and behavioral difficulties and respond poorly to conventional therapy.[15]

The prognosis of children with CAE is excellent. The typical absence usually responds very well to VPA. Remission has been reported varying from 70 to 90% of cases.[6,16] Accurate seizure recognition as well as complete seizure records, either by parents, sitters or teachers, are necessary to precisely determine the outcome of the therapy, although some absences may go undetected. Our case shows a clear dose response relationship between the VPA and the numbers of absences. Therefore the VPA should be increased to its highest tolerated dose and seizures reliably measured in order to acheive complete seizure control.

About 40% of children with CAE will develop GTCs when approaching puberty.[2] Because VPA has a broad spectrum property, it

is therefore considered the AED of choice. Premature discontinuation of VPA after the patient had become seizure free was found to be associated with a higher incidence of late-developing GTCs.[3] VPA should then be maintained and the patient followed to adolescence.

Behavioral problems in CAE are postulated as consequences of frequent seizures, of parents' attitude and of AED therapy.[2] However, in our case, attention deficit was not shown to be related to absence frequency. He continued to be hyperactive even after being free from seizures. Although VPA may exert some effects on mood and cognitive function,[17] it did not seem to help in our case. It was clear that his behavior and intelligence scores did not improve until methylphenidate was added. Our case demonstrates that attention deficit in CAE is unrelated to seizure or AED treatment.

Summary

Recognition of absence seizures leads to the correct diagnosis and appropriate theapy of CAE as demonstrated in our patient. A detailed history along with video/EEG recording are the most fruitful means to diagnose typical absence attacks. Hyperventilation helps increase the sensitivity of EEG positivity. Associated attention deficit does not seem to be a result of seizures or their therapy. Identifying CAE as a distinct epileptic syndrome is noteworthy for prognostic implication. Adequate dose and duration of VPA should be administered for complete seizure control and preventing late developing GTCs in this syndrome.

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