# Atypical juvenile myoclonic epilepsy with structural brain abnormalities and cognitive impairment: A case report

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## ABSTRACT

Juvenile myoclonic epilepsy (JME) is an idiopathic generalized epilepsy affecting 5–10% of epilepsy patients. Its exact cause remains unknown, but recent studies indicate frontal region involvement. It responds well to anticonvulsants but is often misdiagnosed with focal-onset epilepsy. We present a 9-year-old girl with myoclonic, absence, and generalized tonic-clonic seizures happening over three months. EEG revealed slow spike and wave complexes with generalized poly-spikes, while brain MRI identified encephalomalacia cysts with right frontotemporal lobe hemiatrophy. Valproic acid treatment led to seizure-free status for one month. In conclusion, timely EEG and neuroimaging are pivotal in identifying structural abnormalities in JME patients with pronounced cognitive impairment, enabling tailored treatment and better outcomes.

**Keywords:** Juvenile myoclonic epilepsy, cognitive impairment, structural abnormalities

## List of abbreviations

AED – Antiepileptic drugs
AS – Absence seizure
CAE – Childhood absence epilepsy
EEG – Electroencephalography
GTCS – Generalized tonic-clonic seizure
IGE – Idiopathic generalized epilepsies

JAE – Juvenile absence epilepsy
JME – Juvenile myoclonic epilepsy
MRI – Magnetic resonance imaging
MRA – Magnetic resonance angiography
MS – Myoclonic seizure
VPA – Valproic Acid

## INTRODUCTION

The Idiopathic Generalized Epilepsies (IGEs) include four syndromes: childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and epilepsy with generalized tonic-clonic seizures (GTCS) alone [1]. The estimated prevalence of JME is 26.7% of genetic generalized epilepsies, where IGE is one of its distinct subgroups [2]. Birth history and cognitive function are usually normal, but impairments in specific cognitive domains can be seen [3].

The mandatory diagnostic criteria for JME are myoclonic seizure (MS) and the finding of 3 - 5.5 Hz generalized spike-wave or generalized polyspike-wave on electroencephalogram (EEG) [1]. MS usually occur not long after the patient wake up in the morning [1]. MS can stand alone or combined with GTCS and absence seizure (AS), which might present in 80-95% and 15-30% of cases, respectively [4].

Avoidance of precipitating factors and suitable antiepileptic drugs (AEDs) are the mainstay of treatment [2]. Overall response to therapy is good (65-92% drug-responsive patients) [2], but lifelong medication

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is often necessary due to a high risk of relapse after drug withdrawal [1,5]. Since the 1980s, valproic acid (VPA) has been the first AED of choice in JME due to its availability, broad spectrum, and high response rate [2,6]. The role of newer AEDs is increasing, but the data on comparative effectiveness are still lacking [6].

Establishing the diagnosis of JME can pose a challenge for clinicians, especially those with limited experience in pediatric neurology. Subsequently, this may increase the risk of delayed and/or misdiagnosis, resulting in poor outcomes. This case report may give clinicians valuable perspective regarding the best approach to JME and treatment considerations based on the most recent scientific evidence.

## CASE REPORT

A 9-year-old female was referred to the neuropediatric outpatient clinic with a chief complaint of multiple seizures starting three months ago. Seizure was described as stiffness continued by rhythmic jerks of all extremities lasting for eight to ten minutes with the frequency of up to five times daily. She was unresponsive during the attack. Before this seizure happen, she initially experienced a brief, sudden, and irregular movement in her arm when she woke up in the morning but did not seek for help because she was still alert. The patient's mother added that there are times when the patient would stop mid-sentence when she speaks and stare blankly for a few seconds.

At one-month-old, she had her first unprovoked seizure in the form of right arm stiffness lasting for five minutes. At eight months old, she had her second unprovoked seizure in the form of stiffness followed by repetitive jerking movement in all extremities. She received AED for three months, but her mother stopped the medication because she was already seizure-free.

There was no family history of seizures. Her mother denied any illness and consumption of drugs during pregnancy. She was born through spontaneous delivery during 34-35 weeks of gestation and weighed 2400 grams. Her birth body length was 49 cm, with a head circumference of 36 cm. She received exclusive breastfeeding and complete immunization. She was academically behind with a history of repeating her class once. The patient usually insists on helping her mother with work after school, causing her to sleep late and irregularly. She rarely plays with her peers because she feels ashamed of her condition.

Her weight and height were 23 kilograms and 124 cm, respectively. Using the Centers for Disease Control and Prevention growth chart curve, the patient's anthropometry was considered normal, with her weight-per-age and height-per-age scoring higher than the 10th percentile and an ideal body weight of 92%. There were no abnormalities found during general physical examination and detailed neurological examinations. Higher mental function and speech skills were within normal limits.

The patient baseline investigations, which included complete blood count, liver function test, serum electrolytes, and thyroid stimulating hormone, were within normal range. EEG result during sleep-wake cycle stage II was abnormal with slow spike and wave complexes, sharp waves in the right temporal region, and generalized polyspikes (Figure 1). Brain
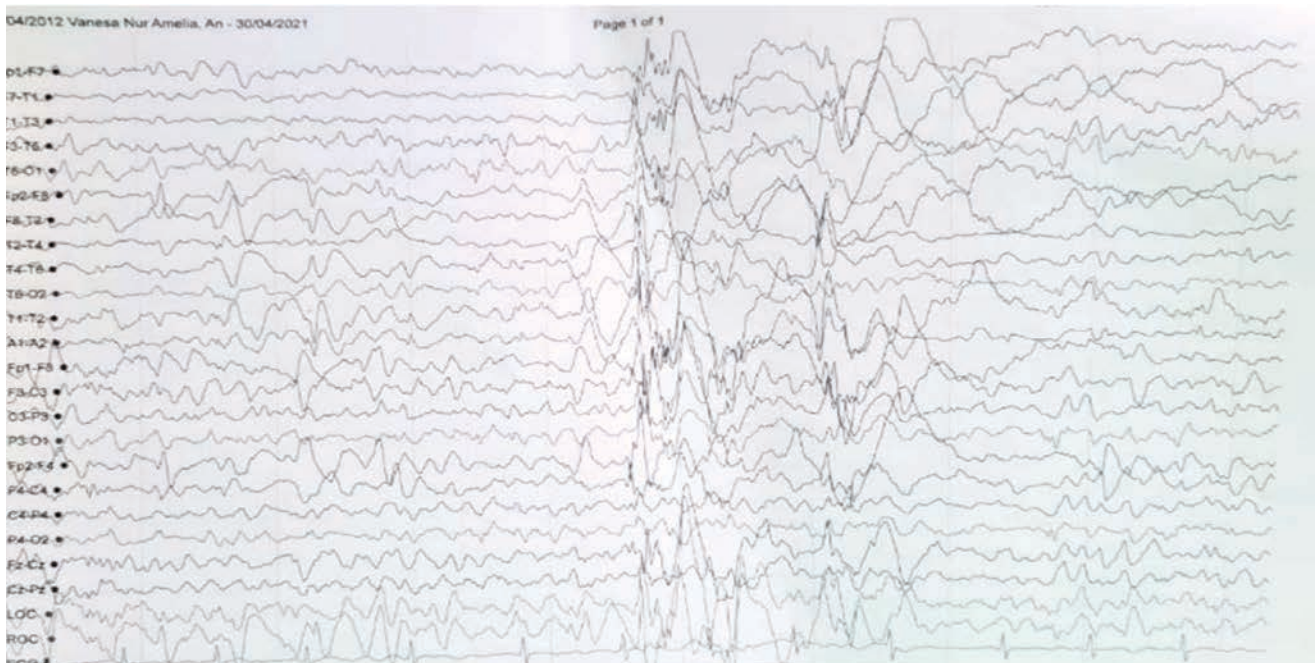


**FIGURE 1.** EEG showing slow spike and wave complexes, sharp waves, and general polyspike
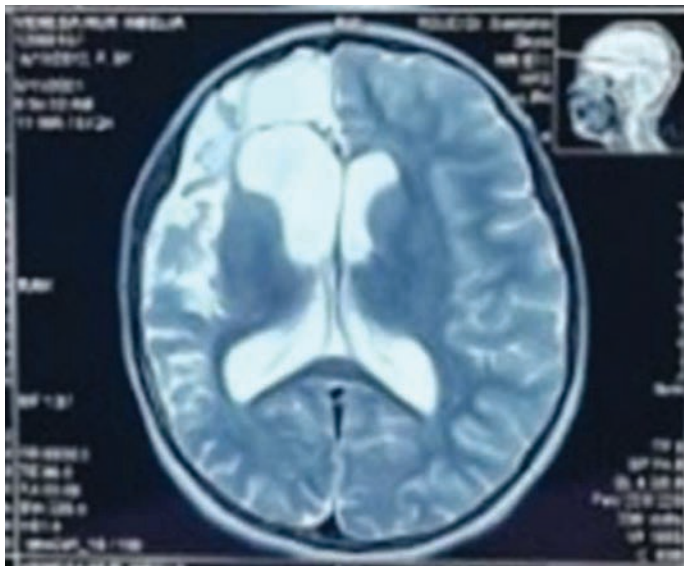
**FIGURE 2.** Brain MRI imaging with contrast revealed encephalomalacia cyst, lateral ventricle retraction, and right frontotemporal lobe and hippocampus atrophy

magnetic resonance imaging (MRI) with contrast revealed an encephalomalacia cyst with hemiatrophy in the right frontotemporal lobe, lateral ventricle retraction extending to the temporal horn and midline to the right side, and right hippocampus atrophy (Figure 2). Volume of the right and left hippocampus is 1.17 cm and 2.2 cm, respectively. Magnetic resonance angiography (MRA) revealed right middle cerebral artery stenosis in the M2 and M3 segments. The patient was treated with VPA 20mg/BW/day which led to seizure-free status for one month.

## DISCUSSION

The patient's seizure onset, which began at 9, is consistent with the JME range of onset, albeit slightly earlier [1]. Antenatal history was normal, however, the patient had a history of preterm birth and low birth weight, which might indicate suboptimal brain development in utero [7,8]. She has a classical phenotype of JME (found in 62.5% cases) where classical Herpin-Janz triad (AS, MS, and GTCS) was present [9]. Despite her MS preceding the GTCS, she did not consider those myoclonic jerks as seizures. This finding is consistent with ILAE statement on JME that MS are frequently recognized retrospectively after GTCS [1]. According to her mother's report, AS happened after MS and GTCS were present. In reality, it is hard to accurately pinpoint the onset of AS, due to its brief and variable nature, causing subtle impairment on awareness [1]. AS can be easily mistaken for daydreaming by parent or teacher.

She met the mandatory diagnostic criteria for JME [1]. Other characteristic features, which are upper extremities involvement, time occurrence, precipitating factors, along with no progressive cognitive deterioration were also identified [1,6]. Normal physical and neurological examination further strengthened our initial suspicion of JME. It is important for clinicians to conduct EEG as soon as possible after a seizure occurs to detect pathological abnormalities in more details [10]. Although cognitive function is usually normal in JME, her marked but stable cognitive impairment might be due to underlying structural abnormalities. Frontal lobe damage can impair attention, memory, language, problem solving, and general compartment (e.g. social behaviors) [11]. Temporal lobe damage can impair semantic, emotional, visual, memory, and visuospatial processing [12]. Hippocampus atrophy can hinder declarative memories [12]. Encephalomalacia cysts might indicate a history of prenatal or perinatal hypoxia which may cause initial neurological damage [13].

She responded positively to VPA. This is consistent with previous studies, which suggest that VPA is superior to most other AEDs for JME treatment [2.6]. Since patients usually respond positively even to low doses, it is better to aim initially for lower doses to minimize its side effects [6]. Every clinician should be careful when informing prognosis in order to set hopeful but realistic expectations. Once an individual becomes seizure-free on AEDs, clinicians should consider prescribing life-long therapy due to a high risk of relapse following drug withdrawal [5].

Meta-analysis identified six prognostic factors for refractoriness: having three seizure types (AS, MS, GCTS), AS, psychiatric comorbidities, earlier age at seizure onset, history of CAE, and praxis-induced seizure [1,5]. Febrile seizure and epileptiform runs ≥3s might also be associated with poor long-term seizure outcome [14]. Found in this patient were the presence of three seizure types, earlier age at onset, and epileptiform runs. Therefore, maintaining seizure control might be difficult. It is crucial to monitor VPA side effects, including weight gain, dysmetabolic syndrome, impaired liver function, tremor, hair loss, and polycystic ovarian syndrome [2].

She has no family history of seizure. Despite being a part of IGE, the term "genetic" is often misconstrued since it refers to the cause and not the inheritance [1]. Although a family history of epilepsy associated with generalized seizures is supportive for making the diagnosis of JME, it is common for patients with IGE not to have a family history of epilepsy [1].

She spends most time in her home due to her fear of being mocked. Untreated, this might lead to anxiety and depression, which are common psychiatric comorbidities in JME [1]. 78% patients with JME also have at least one serious adverse social outcome, such as failure to complete high school, unplanned pregnancy, and unemployment [15]. Child psychiatry

assessment and consultation might be beneficial to increase the quality of life in this situation.

## CONCLUSION

If marked cognitive impairment is present in JME, thorough history-taking can help clinicians discover possible risk factors. Brain imaging can reveal under-lying structural abnormalities, if any. EEG must be conducted as soon as possible after seizure to detect detailed pathological abnormalities. Consultation regarding the possibility of having life-long prescription of AEDs is recommended due to a high risk of relapse following drug withdrawal. Clinicians should also identify prognostic factors and routinely monitor side effects for a better clinical outcome.

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