Late-onset Juvenile Myoclonic Epilepsy or Frontal Lobe Epilepsy with Myoclonus

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To the Editor: The term myoclonus refers to a form of fast, transient, lightning-like muscle twitch that originates in the nervous system. It is usually a manifestation of neurological dysfunction or intractable epilepsy and is clinically divided into cortical myoclonus, spinal myoclonus, physiological myoclonus, etc. It is also categorized as epileptic myoclonus or nonepileptic myoclonus. Juvenile myoclonic epilepsy (JME) is the most common form of epileptic myoclonus, while frontal lobe epilepsy (FLE) with myoclonus is relatively rare. The clinical manifestations of these two forms of epilepsy include shock-like muscle activity appearing in the upper limbs or involving the shoulder and arms together, with irregular and arrhythmic clonus in the morning after waking up that typically results in an involuntary hurtling of objects held in the hands. It is hard to make a distinction between the two conditions clinically. Herein, we report a case of FLE with myoclonus to provide clues to distinguish between the two.

The 38-year-old Chinese female presented at our hospital on September 23, 2015, due to paroxysmal limb shaking accompanied by convulsive seizures for 20 years, which initially manifested as hand tremors at the age of 18 years when she inadvertently dropped a comb while combing her hair early in the morning. She experienced an occasional recurrence of such episodes without unconsciousness. Symptoms typically occurred in the mornings with attacks sometimes occurring in clusters. Generalize tonic-clonic seizure (GTCS) appeared when she was about 23-year-old, she did not take medicine until it occurred frequently in 2012. The episode typically occurred just before retiring to bed in the night and usually triggered by anger and poor sleep. She was diagnosed as a case of myoclonus and treatment with oral levetiracetam (LEV; 500 mg, 2 times/day) initiated. The symptoms were largely alleviated with no attacks experienced from May 2013. After a regular treatment for 18 months, the dose of LEV was reduced to 500 mg once a day and continued till her visit to our center in September 2015. The patient was completely asymptomatic during the time that she was on medication.The patient was born normally without a family history of epilepsy, febrile convulsions, or brain trauma. In the year 2013, 24 h electroencephalogram (EEG) showed occasional sharp slow waves in the frontal zone, in the backdrop of a generally normal EEG tracing [Figure 1a]. Continuous monitoring showed normal at the time of onset of limb tremors [Figure 1b] and normalization of her several subsequent EEG tracing (2014 and 2015). Positron emission tomography-computed tomography (PET-CT) examination showed that the metabolism within bilateral frontal lobes was not uniform while the head magnetic resonance imaging showed normal.

JME is a common type of idiopathic generalized epileptic syndrome with a complex inheritance pattern. The reported incidence of JME in epileptic patients is 5%–11%.[1] The typical clinical picture comprises a triad of absence seizures, myoclonic seizures, and GTCSs. The condition is thought to have an onset in the 8–22 years age bracket, with the average age at onset being 15 years. Disease onset outside of this age bracket has rarely been reported. The initial symptoms include irregular myoclonus of the shoulders and arms that occurs in the morning immediately after waking up and typically manifests as inadvertent dropping of objects from hands. This characteristic sequence of events is considered essential to the diagnosis of JME. Approximately, 85% of patients are known to develop GTCSs several months or years after the onset, while 10%–15% of these patients develop absence seizures.[2] The abnormal rate of 24 h EEG was up to 95.5% and the EEG findings at onset are typically bilateral and synchronous, with 4–6 Hz spikes/multiple spike and slow-wave discharges (SWDs).[2] The frontal lobe is the largest lobe of the brain housing the motor cortex, supplementary motor area, the center for lateral gaze, and the language center. Its anatomical structure and functions are exceedingly complex. FLE is a form of site-associated epilepsy syndrome, and the patients often experience motor deficits, including impaired coordination, decreased dexterity, and poor

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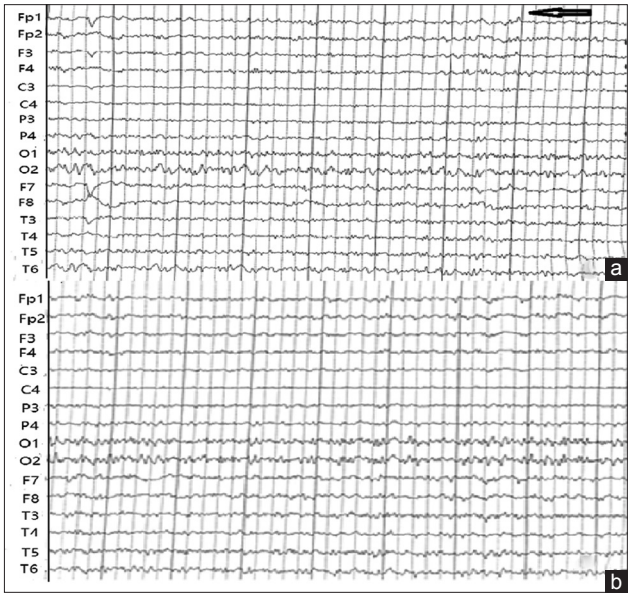

Figure 1: Twenty-four hours electroencephalogram monitoring (May 5, 2013). (a) Electroencephalogram tracing showing normal background activity and occasional sharp slow waves in the frontal area (arrow). (b) Normal electroencephalogram tracing during an episode of limb jitter.

motor planning skills. The International League Against Epilepsy laid down the following diagnostic criteria for FLE:[3] (1) typical clinical manifestations suggesting the involvement of the frontal lobe and (2) epileptic discharge in the frontal lobe during an attack. A long-term video EEG is helpful in determining the seizure type correctly.[4] Other associated clinical symptoms of FLE could indicate the epileptic foci. Attacks of myoclonus associated with FLE involving the motor cortex, though, are rarely encountered. It is characterized by seizures that occur at night or in the early morning, and which tends to get aggravated under conditions of sleep deprivation and exhaustion. The motor involvement may be unilateral or bilateral, and largely involve the facial and distal limb muscles. EEG showed that the abnormal discharges or frontal slow wave activity accompanied by a single sharp wave that is observed in patients with FLE are different from the bilateral spike/multiple spike wave EEG pattern during the intermittence of attack in patients with JME.

In this case, the patient had hand shaking and hurtled items held in her hands. These behaviors were consistent with those typical manifestations of JME. However, the onset was at the age of 18 years, which is different from the common age at the onset of JME. Second, the condition of our case remains stable during the initial 5-year phase of the disease, and this patient was supposed to be secondary GTCS. For epileptic discharges originated from the frontal lobe can spread to the other side or other lobes and induce generalization. This is the reason why FLE is easily misdiagnosed as primary GTCS. The characteristic features of JME include spikes or multiple spike waves, a decline in cognitive and motor function, and morphological changes within frontal lobes with special imaging algorithms. PET studies in patients with JME have shown a decrease in fluorodeoxyglucose in the dorsal lateral prefrontal cortex and premotor area, which indicates a decline in frontal lobe metabolism and activity.[5] This adds to the challenge in distinguishing between the two conditions. In general, the patient showed uniform metabolism in bilateral frontal lobe (PET-CT), occasional sharp slow waves in the frontal zone (24 h EEG), and no typical SWDs or multiple spike waves during episodic hand tremor (documented with video-EEG monitoring). Third, the patient showed multiple myoclonus episodes at night and GTCSs followed by shouting as her condition aggravated. This clinical picture was consistent with FLE more. Besides, she had normal intelligence and physical examination of the nervous system was unremarkable. Finally, the patient readily responded to treatment with LEV, and no recurrence of seizures was experienced after dose-reduction, that was different from JME, in which the withdrawal of the medication was reported to be difficult due to the high frequency of relapse.

Taken together, the patient was diagnosed as a case of FLE with initial myoclonic epilepsy rather than late-onset JME, while the possibility of the coexistence of the two diseases was not considered. FLE is a rare clinical entity that is liable to be easily misdiagnosed. Objective distinction between these two forms of epilepsy is exceedingly important since their treatment and prognosis are different. Drug therapy for JME is useful, though the effect is not sustained after withdrawal. Sodium valproate is the treatment of choice, while carbamazepine and oxcarbazepine are contraindicated due to the associated risk of aggravation of myoclonic seizures. On the other hand, treatment with carbamazepine and oxcarbazepine is effective and considered a routine treatment in patients with FLE, and carbamazepine is also the most effective drug monotherapy in partial epileptic patients.[6] Therefore, it is crucial to accurately identify these conditions to avoid misdiagnosis.

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Conflicts of interest

There are no conflicts of interest.

References

1. Harden C. Juvenile myoclonic epilepsy-what does the future look like? Epilepsy Curr 2014;14:150-1. doi: 10.5698/1535-7597-14.3.150.
2. Akgun Y, Soysal A, Atakli D, Yuksel B, Dayan C, Arpaci B. Cortical excitability in juvenile myoclonic epileptic patients and their asymptomatic siblings: A transcranial magnetic stimulation study. Seizure 2009;18:387-91. doi: 10.1016/j.seizure.2009.02.002.
3. Lazow SP, Thadani VM, Gilbert KL, Morse RP, Bujarski KA, Kulandaivel K, *et al.* Outcome of frontal lobe epilepsy surgery. Epilepsia 2012;53:1746-55. doi: 10.1111/j.1528-1167.2012.03582.x.
4. Braakman HM, Vaessen MJ, Jansen JF, Debeij-van Hall MH, de Louw A, Hofman PA, *et al.* Pediatric frontal lobe epilepsy: White matter abnormalities and cognitive impairment. Acta Neurol Scand 2014;129:252-62. doi: 10.1111/ane.12183.
5. Swartz BE, Simpkins F, Halgren E, Mandelkern M, Brown C, Krisdakumtorn T, *et al.* Visual working memory in primary generalized epilepsy: An 18FDG-PET study. Neurology 1996;47:1203-12. doi: 10.1212/WNL.47.5.1203.
6. Zhu F, Lang SY, Wang XQ, Shi XB, Ma YF, Zhang X, *et al.* Long-term effectiveness of antiepileptic drug monotherapy in partial epileptic patients: A 7-year study in an Epilepsy Center in China. Chin Med J 2015;128:3015-22. doi: 10.4103/0366-6999.168968.