Autosomal dominant cortical tremor, myoclonus, and epilepsy (ADCME): Probable first family from India

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Abstract

Autosomal dominant cortical tremor, myoclonus, and epilepsy (ADCME) is an extremely rare syndrome characterized by familial occurrence of postural and action-induced tremors of the hands but showing electrophysiologic findings of cortical reflex myoclonus. Patients also have cognitive decline and tonic-clonic seizures, often precipitated by sleep deprivation or photic stimulation. We describe probably the first family from India of this ill-defined syndrome.

Key Words

Cortical tremor, myoclonus, photic stimulation

Introduction

The association of hereditary tremor and epilepsy was first described in a Japanese family.\(^1\) In 1990, Ikeda reported sporadic cases of “tremor” consisting of irregular distally prevailing twitches of the limbs associated with seizures.\(^2\) Familial cases of cortical tremor and epileptic seizures, representing autosomal dominant inheritance, were initially described as “familial cortical myoclonic tremor.”\(^3\) Subsequently, these symptoms were recognized as an idiopathic syndrome that was renamed benign adult familial myoclonic epilepsy (BAFME).\(^4\) and Japanese families were linked to chromosome 8q23.3-q24.1.\(^5\) The disease usually has a benign course, although drug-resistant partial seizures or slight mental retardation occurs in some cases. A worsening of cortical tremor and myoclonus is common in advanced age. We describe a family with tremors, myoclonus, tonic-clonic seizures precipitated by sleep deprivation and photic stimulation and worsening of myoclonus with advanced age and cognitive decline with advanced age. This is to our knowledge the first family of autosomal dominant cortical tremor, myoclonus, and epilepsy (ADCME) from India.

Report of cases

The pedigree of the family is shown in Figure 1; there was no consanguinity between parents.

Case Reports

Case 1 (III-2) (index case)

A 65-year-old male, a farmer by occupation, with normal birth and developmental history presented with 30-year duration of nonprogressive postural and action tremors of the fingers. There was no ataxia of limb or stance. These tremors did not interfere with his tasks of daily living. Since past 5 years he started having myoclonic jerks, which were present both in limbs and axial musculature. The myoclonic jerks were more frequent at night and were precipitated by sleep deprivation. He also had severe photic stimulation sensitive tonic-clonic seizures, often precipitated by sleep deprivation or photic stimulation. These seizures were often precipitated by sleep deprivation or photic stimulation. The disease usually has a benign course, although drug-resistant partial seizures or slight mental retardation occurs in some cases. A worsening of cortical tremor and myoclonus is common in advanced age. We describe a family with tremors, myoclonus, tonic-clonic seizures precipitated by sleep deprivation and photic stimulation and worsening of myoclonus with advanced age and cognitive decline with advanced age. This is to our knowledge the first family of autosomal dominant cortical tremor, myoclonus, and epilepsy (ADCME) from India.
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Case 3 (V-1)

A 20-year-old male, son of the patient described in case 2, had a normal birth and developmental history. He presented with a 5-year history of nonprogressive postural and action tremors of the fingers. He also has history of myoclonic jerks since 3 years, which are more on awakening and on exposure to bright light. He also has tonic-clonic seizures that are more on sleep deprivation. The seizures are well controlled on antiepileptic drugs in form of sodium valproate. There is no limb or gait ataxia. There is no cognitive decline. The clinical examination is normal except for action and postural tremors and presence of myoclonic jerks. MRI brain is normal. EEG showed paroxysm of sharp and slow wave complexes mostly localized over posterior regions. IPS at frequencies between 10-25 Hz triggered generalized spike and wave complexes.

The cases V (2,4) are affected in the form of action and postural tremors of the fingers, myoclonic jerks that are not stimulus sensitive, and seizures that are generalized tonic-clonic type. The seizures are well controlled on sodium valproate.

The patient IV (2) has similar phenotype as IV (1).

The patient II (1) had tremors of upper limbs, myoclonic jerks, and seizures in form of generalized tonic-clonic type. He died of cardiac arrest. He was never investigated for the disease.

The patient I (1) had only tremors of fingers. Detailed history of myoclonic jerks and seizures was not present. She was never investigated for the disease.

Discussion

The association of ADCME was first recognized in Japanese families and is now increasingly reported worldwide. Despite being a well-delineated condition with remarkable features, it is not officially recognized from International League Against Epilepsy (ILAE), and its nosologic placement is still debated. Its clinical features (age of onset, seizure types, occurrence on awakening) are different from those of juvenile myoclonic epilepsy and other idiopathic generalized epilepsies. The lack of rapid cognitive decline and the less severe and prolonged clinical course distinguishes this syndrome from progressive myoclonic epilepsies.

In a study by Coppola et al.,[6] were described clinical, electrophysiologic, and treatment data of 14 patients (age group 11-80 years) from three families with ADCME. Cortical tremors and myoclonic jerks were present in 71.4% of the patients. Myoclonic jerks were of minor severity at the beginning of the disease, but with age myoclonic jerks increased in severity and led to progressive impairment of activities. Seizures in form of tonic-clonic seizures, precipitated by sleep-deprivation, or photic stimulation were present in 42.8% of their patients. Generalized anxiety disorder was present in 42.8 % of their patients, but none of the patients had cognitive decline.

In a study by Maurizio et al.,[7] was described a European family with cortical tremor, epilepsy, and mental retardation, the pedigree of which indicates an autosomal dominant inheritance of the disease. The EEG showed diffuse spike-and-wave complexes and/or posterior spikes and a photoparoxysmal response in the four subjects.
In a study by Elena et al.,[8] they studied a large Italian family of 23 members. Of these, 16 members were affected in form of rhythmic cortical myoclonic jerks, seven members had photic-induced myoclonic jerks, and epilepsy was present in five of the patients. Most of their patients had behavior abnormality but none had cognitive impairment.

In the Indian family described by us, eight members out of a total 24 are affected in five consecutive generations. The pattern of inheritance seems to be autosomal dominant as members of both sexes are affected and no generation is spared. All the affected members have tremors that are action and postural tremors and are nonprogressive in nature. Cortical tremor is the term coined by Ikeda et al.,[2] to define action and postural tremors, often accompanied by seizures, characterized by giant somatosensory-evoked potentials (SEPs), enhancement of C-reflex, and premyoclonic jerks spike detected by means of jerk-locked-average method. We were not able to do these detailed electrophysiological studies in our patients, and this is a drawback of our study.

Photosensitive myoclonic jerks were present in at least four out of the eight (50 %) of the affected members. The myoclonic jerks seemed to progress in severity with age as was seen in patients III (2), IV (1), IV (2).

Seizures in form of generalized tonic-clonic type were present in at least seven out of the eight (87.5%) affected patients. We got the EEG record in three affected members, and all of them showed paroxysm of sharp and slow wave in the posterior leads, with generalized spike and slow wave discharges on IPS. The seizures in all affected members were well controlled with sodium valproate.

Cognitive decline in form of executive dysfunction and recent memory loss was present in at least three affected members but was mild in two of them: IV (1), IV (2), and severe in one (III-2). There were no significant behavior changes in any of the other affected members.

To our knowledge this is probably the first family of ADCME from India. The genetic background of this condition is heterogenous. Japanese families are linked to 8q24 and Italian to 2p11.1-q12.2.[2] However, no causative genes have been identified. As no definite genetic locus for this disease has till now been found, we could not get a definite genetic proof of this disease.

This case report highlights the following points:

ADCME is an extremely rare syndrome, and a family of this has probably never been reported from India.

The presence of postural and action tremor, stimulus-sensitive myoclonus, tonic-clonic seizures precipitated by sleep deprivation, and photic stimulation and cognitive decline late in the course of the disease are its core features.

The good response of seizures and myoclonus to drugs and its relative benign course helps to differentiate this syndrome from other progressive myoclonic epilepsies.

In conclusion, we describe the data for a age-dependent progression and alongside the already-reported clinical features the presence of cognitive decline in this unique and rare syndrome.

References

1. Wakeno M. A family with heredofamilial tremor associated with epileptic disorders. Seishin Shinkeigaku Zasshi 1975;77:1-18.
2. Ikeda A, Kakigi R, Funai N, Neshige R, Kuroda Y, Shibasaki H. Cortical tremor: A variant of cortical reflex myoclonus. Neurology 1990;40:1561-5.
3. Terada K, Ikeda A, Mima T, Kimura M, Nagahama Y, Kamioka Y, et al. Familial cortical myoclonic tremor as unique form of cortical reflex myoclonus. Mov Disord 1997;12:370-7.
4. Yasuda T. Benign adult familial myoclonus epilepsy (BAFME). Kawasaki Med J 1991;17:1-13.
5. Plaster NM, Uyama E, Uchino M, Ikeda T, Flanigan KM, Kondo I, et al. Genetic localization of the familial adult myoclonic epilepsy (FAME) gene to chromosome 8q24. Neurology 1999;53:1180-3.
6. Coppola A, Santulli L, Del Gaudio L, Minetti C, Striano S, Zara F, et al. Natural history and long-term evolution in families with autosomal dominant cortical tremor, myoclonus, and epilepsy. Epilepsia 2011;52:1245-50.
7. Elia M, Musumeci SA, Ferri R, Scuderi C, Del Gracco S, Bottitta M, et al. Familial cortical tremor, epilepsy, and mental retardation: A distinct clinical entity? Arch Neurol 1998;55:1569-73.

8. Gardella E, Tinuper P, Marini C, Guerrini R, Parrini E, Bisulli F, et al. Autosomal dominant early-onset cortical myoclonus, photic-induced myoclonus, and epilepsy in a large pedigree. Epilepsia 2006;47:1643-49.

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