



## Case Report

# Juvenile Huntington's disease masquerading as progressive myoclonus epilepsy



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## ABSTRACT

Juvenile Huntington's disease (JHD) has an onset before 20 years of age, and is characterized by behavioural issues, epilepsy, rigidity, bradykinesia and dystonia. It contributes to 0.5–5% of all Huntington disease (HD) cases. JHD demonstrates a more rapid progression and is characterised by dystonia, as opposed to the slow progression with predominant chorea seen in adult-onset HD. Seizures are described in 38% of JHD as compared to 2% in the adult onset HD. The different types of seizures reported in JHD are generalized seizures, myoclonus, absence seizures and less commonly tonic and focal seizures with impaired awareness. JHD patients have good seizure control initially and develop drug-resistant epilepsy in the later stages of the disease which is rarely reported. Here, we report the case of a 13-year-old boy, who initially presented with generalized tonic-clonic seizures followed by myoclonic jerks, with subsequent cognitive decline, ataxia, involuntary movements and drug resistant epilepsy mimicking a progressive myoclonus epilepsy. His EEG changed from normal background with generalized interictal epileptiform discharges to diffuse slowing with fast activity devoid of epileptiform activity to reflect electroclinical evolution of the disease process.

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## Introduction

Huntington's disease (HD) is a neurodegenerative disorder of autosomal dominant inheritance, beginning in midlife and characterized by movement disorder, mood and personality changes, followed by cognitive decline. In contrast, Juvenile Huntington's disease (JHD) presents before 20 years of age and is characterized by behavioral issues, epilepsy, rigidity, bradykinesia and dystonia [1,2]. Overall JHD is thought to account for 0.5–5% of all HD cases, 20% of which has an onset, at or before 10 years of age [3]. HD and JHD are both caused by the expansion of CAG trinucleotide repeat within the first exon of the huntingtin gene (IT-15) on the short arm of chromosome 4 [1,4]. CAG trinucleotide repeat length is >60, usually in the range of 80 to 100 in JHD compared to more than 36 in HD [4,5]. In this way, JHD has a high expansion range, more rapid progression of disease and dystonia in contrast to HD. Seizures are reported in 38% of individuals with JHD, which can be generalized seizures, myoclonus, absence seizures and less

commonly tonic seizures and focal seizures with impaired awareness [6]. The exact mechanism of seizures in JHD is not known but current thinking is that seizures are secondary to primary neuronal degeneration and changes in striatal synapses [7]. Here, we report the case of a 13-year-old boy, who initially presented with generalized tonic-clonic seizures followed by myoclonic jerks suggesting genetic generalized epilepsy. He subsequently developed cognitive decline resembling the progressive myoclonus epilepsies, with chorea appearing very late in the disease course.

## Case

## Presentation

A thirteen-year-old boy, born of non-consanguineous marriage with normal birth and development history presented at five years of age with a single generalized tonic-clonic seizure. He had a normal neurological examination, and EEG and MRI brain were also normal. He was initially started on oral levetiracetam, which was changed to valproate after 6 months following a second generalized seizure. He remained seizure-free for four years on valproate monotherapy. By 10 years of age, he started demonstrating

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hyperactivity and behavioural issues like irritability, aggressive behavior and stubbornness. Around the same time, he also developed myoclonic jerks and sudden forward falls, which were infrequent initially, but increased to multiple daily episodes the following year. There was further deterioration manifesting as ataxia, frequent falls, decreased word output and cognitive decline, due to which he dropped out from the 6th grade. Neurological examination at the time revealed intermittent myoclonic jerks with hypotonia, brisk reflexes and ataxia in the context of hyperactive behaviour. His fundus examination was normal. Prolonged video EEG showed, slowing of background activity with frontally dominant generalized spike- and polyspike-and-wave discharges, 3-Hz generalized spike-wave discharges with a photoparoxysmal response and bilateral independent occipital spikes. Multiple myoclonic jerks were recorded with EEG showing frontally dominant generalized discharges (see Fig. 1). In view of epilepsy with myoclonic jerks, and cognitive decline with above mentioned EEG changes a diagnosis of a progressive myoclonus epilepsy (PME) like Lafora body disease (LBD), myoclonic epilepsy with ragged red fibres (MERRF syndrome), dentatorubral pallidoluysian atrophy (DRPLA), neuronal ceroid lipofuscinosis (NCL), subacute sclerosing panencephalitis (SSPE) and sialidosis were considered [8]. Further evaluation for PME was planned but he failed to follow up until six months later wherein he had developed chorea and intermittent leg dystonia with further worsening of cognition. His repeat MRI brain showed caudate and lentiform nuclei atrophy with FLAIR hyperintensity as well as cerebral and cerebellar atrophy (Fig. 2). In the presence of behavioral issues, myoclonus, chorea and imaging features, a diagnosis of Huntington's disease was considered. His genetic study showed the presence of 81 CAG repeats. His father was living separately from the family for the last six years, so available family history was limited. After a diagnosis of the index case, on inquiry, it was found that the father was also demonstrating some abnormal movements of limbs and gait issues for the past

year. This confirmed the phenomenon of genetic anticipation with early onset of HD in the index case.

Further along the disease course, he continued to worsen with weekly generalized seizures despite the combination of multiple antiseizure medications like valproate, lamotrigine, levetiracetam, and clobazam. His follow up EEG, ten months later, showed significant slowing of background activity with bilateral occipital delta intermixed with fast activity and focal occipital discharges without any generalized discharges as compared to the first EEG (Fig. 3).

### Discussion

Our patient with JHD presented with generalized seizures and myoclonus in the early stages of illness, followed by cognitive decline and chorea relatively late into the illness, mimicking PME. A systematic review by Cronin et al. reported seizures as the presenting feature in 15% of cases of JHD [9], previously thought to be a rare presenting feature. In the study by Cloud et al., generalized tonic-clonic seizures were the most common seizure type in JHD followed by myoclonic, tonic seizures and multiple seizure types that were described in the same individual [6]. Our patient had generalized tonic-clonic seizures as the presenting feature and later manifested multiple seizure types. Initially, the child had only two episodes of seizures and responded well to a single antiepileptic medication without any cognitive decline. An age-specific genetic generalized epilepsy like juvenile myoclonus epilepsy (JME) was considered after the onset of myoclonus and some cognitive impairment. JME cases usually demonstrate normal background activity in EEG with frontally dominant generalized discharges and photosensitivity with good response to valproate. The cognitive dysfunction in JME is usually executive dysfunction [10] while HD, is characterised by additional impairment of emotional expression, learning and working memory along with language dysfunction which is progressive [4,11].

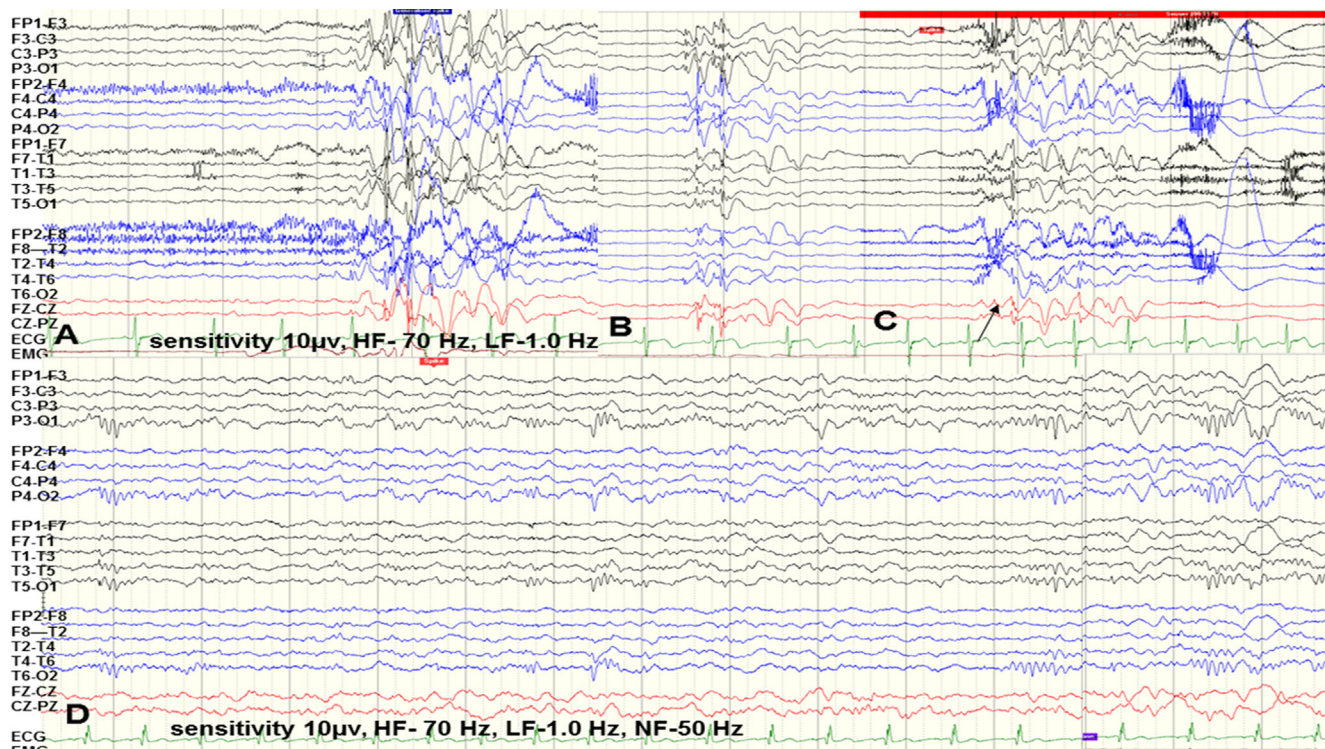
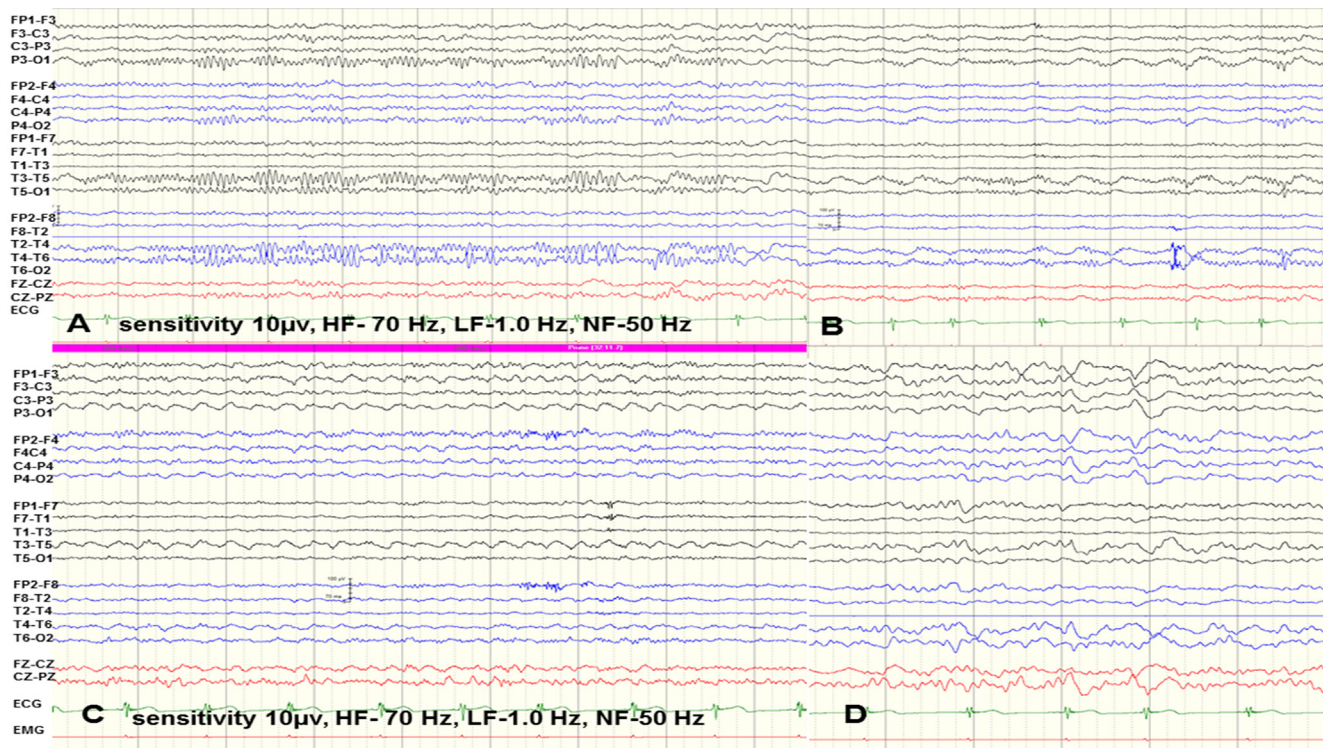
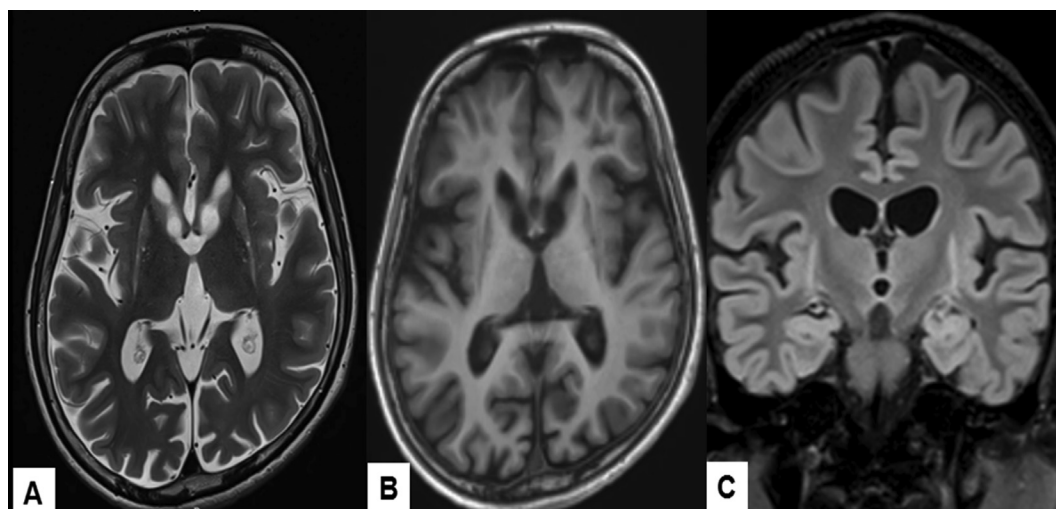


Fig. 1. EEG in bipolar montage sensitivity 10µv, HF- 70 Hz, LF-1.0 Hz, NF-50 Hz. (A) Frontally dominant 3–3.5 Hz generalized spike- and polyspike-and-wave discharges (B) Generalized frontally dominant spike wave discharges (C) Myoclonic jerk (arrow) correlating with burst of frontally dominant spike, polyspike wave discharge (D) Bilateral occipital spikes and rhythmic spikes.



**Fig. 2.** Follow up EEG Bipolar montage sensitivity 10µv, HF- 70 Hz, LF-1.0 Hz, NF-50 Hz A) Bilateral occipital fast activity B) bilateral occipital delta rhythm intermixed with fast activity and spikes C) Generalized delta activity predominantly over occipital region D) sleep record with vertex waves.



**Fig. 3.** A) T2 W axial image showing caudate and lentiform nuclei atrophy with lentiform nuclei hyperintensity as well as cerebral atrophy B) T1 W axial image showing caudate and lentiform nuclei atrophy with corresponding lentiform nuclei hypo intensity C) FLAIR coronal image showing diffuse brain volume loss involving both grey and white matter along the cerebral hemispheres, including marked bilateral caudate and putaminal atrophy with bilateral putamen FLAIR hyperintensities and mild dilated 3rd ventricle.

His further deterioration with behavioral issues, myoclonus, ataxia and cognitive decline, pointed towards PME like Lafora body disease (LBD), MERRF syndrome, DRPLA, NCL, SSPE, and sialidosis. LBD patients have behavioral changes, depression along with myoclonus, ataxia, cognitive decline and normal MRI with spikes, poly-spikes and generalized epileptiform discharges with photosensitivity on EEG and autosomal recessive inheritance. MERRF on the other hand, involves features of neuropathy, myopathy, cardiomyopathy or hearing loss, in addition to seizures and cognitive decline. DRPLA has onset before the age of twenty with

seizures, myoclonus, ataxia, behavioural issues and progressive intellectual deterioration with later choreoathetosis movements like seen in our patient. NCL was excluded in the absence of visual symptoms and optic atrophy as was sialidosis because a cherry-red spot macula and gaze palsy were absent. In SSPE, EEG has characteristic generalized periodic discharges which were absent in our patient [8].

EEG characteristics in JHD have been rarely described in the literature, with details pertaining to the progression in EEG over time largely absent. The reported EEG characteristics are from normal

EEG to generalized spike-polyspike-and-wave discharges, focal or multifocal epileptiform discharges, specifically bilateral parieto-occipital discharges and focal occipital discharges, 3-Hz spike-and-wave discharges as well as paroxysmal slowing [6,12–15]. In our patient, EEG was normal initially and subsequently showed background slowing with focal and generalized discharges with photosensitivity suggestive of PME. Only seven out of 24 patients described in a study by Landau et al, had photosensitivity but confirmed genetic diagnosis was not available for every case [14]. The exact mechanism of photosensitivity is not known but it is largely thought to be owing to reduced connectivity between the prefrontal and frontopolar regions with increased connectivity between an occipital and supplementary motor area with expression through the striato-thalamocortical system [16].

The MRI finding of JHD includes atrophy of the caudate nucleus and increased signal intensity on T2-weighted imaging in the basal ganglia and thalamus with nonspecific subcortical hyperintensities in a few cases and ventriculomegaly in the late stage of the disease. Also, volume loss in basal ganglia, thalami, hippocampi, substantia nigra, and cerebellum have been described [2,17]. Our patient had similar imaging features on repeat MRI scan. There are no distinguishing imaging features between JHD and HD.

In the study by Sipilä et al, the prevalence of epilepsy in adult-onset HD was similar to the general population (around two percent) and was easily controlled with antiseizure medication [18]. Seizures in JHD are well controlled in the initial stage of the disease and become drug-resistant in the later stages of the disease. Although valproate is found to be the most effective drug, other commonly used antiseizure medications are phenytoin and carbamazepine, with clonazepam, ethosuximide, gabapentin, zonisamide, and lamotrigine being less commonly used [2]. In the report by Khair et al, the combination of oxcarbazepine, levetiracetam, and clobazam proved to be the most successful [13].

In a study by Gambardella et al, a patient who presented with PME-like features had a good response to valproate with the EEG showing generalized and focal discharges without photosensitivity [12]. In comparison, our patient had drug-resistant epilepsy and EEG showed generalized epileptiform discharges with photosensitivity. His follow-up EEG showed further worsening with diffuse slowing with fast activity devoid of epileptiform activity suggesting further evolution of the disease, similar to SSPE, where there is loss of periodic discharges with slowing of background activity, in advanced stages of the disease. This progression of EEG in JHD has not been described. Early diagnosis avoids further searching for the etiology of epilepsy, unnecessary tests and parental anxiety in addition to providing proper treatment to improve patient care.

## Conclusion

Our case highlights the importance of considering JHD in the differential diagnosis of patients with clinical and EEG features of progressive myoclonus epilepsy. In our patient the EEG changed from normal background with generalized interictal epileptiform discharges to diffuse slowing with fast activity devoid of

epileptiform activity to reflect electroclinical evolution of the disease process.

## Ethical publication statement

'We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.' Written informed consent for publication has been obtained from patient's mother.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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