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Case report

Autistic features in Unverricht–Lundborg disease

Ruchika Tandon, Sunil Pradhan *

Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow 226014, India

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ABSTRACT

We studied three patients with Unverricht–Lundborg disease for autistic features along with other clinical features associated with progressive myoclonus epilepsy.
We diagnosed this disease based on noise and touch sensitive myoclonus, ataxia, cognitive decline, typical EEG features, normal MRI of the brain and applied Children's Global Assessment Scale and Childhood Autism Spectrum Test to these children.
The CGAS score was 35 in two and 50 in one of them. CAST scores were above 15 in all of three of them.
Autistic features may be an important clinical feature of this disease. History and physical examination for myoclonus should probably be taken in autistic children.

1. Introduction

Unverricht–Lundborg disease is an autosomal recessive progressive myoclonus epilepsy characterized by onset at the age of 6–15 years, severe incapacitating stimulus-sensitive progressive myoclonus, tonic–clonic seizures, absence seizures and characteristic abnormalities in the electroencephalogram (EEG) [1–3]. Neuropsychiatric disturbances are a recognized feature of Unverricht–Lundborg disease [4]. However, autistic features have not recived much detail in these patients. Autistic features may however be co-associated with epilepsy [5]. Hence, we studied three patients with this disease for autistic features along with other clinical features.

2. Case series

The study was conducted on patients with Unverricht–Lundborg disease who presented to Sanjay Gandhi Post Graduate Institute of Medical Sciences in Lucknow, India. The patients were diagnosed due to myoclonic seizures triggered by loud noise and tactile stimulation along with ataxia and cognitive decline, electroencephalogram changes of intermittent transient slowing and generalized epileptiform discharges along with a normal MRI scan [6]. We applied the Children's Global Assessment Scale to assess the level of function in these patients [7]. Treatment included antiseizure drugs and comorbid symptom management. The ages of the children ranged between 3 years and 15 years and the age at onset of seizures was between 1 year and 15 years. Two patients had atonic seizures in addition to generalized tonic-clonic seizures (GTCS). Triggers included flickering lights, movement and vibration in one patient and scolding in none of them. Hyperactivity was present in two children and mental retardation was moderate in one and mild in the other two. Children's Global Assessment Scale score was 35 in two of the children and 50 in one of them (range 1–90; high scores reflect better function). Psychiatric features included running amok, wandering, inappropriate smiling, depression and violent behavior (Table 1). Cranial nerve involvement (left facial palsy and decreased visual acuity) was present in one patient, and sensorineural hearing loss occurred in the other child. All of them exhibited spasticity and hyperreflexia. Fig. 1 shows EEG changes for one of the patients. There was a partial response to antiseizure drugs in two patients and one of them responded poorly to treatment (Table 1). Antiseizure drugs utilized included sodium valproate, zonisamide, clonazepam and levetiracetam. GTCS were controlled in two of the patients and atonic and myoclonic seizures showed partial response to treatment.

We suspected autism on the basis of absent eye contact, avoidance behavior and absence of attachment to their parents. Subsequently, we assessed these children using the Childhood Autism Spectrum Test (CAST), which yielded a score of >15 in all the three children (Table 2) [8]. Hence, they were classified as having autism.

3. Discussion

In this study, the ages of children ranged between 3 years and 15 years and the age at the onset of seizures ranged between 1 year and 15 years consistent with previous studies [6]. Myoclonic seizures are a presenting symptom in most of the patients [9]. In the present study, myoclonic jerks were the first clinical feature in two patients. Various stimuli like noise, light or touch may trigger myoclonic jerks in these patients [1,6,10]. Our patient's had myoclonus aggravated by

* Corresponding author.
E-mail address: drspradhan@rediffmail.com (S. Pradhan).

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Table 1
Demographic and clinical features of patients of Unverricht-Lundborg syndrome.

Patient number	1	2	3
Age	11 years	15 years	3 ½ years
Age at onset of myoclonic seizures	3 years	15 years	3 years
Age at onset of atonic seizures	1 year	13 years	–
Age at onset of GTCS	10 years	–	3 ½ years
Frequency of GTCS	Around once every 3 months	–	Around once every 15 days
Frequency of myoclonic seizures	200–300 episodes per day	Hundreds of episodes per day	Approximately 200 episodes per day
Triggered by loud noise	Yes	Yes	Yes
Triggered by touch	Yes	Yes	Yes
Triggered by flickering lights	No	Yes	No
Triggered by scolding	No	No	No
Triggered by movement	No	Yes	No
Triggered by vibration	No	Yes	No
Hyperactivity	Yes	No	Yes
Children's Global Assessment Scale	50	35	35 ???
Psychiatric features	??? Running amok, wandering, smiles often	Depression	Violent, fights, bites
Intelligence Quotient (range)	70–79	80–89	80–89
Cranial nerves	None affected	Left facial palsy partially decreased visual acuity	Bilateral profound sensorineural hearing loss
Motor system	Generalized weakness, hyperreflexia	Hyperreflexia	Spasticity, hyperreflexia
Cerebellar signs	Gait ataxia	Gait ataxia, cerebellar signs present in upper limbs	Gait ataxia
BAER	–	–	Bilateral profound hearing loss
EEG	Intermittent transient slowing	Intermittent transient slowing	Generalized epileptiform discharges
MRI	Normal	Normal	Normal
Response to treatment	Partial	Poor	Partial

flickering lights, movement and vibration as triggering factors in one patient and scolding in none of them. We noted that vibration was able to trigger myoclonus. This stimulus has not received attention as a trigger for myoclonus. We found comorbidities of hyperactivity in two children, impaired function, and mental retardation and behavioral features in our cohort similar to prior reports [2–4,11]. Our patients had only a partial response to antiseizure drug treatment as expected in Unverricht–Lundborg disease [2].

Autistic features seen in our patients are a new comorbidity that has not been detailed in the past to our knowledge. This was severe in the

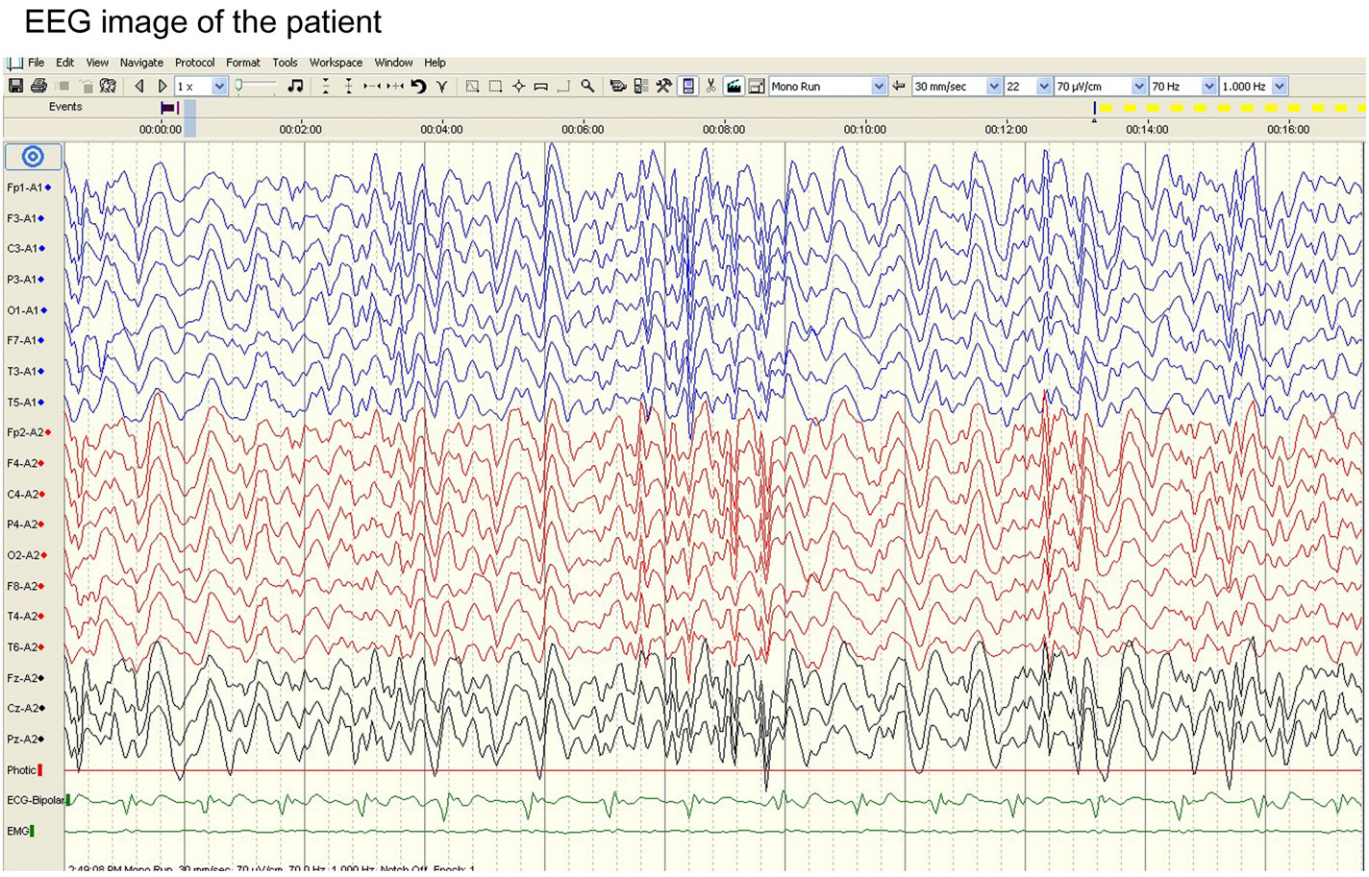

Fig. 1. EEG of a patient with Unverricht–Lundborg disease.

Table 2
Autistic features in Unverricht–Lundborg syndrome.

Main autistic features drawing attention to the presence of autism	No response to commands, not attached to parents	Avoids strangers, no eye contact	Not attached to parents, runs amok but maintains eye contact
Childhood Autism Spectrum Test (CAST)	20	21	17

diagnosis of autism as judged by the Childhood Autism Spectrum Test. Hence, we recommend assessing autistic features in patients with Unverricht-Lundborg disease. This may be an important comorbid clinical feature in patients with the disease and may also suggest a possible overlap between autism spectrum and other progressive myoclonus epilepsies. Conversely, obtaiing a history of myoclonus in children who present with autism may help elucidate the diagnosis. Further study involving more patients may help in defining the true incidence of autism in the Progessive Myoclonus epilepsies.

Declaration of Competing Interest

None.

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