Case Report

Myoclonic status misdiagnosed as movement disorders in Rett syndrome: A video-polygraphic study

Giuseppe d’Orsi*, Vincenzo Demaio, Mauro G. Minervini

Epilepsy Center, Neurological Unit, Casa Divina Provvidenza, Opera Don Uva, Via Bovio 78, 70052 Bisceglie (BAT), Italy

ABSTRACT

Myoclonic jerks and myoclonic status (MS) are sometimes difficult to distinguish clinically from movement disorders such as hand stereotypies, tremor, and dystonia in Rett syndrome. We describe a rare and complete video-polygraphic study of a girl with Rett syndrome (MECP2 mutation) and MS misdiagnosed as movement disorders and disclosed after video-polygraphic recordings. Corresponding to closely recurring activity of diffuse spike and polyspikes–wave-type paroxysms, rhythmic and, especially, arrhythmic myoclonias, usually asymmetrical and asynchronous, involving mainly right muscle deltoid and rarely followed by an inhibitory phenomenon, appeared. The MS improved and, most importantly, disappeared after the use of levetiracetam, with an evident antimyoclonic efficacy and a marked improvement of daily life for the patient and her caregivers. The difficulty in differentiating some typical nonepileptic behavioral features and movement disorders of patients with Rett syndrome from seizures was overcome using prolonged video-polygraphic recordings in our case.

1. Introduction

Recently, Caraballo et al. [1] described the electroclinical features of myoclonic status (MS) in nonprogressive encephalopathies as characterized by the recurrence of long-lasting status associated with absences and myoclonias, mixed with other abnormal movements; the etiology is mainly genetic (Angelman syndrome and 4p syndrome) and developmental cortical malformations. Of seven patients with epilepsy and Rett syndrome (RTT) with a proven MECP2 mutation, we report a rare and complete video-polygraphic study of a girl whose clinical manifestations and polygraphic features were compatible with MS and were misdiagnosed as movement disorders.

2. Case study

The patient was an 8-year-old girl with a psychomotor development that was normal until the age of 12 months, but then progress stagnated, and it became difficult to get in touch with her. From the age of 18 months, she developed movement disorders, including hand stereotypies, tremor, and dystonia; moreover, the child experienced paroxysmal episodes of hyperventilation and apnea during wakefulness. She became severely retarded with autistic traits and, at the age of 2, was diagnosed as having RTT with a truncating nonsense mutation in the MECP2 gene. When she was 3 and 4, during nocturnal sleep, she had repetitive generalized tonic-clonic seizures, resistant to rectal diazepam. Focal seizures (brief loss of contact) also started at age 4, and the decision was made to initiate treatment with carbamazepine (200 mg/day), which she tolerated well, resulting in a 3-year seizure-free period. At the age of 7, she was admitted to our epilepsy center because her condition had insidiously deteriorated; the parents noticed progressive deterioration of contact, and the child had become more and more ataxic with jerks in the extremities, predominantly asymmetrical and asynchronous, misdiagnosed as movement disorders and nonepileptic behavioral features. In fact, subcontinuous myoclonic jerks were intermingled with hand stereotypies, tremor, and dystonia, and a firm diagnosis of MS could be established using prolonged video-polygraphic recordings (polygraphic parameters: EEG; electromyographic activity from right and left deltoid muscles, right and left flexor and extensor hand muscles, right and left tibialis anterior muscles; ECG; thoracic respiration). The EEG showed closely recurring activity of diffuse spike and polyspike–wave-type paroxysms, involving mainly the anterior regions, intermingled with multifocal spikes, occasionally resulting in spike–wave complexes, predominant in frontocentral regions. From the electromyographic point of view, corresponding to the diffuse paroxysms, rhythmic and, especially, arrhythmic myoclonias, usually asymmetrical and asynchronous, involving mainly right deltoid muscle and rarely followed by an inhibitory phenomenon, appeared (Fig. 1). Because myoclonic jerks were intermingled with movement disorders, and especially with hand stereotypies, the...
misdiagnosis could be justified. This “epileptogenic encephalopathy,” which insidiously arose a few months before, was resistant to intravenous benzodiazepine, phenytoin, and steroids, and persisted after withdrawal of carbamazepine. Consequently, oral levetiracetam (LEV) was added at 500 mg and increased to 1000 mg/day over the next 7 days. The MS improved significantly after approximately 48 h of receiving LEV (500 mg/day) and disappeared completely after 8 days (LEV 1000 mg/day) (Fig. 2); the deterioration of contact also improved and the patient could walk. LEV totally controlled epileptic seizures, and was maintained during follow-up because of the favorable combination of efficacy and tolerability.

3. Discussion

Children affected by MS usually have myoclonic–astatic epilepsy [2] and, alternatively, a peculiar form of myoclonic epilepsy in nonprogressive encephalopathies [3] or genetic etiology such as Angelman syndrome [4] and 4p syndrome [5]. MS recognition is more difficult in these cases because it develops insidiously in previously hypotonic patients who become more and more hypotonic and often dystonic, and only close observation combined with prolonged polygraphic recording reveals the deterioration that results from MS. The electroclinical features are characterized by myoclonic absences and rhythmic myoclonias, and a refractoriness to different antiepileptic drugs including ACTH is often evident [1]. Nevertheless, several authors have described a quite electroclinical picture of MS in patients with Angelman syndrome and 4p syndrome [4,5], but few of them have stressed the electroclinical picture in RTT with MECP2 mutations [1]. In our patient with RTT, peculiar clinicopolygraphic features of MS were subcontinuous jerks, at times rhythmic or arrhythmic, and absences with myoclonic components corresponding to diffuse paroxysms. Subcontinuous myoclonic jerks were difficult to distinguish clinically from hand stereotypes, tremor, and dystonia, and in our case a firm diagnosis could be established using prolonged video-polygraphic recordings. In fact, RTT is one of the best human conditions in which to study movement disorders such as hand stereotypes, tremor, chorea, myoclonus, ataxia, and dystonia [6]. In particular, myoclonus has been estimated to occur in about 50% of patients with RTT older than 4 years [7] who usually show a distinctive pattern of cortical reflex myoclonus with prolonged intracortical delay of the long-loop reflex [8]. Despite its high frequency, myoclonus has a highly variable severity, never representing a prominent clinical feature. Moreover, an early-onset epileptic encephalopathy in infancy that evolves into myoclonic seizures in childhood has been described in three girls with a mutation of the CDKL5 gene [9]. MS is rarely recognized and often misdiagnosed [1]. Our case highlighted the difficulty of differentiating movement disorders from seizures and proved the usefulness of prolonged video-polygraphic recordings in studying patients with RTT. Drugs such as carbamazepine, vigabatrin, and lamotrigine may precipitate MS due to myoclonic–astatic epilepsy and severe myoclonic epilepsy in infancy [10,11]. In our case, we ruled out the involvement of carbamazepine in MS. In fact, this “epileptogenic encephalopathy” was resistant to intravenous benzodiazepine, phenytoin, and steroids and, most importantly, persisted after withdrawal of carbamazepine. Finally, benzodiazepines and steroids were only transiently effective; the status proved to be refractory to different antiepileptic drugs. In some cases, valproate associated with ethosuximide may improve MS [1]. In our case, the MS improved and, most importantly, disappeared after the administration of LEV, with an evident antmyoclonic efficacy and a marked improvement of daily living for the patient and her caregivers. Because of the favorable combination of efficacy and tolerability, LEV may appear as a
first-line option in the treatment of myoclonic seizures and MS in patients with RTT in the future: our clinical observation should be confirmed in larger series and in a randomized controlled trial.

References


Fig. 2. Polygraphic features after the administration of LEV: the MS disappeared and only right-hand stereotypes appeared.