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Case study

Myoclonic epilepsy with photosensitivity in infants with Pallister-Killian Syndrome

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ABSTRACT

Introduction: Pallister-Killian Syndrome (PKS) (OMIM #601803) is a rare genetic disorder caused by a mosaic tetrasomy of the short arm of chromosome 12. Epilepsy is a frequent concern in PKS patients.

Methods: we report 3 PKS patients, with early-onset myoclonic epilepsy and photosensitivity. In these children, we analysed epileptic history and the EEG phenotype.

Results: Epilepsy onset was in the first 2 years of life in all patients and in 2 of them myoclonic seizures were the only seizure type. In all children photosensitivity was observed and myoclonic seizures were mainly related to low-frequency (1–6 Hz) intermittent photic stimulation. Levetiracetam was effective and well tolerated in the 2 treated patients.

Conclusions: early-onset myoclonic epilepsy is a possible clinical manifestation of PKS. Low-frequency photosensitivity is a peculiar bioelectrical marker in these children.

1. Introduction

Pallister-Killian Syndrome (PKS) (OMIM # 601803), is a rare genetic disorder caused by a mosaic tetrasomy of the short arm of chromosome 12. PKS is characterized by variable degrees of neurodevelopmental delay and intellectual disability, seizures, typical craniofacial dysmorphisms, skin pigmentation abnormalities and multiple congenital malformation.[1]

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Epilepsy is a frequent concern in PKS patients, being present in about 40–60% of cases. Onset of epilepsy is often during infancy and the most common seizure types reported are epileptic spasms, myoclonic and focal seizures.[1–3]

Myoclonic seizures were reported by parents in 15 out of 27 patients in a questionnaire-based study by Candee[1] and in 9 out of 22 patients in a cohort presented by Blyth[2]; moreover, myoclonic epilepsy was described in only 2 out of 13 patients of the case series of Giordano.[3]

Here we report 3 young patients with genetically confirmed PKS and myoclonic epilepsy, focussing on the epileptic history and the EEG phenotype with the aim to contribute to better define the electroclinical phenotype of PKS. Informed consent was obtained by parents.

2. Patients

2.1. *Case 1*

Male, 5 years and 1 month old. No disease of neurological interest in family history. At birth facial dysmorphisms suggest the genetic diagnosis of PKS that was evidenced by karyotype on peripheral blood lymphocytes and than confirmed by FISH. The patient presented a severe psychomotor developmental delay. The onset of epilepsy was at 18 months with frequent sudden jerks, massive or involving the upper limbs, sometimes induced by photic stimulation; sporadic brief tonic seizures were reported too. Brain MRI at 20 months was normal. First polygraphic EEG at the Department of Child Neurology and Psychiatry of the University of Bologna (4 years and 5 months) showed slowing of background activity. We recorded both spontaneous and photo-induced head and limbs' myoclonic events. Myoclonic seizures were triggered by intermittent photic stimulation (IPS) at low frequencies (1–6 Hz) and were correlated to spike and high slow wave complexes more represented on the posterior regions tending to diffusion.

Both epileptic manifestations were well controlled by Levetiracetam started at 4 years and 6 months.

2.2. *Case 2*

Male, 3 years and 8 months old. Family history negative for neurological disease. Psychomotor developmental delay and facial dysmorphisms led to genetic diagnosis of PKS confirmed with array-CGH on fibroblast cells obtained by buccal smear.

At 6 months parents noticed onset of sudden jerks affecting the upper limbs and less intensely the lower limbs, during breast-feeding, awakening, drowsiness and tiredness. The episodes did not seem to bother the child and no antiepileptic therapy was started. Brain MRI at 7 months revealed only a pituitarian cyst.

The first EEG at the Department of Child Neurology and Psychiatry of the University of Bologna (3 years and 4 months) documented slowing of background activity. Massive myoclonic jerks were observed triggered by switching the room light suddenly on, during IPS at low frequencies (1–6 Hz) and while eating. The EEG showed generalized discharge of spike and high slow wave complexes, corresponding to the myoclonic seizures.

At the age of 3 years and 5 months the patient presented about 20 subtle myoclonic seizures a day without traumatic injuries and no treatment was started.

2.3. *Case 3*

Female, 2 years and 6 months old. Family history negative for neurological disease.

At birth evidence of facial dismorphisms, ogival palate and anteriorized anus. Subsequent investigations showed bilateral pielectasia, iris coloboma, patency of the oval foramen and a cochlear deafness: these findings, after a negative investigation of the karyotype in peripheral blood cells, led to the genetic diagnosis of PKS obtained by array-CGH on the same material.

Brain MRI performed at 9 months showed macrocrania and enlargement of cerebral sulci. The corpus callosum appeared globally thinned and the cisterna magna was modally wide.

She presented severe psychomotor developmental delay. At 11 months the patient presented the onset of sudden asymmetric extension jerks of the upper and lower limbs associated with a slight head hyperextension. These episodes occurred only upon awakening or when induced by switching the room light suddenly on, with daily frequency, grouped in clusters with spontaneous resolution.

At 1 year, after an initial diagnosis of epileptic spasms, Vigabatrin was started without any benefit. These events continued several times a day. At our evaluation, EEG was characterized by slowing of background activity and brief generalized discharges of spike and wave complexes clinically associated with upper limbs myoclonic jerks at low frequencies of IPS (1–6 Hz) and when the room light was switched suddenly on.

Vigabatrin was stopped and Levetiracetam was started with good response: only palpebral myoclonia during photic stimulation persisted. Parents also reported an improvement in cognitive performances.

3. Discussion

This is the first report of myoclonic epilepsy with low-frequency photosensitivity in Pallister-Killian Syndrome. In all patients myoclonic jerks were mainly related to low-frequency photic stimulation (see Fig. 1), and in 2/3 myoclonic seizures were the only seizure type.

A few authors focused on epilepsy in PKS. The most frequent seizure types reported in infancy were epileptic spasms and myoclonic seizures: in particular Giordano et al.[3] noticed in his case series a prevalence at onset of epileptic spasms while Candy et al.[1] described a most common presence of myoclonic seizures in a study based on parent structured questionnaires.[1,3] Our experience (in particular patient 3) shows that the differential diagnosis between epileptic spasms and myoclonic seizures can be challenging in these patients; however a correct diagnosis is mandatory, because they differ both in therapeutic management and evolution. We suggest that obtaining a polygraphic EEG is the gold standard approach to differentiate these events.

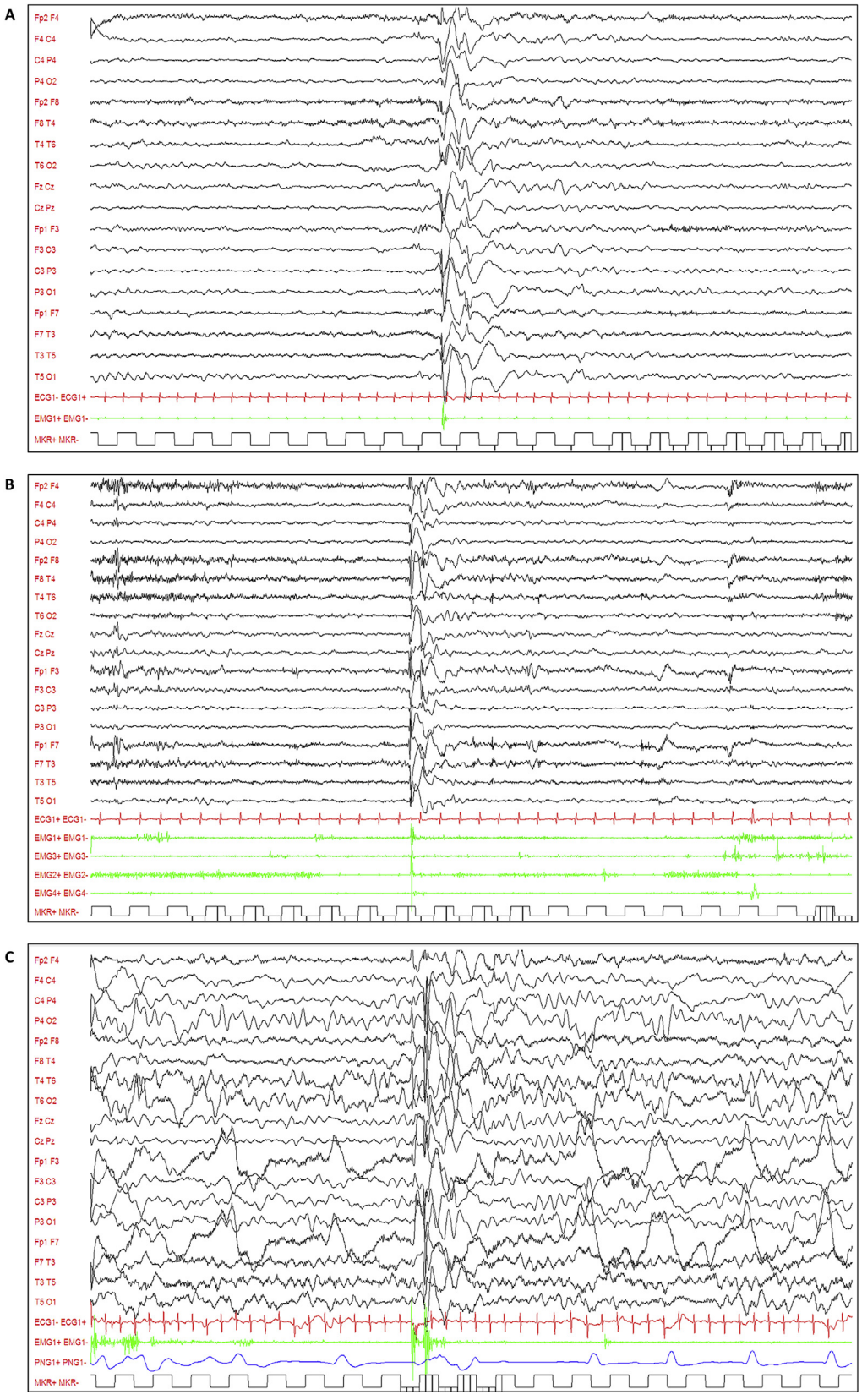

Fig. 1 – Myoclonic seizures at low frequency intermittent photic stimulation. (A) Patient 1, 4 years old: myoclonic seizure triggered by IPS at 1 Hz correlated to generalized EEG discharge of spike and waves (B) Patient 2, 3 years old: massive myoclonic jerk triggered during IPS at 3 Hz: the EEG shows generalized discharge of spike and waves. (C) Patient 3, 1 year old: brief generalized EEG discharges of spike and waves clinically associated with upper limbs myoclonic jerks at 6 Hz IPS.

Myoclonic seizures are frequently reported in infants with genetic syndromes and chromosomopaties, e.g. Angelman syndrome, Wolf-Hirschhorn syndrome and 1p36 deletion syndrome, although a myoclonic epilepsy with photosensitivity is less common in these children.[4] Moreover, low-frequency photosensitivity, as observed in our patients, is a very rare condition, mainly related to progressive myoclonic epilepsies.[5] Interestingly, a similar pattern of photosensitivity was previously described in Patau syndrome, another chromosomal aneuploidy disorder.[6]

On this basis we recommend to consider also the diagnosis of PKS in infants with syndromic features presenting myoclonic epilepsy and low-frequency photosensitivity. Furthermore, we underline the importance to include low frequencies of IPS during routine EEG in children.

Moreover, the observation in patient 2 of myoclonic seizures while eating in addiction to photosensitivity suggests a particular susceptibility to develop reflex seizures in our patients.

As previously described by other studies, Levetiracetam was effective and well tolerated in our patients with PKS.[1,3]

In conclusion, our experience shows that early-onset myoclonic epilepsy is a possible clinical manifestation of PKS. Low-frequency photosensitivity is a peculiar bioelectrical marker in these children. Further studies are needed to better define the electroclinical phenotype and the mechanism of epileptogenesis in PKS.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejpn.2019.05.012.

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