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CASE REPORT

Late-onset myoclonic epilepsy in Down's syndrome (LOMEDS)

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The aim of this paper is to report a patient with late-onset myoclonic epilepsy in Down's syndrome (LOMEDS) as a differential diagnosis of adult-onset progressive myoclonic epilepsies.

A 55-year-old male with Down's syndrome (DS) is described who developed progressively frequent myoclonus and generalized myoclonic–tonic seizures (GMTSs) at the age of 52. EEG recordings demonstrated background slowing and generalized polyspike-wave discharges occasionally associated with myoclonic jerks, leading to the classification of primary generalized epileptic myoclonus. Descriptions of late-onset epilepsy in DS patients are rare. However, a review of the pertinent literature revealed at least two other cases of elderly DS patients developing progressive myoclonic epilepsy after the onset of dementia.

We suggest that late-onset myoclonic epilepsy in Down's syndrome as characterized here should be considered in the differential diagnosis of adult-onset myoclonic epilepsies. LOMEDS apparently shares features with myoclonic epilepsy in Alzheimer's disease (AD) and Unverricht–Lundborg disease (ULD) caused by a mutation on chromosome 21. Since life expectation of DS patients has markedly increased, LOMEDS may be more frequent than currently acknowledged.

Key words: trisomy 21; progressive; myoclonus; dementia; chromosome 21.

INTRODUCTION

Epilepsy in Down's syndrome (DS) has been frequently observed and its prevalence increases with age, reaching 46% in patients over 50 years compared to approximately 9% in patients over 18 years[1–3]. A bimodal onset of seizures in DS with a peak incidence during early childhood and in middle age has been described by several authors[4,5]. A triphasic distribution of seizure onset has also been suggested, i.e. during infancy, early adulthood and a particular epilepsy in patients over 50 years[1,4]. As longevity of subjects with DS is increasing, epilepsy with late onset will be more frequently encountered in the future[6].

Thus far, descriptions of epilepsy with onset during or after the fifth decade in DS have been rare, but include at least two individuals featuring myoclonic as well as generalized tonic–clonic seizures (GTCSs)[7,8]. Here we report a further case of late-onset progressive myoclonic epilepsy in DS and discuss the pertinent literature.

CASE REPORT

A 55-year-old male patient with DS was admitted to our hospital with the first occurrence of a generalized myoclonic–tonic seizure (GMTS). Apart from increased muscle tone and gait disturbance, physical examination did not reveal any significant neurological abnormalities. Due to mental retardation, mini-mental-state examination yielded a score of one point while a CT scan revealed cortical atrophy. MRI examination was not possible due to non-compliance of the patient. The clinical diagnosis of DS was confirmed by cytogenetic analysis.

Approximately 3 years before admission, myoclonic jerks, particularly of the upper extremities, had started.

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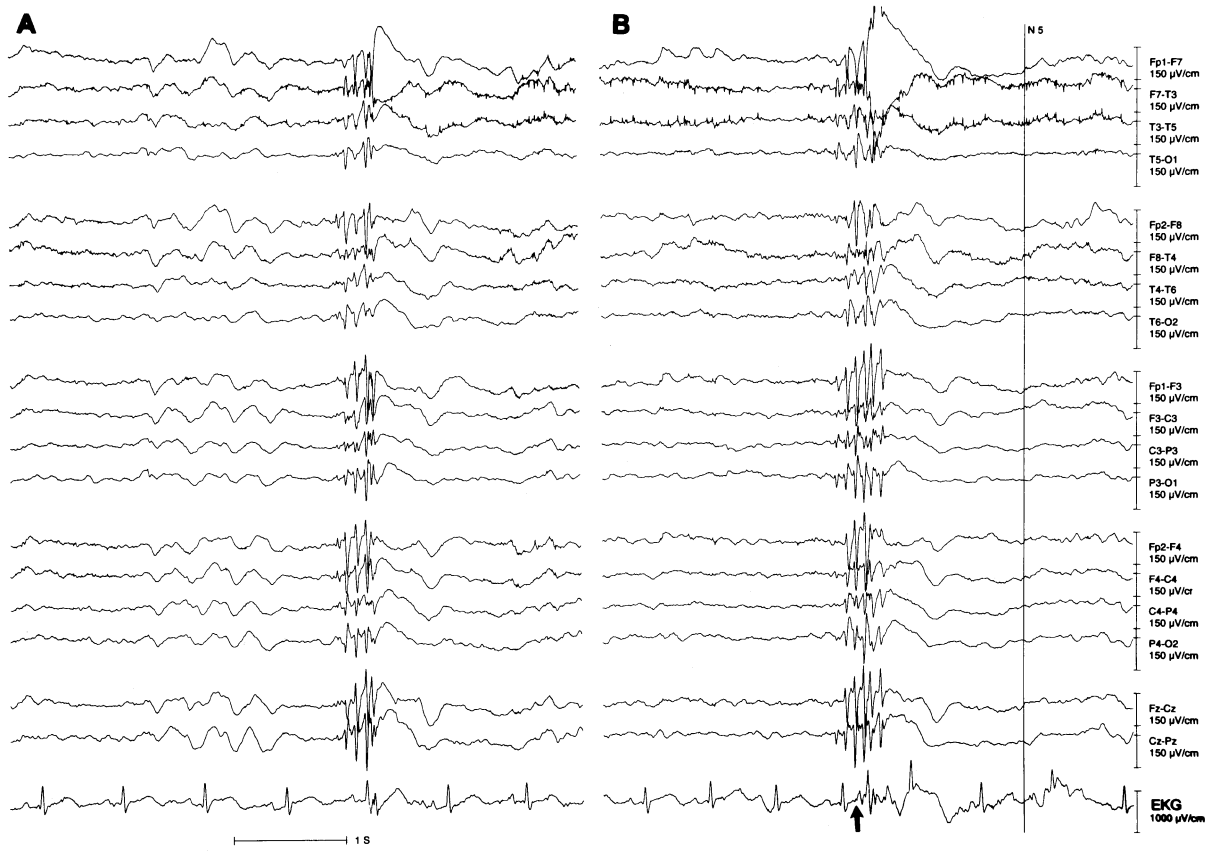

Fig. 1: EEG of the patient showing generalized continuous slowing, generalized intermittent rhythmic slowing and polyspike-wave complexes (a and b). (b) shows a polyspike-wave complex followed by a myoclonic jerk about 185 ms after onset of the polyspike component as visible in the ECG lead (arrow) and noted by the technician (marker line).

These usually occurred in the morning and could be improved by administration of sodium valproate (1800 mg per day). Reduction of this compound because of daytime somnolence temporally coincided with the occurrence of the first GMTS as described by a witness. Due to aggressive behaviour during the addition of lamotrigine, the medical regimen was not closely followed, and additional GMTSs occurred. On a low dose of sodium valproate (900 mg per day), GMTSs were finally controlled but myoclonic jerks increased over the subsequent months. Therefore, topiramate (100 mg per day) was introduced, leading to significant and sustained improvement.

EEG recordings, when sodium valproate serum levels were below detection threshold, showed generalized continuous slowing, generalized intermittent rhythmic slowing as well as generalized polyspike-wave complexes (Fig. 1a). The latter were occasionally associated with generalized myoclonic jerks occurring 180–250 ms after the onset of the polyspike component (Fig. 1b). No epileptiform discharges were recorded on monotherapy with sodium valproate 6 months later.

DISCUSSION

Epilepsy in DS characterized by seizure onset after the fourth decade, myoclonic jerks, occasional GTCSs, and progressive dementia has previously been described in two cases[7,8]. In addition, epileptic seizures and myoclonus had already been observed in nine demented elderly DS patients[9]. In a prevalence study of epilepsy in DS, three patients with onset of epilepsy after the age of 45 were identified. Interestingly, each of these individuals was clinically characterized by dementia, myoclonus and GTCSs[10]. EEG documentation, however, was only provided in the two patients mentioned above[7,8]. Our patient presented with myoclonic jerks in the morning and occasional GMTSs with onset after the age of 50. Progressive dementia could not be evaluated due to severe mental retardation. Although, including our case, 15 elderly DS patients could be identified in the literature with probable myoclonic epilepsy, late-onset myoclonic epilepsy in Down's syndrome (LOMEDS) is currently not included among the possible causes of epileptic myoclonus[11]. We therefore propose that LOMEDS, as

characterized above, should be included in the differential diagnosis of adult-onset myoclonic epilepsies.

Generalized epilepsy was proven by demonstration of generalized epileptiform discharges in all cases with EEG documentation. Furthermore, the time-locked association of polyspike-wave complexes preceding the myoclonus in our patient and in the patient reported by Genton and Paglia[7] allows the classification of primary generalized epileptic myoclonus[12]. LOMEDS may be successfully controlled by the administration of valproate and topiramate. However, the latter has to be used with particular caution in DS patients since topiramate may induce further deterioration of cognition. Piracetam and levetiracetam are other treatment options for myoclonic epilepsies.

Myoclonus is also found in the majority of Alzheimer's disease (AD) patients with epilepsy[13]. Since accumulation of beta-amyloid has been found in both individuals affected with AD and ageing DS patients with dementia[14], a common pathogenesis of dementia and myoclonic epilepsy in elderly DS patients and patients with AD appears likely[15]. Possibly, LOMEDS purely indicates comorbidity with AD in patients with DS. There are also similarities between LOMEDS and Unverricht–Lundborg (ULD), such as generalized epileptiform discharges and generalized slowing in the EEG. However, there is no clear evidence of a causal relationship between these two conditions[16].

CONCLUSIONS

In summary, we suggest that late-onset epilepsy in elderly, demented DS patients characterized by myoclonus, occasional GTCSs or GMTSs, generalized epileptiform discharges in EEG, and slow progression may represent a distinct epilepsy syndrome (LOMEDS). Myoclonus in this syndrome can be classified as primary generalized epileptic myoclonus. More subjects suffering from late-onset epilepsy in DS have to be investigated to allow for a more detailed description of this syndrome. It will then be possible to judge whether LOMEDS is a distinct syndrome or a mere association of DS and AD with myoclonic seizures.

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