

Late-onset epileptic spasms may be cured by focal cortical resective surgery

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ABSTRACT – We report the case of a child with isolated late-onset epileptic spasms who significantly improved after focal frontal cortectomy. Clusters of axial and limb tonic contractions with head nodding began at 2 years of age. They occurred only during sleep, lasting 15 to 20 minutes and were pharmacoresistant. The child suffered slight mental delay. Interictal EEG showed left frontal spikes in slow sleep. Ictal video-EEG showed patterns of asymmetric spasms. MRI revealed a distinct white matter abnormality in the left frontal superior gyrus, corresponding clearly to localised cortical hypometabolism on FDG-PET and PET-MRI co-recording. SEEG investigation showed that the first spasm of the clusters corresponded to a localised discharge of rapid rhythms from the electrodes placed within the area identified as a lesion by MRI. Discharges then became more diffuse across the left frontal and temporal electrodes throughout the duration of the cluster. A tailored focal frontal resection was performed at 16 years of age. Spasms were very rare during the following three years (Engel class II). This observation illustrates the fact that isolated epileptic spasms can be cured by focal cortical resection despite a lack of clearly localised EEG surface anomalies. [*Published with video sequences*]

Key words: late-onset epileptic spasms, focal surgery, asymmetric epileptic spasms



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Late-onset epileptic spasms (ES) form a heterogeneous group (Gobbi *et al.*, 2007). They may be associated with various types of seizures, such as partial seizures in partial cryptogenic or symptomatic epilepsies, and some epileptic encephalopathies. We report the case of a child with isolated late-onset ES who experienced a substantial

improvement following focal frontal cortectomy.

Case report

A girl, born in 1991, had no significant perinatal history and early psychomotor development was normal. Clusters of axial and limb tonic

contractions with head nodding were observed by the family at 2 years of age. The clusters occurred only during sleep and lasted 15 to 20 minutes. Neurological examination and awake EEG were normal. Valproate was administered. The girl continued to have clusters, two or three times a week. In the absence of any identified epileptic origin, treatment with valproate

was stopped and the frequency of the clusters was unchanged.

Sleep EEG at the age of 5 years revealed clusters, leading to the diagnosis of epileptic seizures. Interictal EEG showed left frontal spikes during slow sleep. Ictal EEG revealed generalised biphasic slow waves with superimposed fast rhythms lasting 0.5 to 1 second during



Figure 1. (S: 15 μ V/mm; T: 0.1 sec; H: 35 Hz): Interictal sleep EEG: burst of diffuse asymmetric slow spike-and-waves predominantly in the left frontotemporal area.

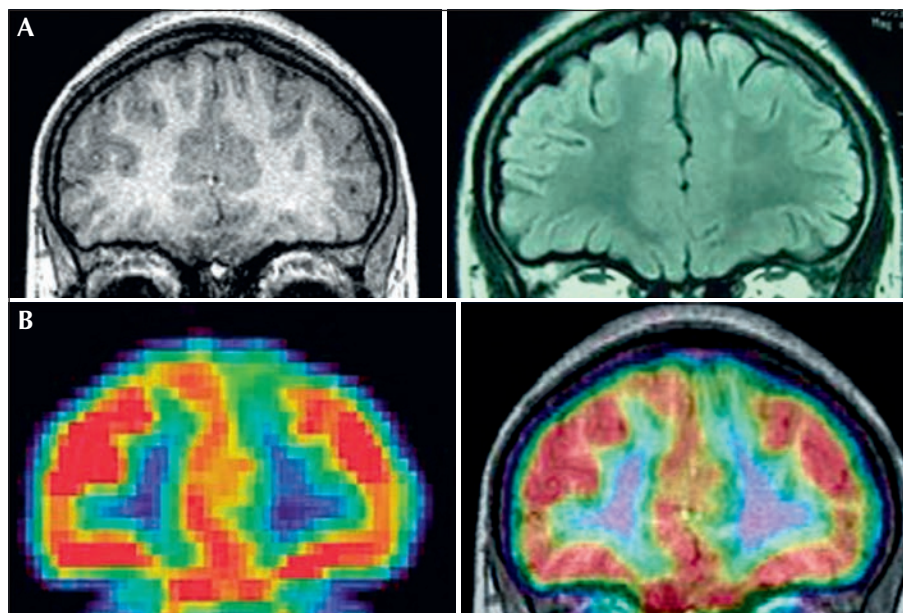


Figure 2. Coronal slices of MRI and PET. (A) MRI of the anterior frontal lobe (left: T1; right: Flair) showing a hypersignal in the white matter in the medial part of the left superior frontal gyrus on Flair sequence. (B) Hypometabolism of the medial part of the left superior frontal gyrus as evidenced by FDG-PET (left) and FDG-PET-MRI co-recording which colocalised anatomically with the white matter abnormalities (right).

axial hypertony, repeated for 10 minutes, and occurring throughout the cluster. Several antiepileptic drugs (carbamazepine, vigabatrin, clonazepam, lamotrigine, topiramate, levetiracetam, and oxcarbamazepine, successively) were tried and ineffective.

Educational difficulties were noted at the age of 7 years, mostly in mathematics. Neuropsychological assessment performed at the age of 10 years showed mild intellectual disability (WISC-III: TIQ: 62) and the girl was oriented towards an adapted school.

A second video-EEG was performed at 14 years of age and a cluster of seizures was recorded during sleep; the patient woke and presented with repeated episodes of sudden head flexion with abduction of the upper limbs and flexion of the lower limbs. The first events were very brief and symmetric. The following motor sequences became longer (lasting 1 to 1.5 seconds) with a tonic component and were asymmetric, the movement of abduction being larger on the right limbs. The patient also had a hiccup (see *video sequence*). The last events of the episode were brief, similar to the start, but remained asymmetric. The frequency and intensity of the events in the cluster increased and then slowly decreased. The cluster lasted 16 minutes. During the cluster, consciousness was preserved and language was normal. During the first events, EEG showed a diffuse high-voltage sharp-and-slow-wave complex, then, as the events became asymmetric and more tonic, a period of voltage attenuation followed the slow-wave pattern which was generally diffuse, symmetric or asymmetric, longer and more evident over left central and temporal regions. The localisation of the slow-wave pattern was diffuse with a maximum peak over the vertex region. Between these events, there was a diffuse theta activity and left frontotemporal delta waves. Interictal activity was normal during the awake state. During slow sleep, there were bursts of generalised asymmetric slow spikes and waves predominantly on the left frontotemporal area (*figure 1*), as well as generalised, symmetric, synchronous slow spikes and waves, in some cases interrupted by slow polyspikes and waves.

FDG-TEP-MRI co-recording demonstrated a localised hypometabolic area over the medial part of the left superior frontal gyrus and a corresponding signal abnormality on MRI (*figure 2*). Because of this concordant result, a stereoelectroencephalography (SEEG) investigation was performed using intracranial multiple contact electrodes. Seven left frontal electrodes and three left temporal electrodes were placed as shown in *figure 3*. Interictal SEEG during the awake state showed multifocal spikes, polyspikes, and spike-waves recorded asynchronously from all electrodes; these discharges became generalised and synchronous during slow sleep. Three infraclinical

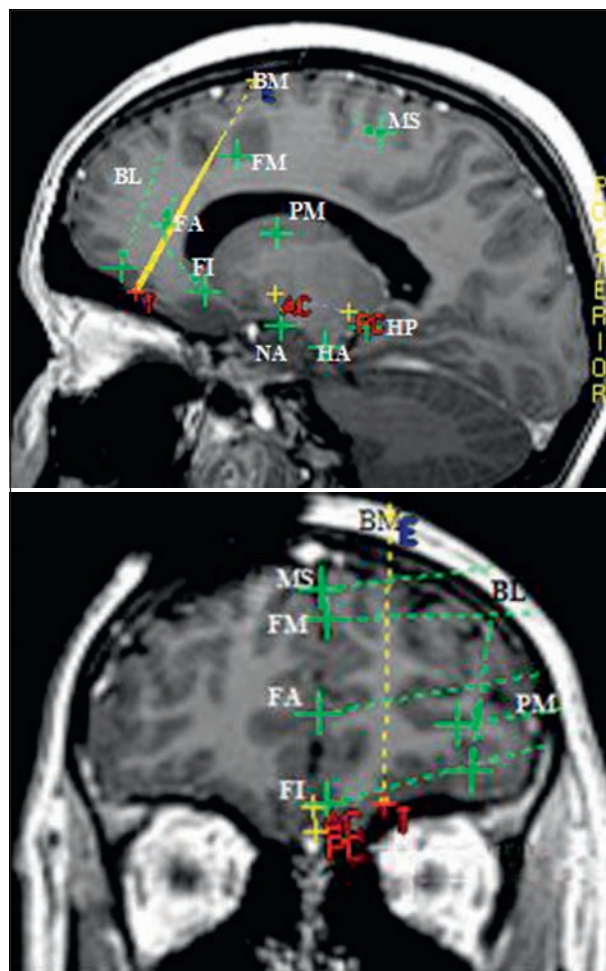


Figure 3. SEEG with location of the ten electrodes: seven frontal electrodes including two vertical (BM: basal medial with external contact located in the lesion; BL: basal lateral) and five orthogonal (FI: frontal inferior; FA: frontal anterior; FM: frontal medium; MS: supplementary motor area; PM: opercular medium) electrodes, and three orthogonal temporal electrodes (NA: uncus; HA: hippocampus anterior; HP: hippocampus posterior). AC: anterior commissure; PC: posterior commissure.

Projection of all electrodes is shown in the sagittal plane (above) and of the seven frontal electrodes in the coronal plane (below). This projection in two single MRI slices does not represent the real trajectory for each electrode, which can only be appreciated with the combination of the two.

rhythmic sharp wave discharges were recorded at the electrodes over the lesion (BM 14-18) with secondary spreading to the frontobasal cortex (BM 1-3); they were continuous at the start of the episode and progressed towards a discontinuous pattern, consistent with burst-suppression, over 1 to 2 minutes (*figure 4*). Eight clusters of seizures were recorded with the same clinical characteristics as observed by surface video-EEG recording. A fast discharge followed by a sharp-wave rhythmic activity on BM 14-18 over the lesion, lasting 50 seconds, preceded the first clinical event.

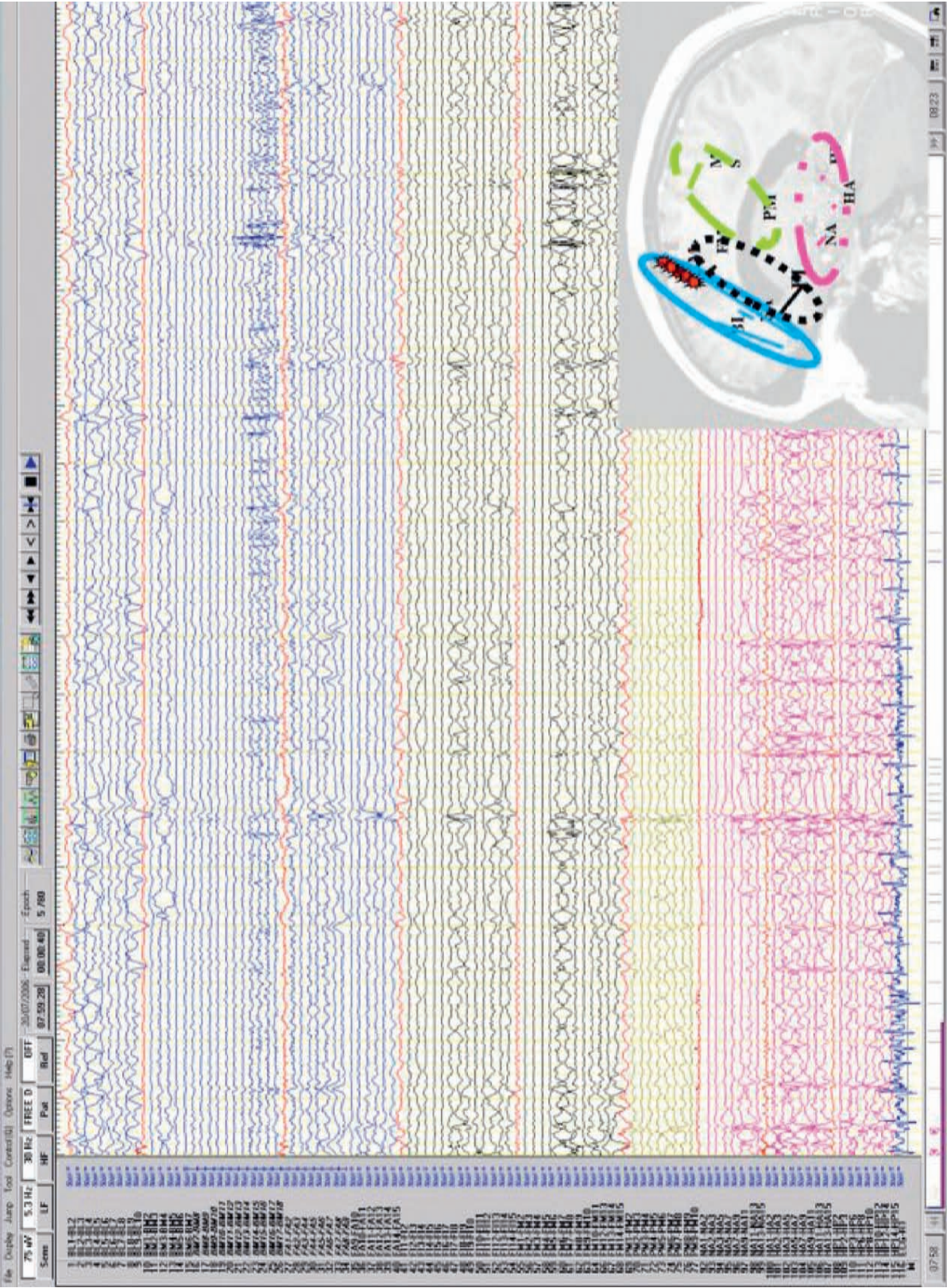


Figure 4. Interictal SEEG: intrafocal rhythmic sharp wave discharges on BM 13-18.

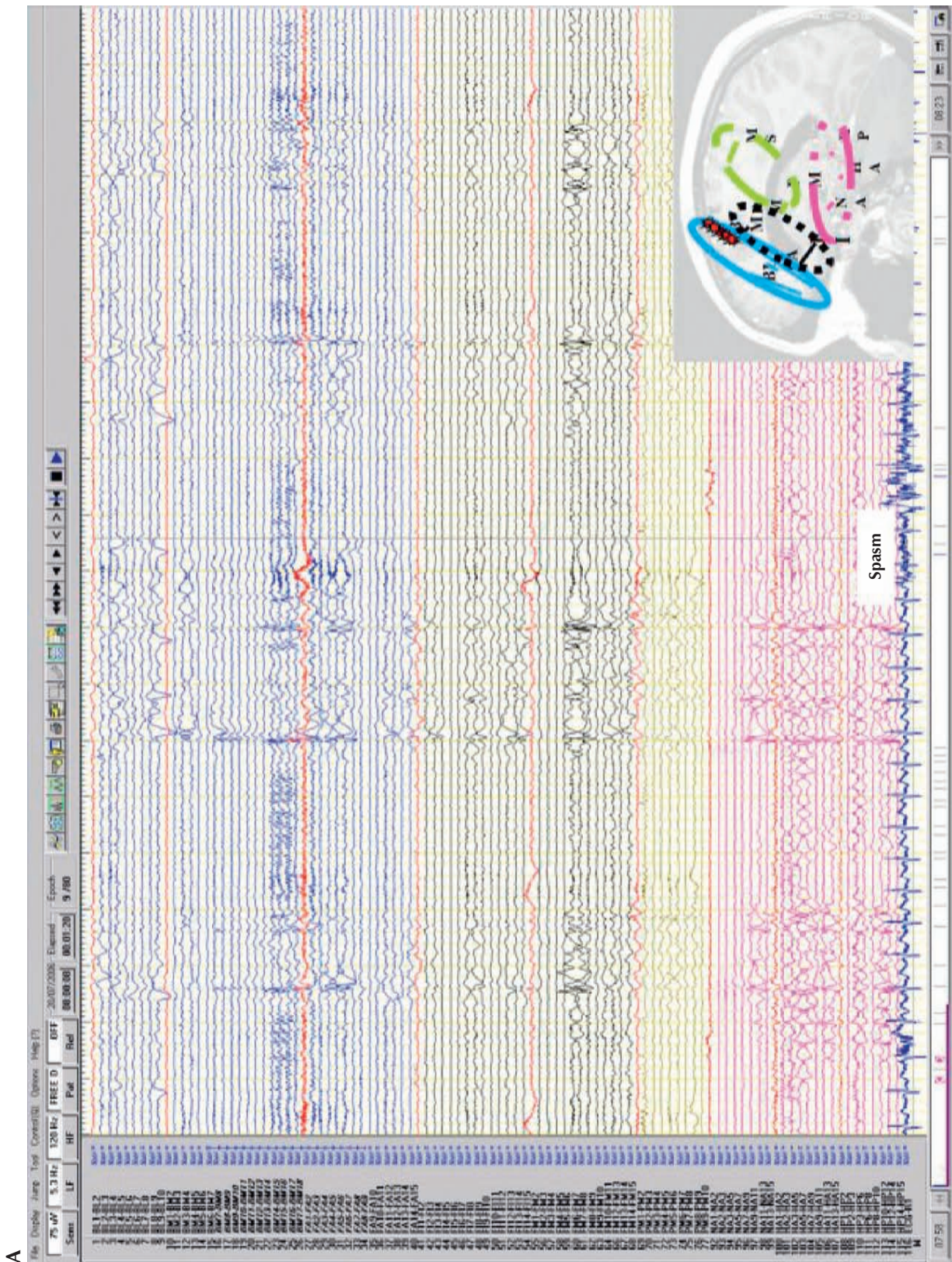
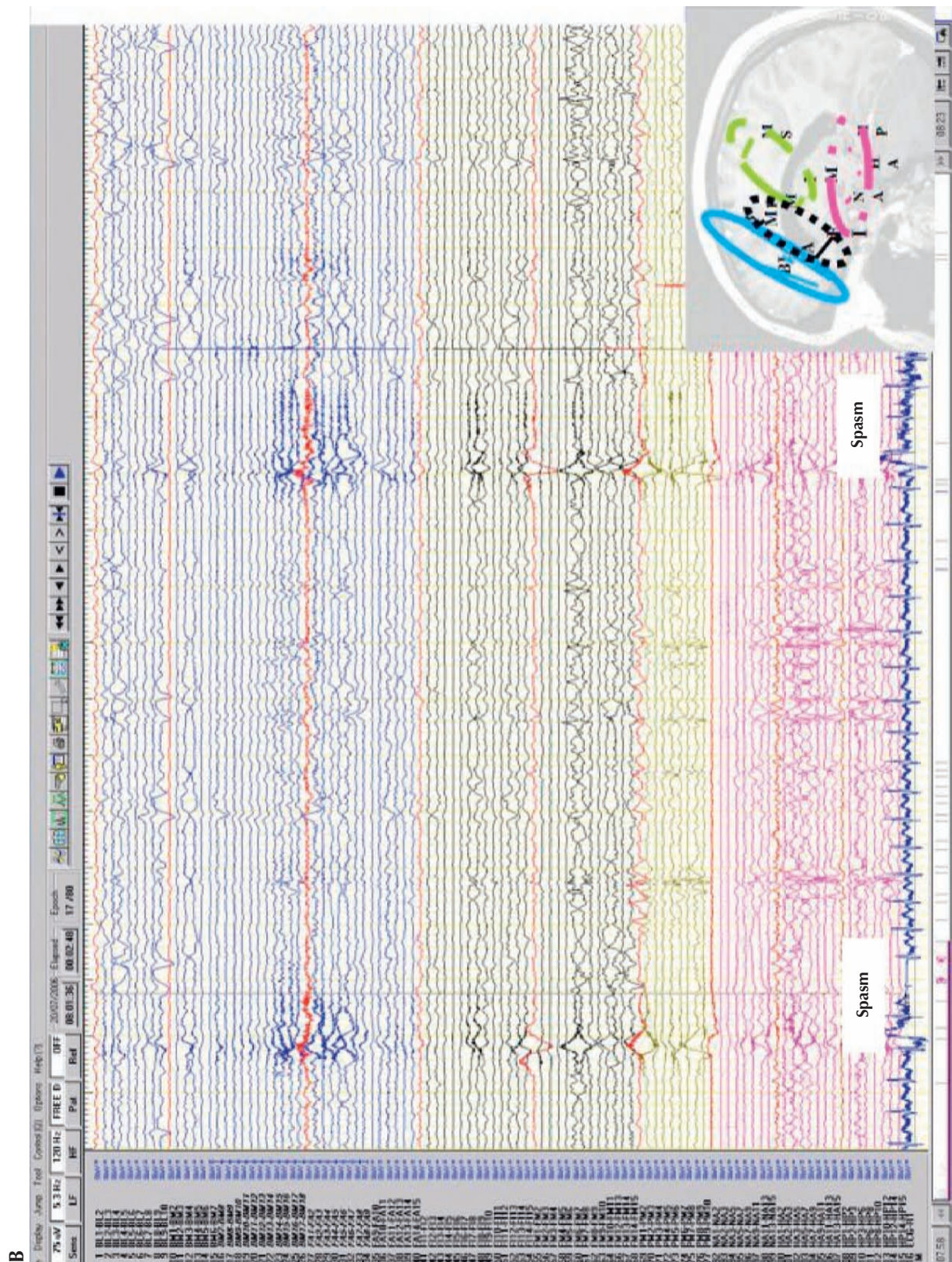


Figure 5. Ictal SEEG. (A) First spasm of the cluster: rhythmic sharp wave discharge on the external contacts of electrode BM (BM 13-18) ceases and is followed by a fast activity spreading mainly to FA 1-7 and coinciding with the first spasm of the cluster. (B) Following spasms of the cluster, fast activity becomes longer and more diffuse.



The ictal EEG pattern consisted of a fast activity on BM 14-18, spreading to nearby electrodes and lasting for one second, followed by a slow-wave component at the same sites. On BM 14-18, however, the fast activity lasted longer (3 seconds). The clinical manifestations occurred during the slow component. Unfortunately, the motor cortex was not investigated. The second clinical event occurred 32 seconds after the first. There was a widespread fast activity, also at the temporal electrodes, followed by a slow component; the clinical manifestations were associated with the slow component. The subsequent events during the cluster were longer but no anatomo-electroclinical correlation was possible due to the sampling bias of SEEG. At the beginning of the cluster, the focal discharge persisted between spasms and then became discontinuous; when the spasm became tonic, the focal discharge disappeared (figure 5).

The patient underwent left anterior frontal cortectomy, corresponding to the external BM area, in December 2007 (neurosurgeon: GD), at the age of 16 years. Anatomo-pathological analysis revealed no dysplasia or ischaemia, but hyaline astrocytic inclusions were found which were identified to be PAS negative but strongly positive for filamin A, by immunocytochemical analysis.

The postoperative outcome was favourable with only three seizures during the three years of follow-up (Engel class II). The patient's performance at school improved and she was able to begin professional education. Her neuropsychological evaluation remained stable (WISC-III: TIQ: 65) with a dysexecutive frontal syndrome.

Discussion

This case presented here illustrates how late-onset isolated epileptic spasms may have a focal origin and be cured by adapted cortical resection.

The patient's epileptic episodes corresponded to the definition of Epileptic Spasms (Vigevano *et al.*, 2001) because the duration of muscular contraction was intermediate between myoclonic movement and tonic seizure. During the cluster, there was a progression from brief and symmetric spasms to tonic asymmetric spasms. The EEG characteristic of the spasms was a diffuse high-voltage, slow-wave complex; when the spasm became tonic and asymmetric, there was a period of symmetric or asymmetric voltage attenuation following the slow-wave pattern. This electroclinical pattern is common in ES (Vigevano *et al.*, 2007).

Using the ILAE classification group, this case of ES corresponds to generalised-onset seizures and to focal-onset secondary generalised seizures, although the focal-onset seizure was noted as "unverified"

(Engel, 2006). When the ES occurred in an isolated manner it was difficult to determine the origin. Our patient presented with no partial seizures and no clear focal scalp EEG anomalies, suggestive of focal epilepsy. This was concordant with the cases of cryptogenic late-onset spasms reported by Eisermann *et al.* (2006) which evoked an epileptic encephalopathy intermediate between West syndrome and Lennox-Gastaut syndrome. A focal onset was nevertheless suspected in our case because FDG-TEP-MRI co-recording showed a localised area of hypometabolism over the medial part of the left superior frontal gyrus, consistent with scalp EEG data. This allowed us to guide implantation of depth electrodes. SEEG showed a clinically silent focal discharge lasting 50 seconds preceding the spasms in the hypometabolism area that was not detected by surface EEG. The first spasm corresponded to fast activity in this area, then, during the cluster there was a widespread fast activity followed by a slow component during spasms. Resection of this area involved in the focal discharge area was associated with a good seizure outcome. Similar data have been obtained from electrocorticography studies showing the dynamic electrocorticographic changes associated with ES; in cases in which a focal-onset seizure zone was identified, based on high frequency oscillations (HFOs) generated by the neocortex and the subsequent propagation to the sensory motor cortex associated with body jerking, surgical resection of the cortical region generating ictal HFOs was associated with a good surgical outcome (RamachandranNair *et al.*, 2008; Nariai *et al.*, 2011). In our case, we can speculate that if there had been depth electrode contacts within the motor cortex, the longer lasting, more tonic seizures would most likely have been shown to be the result of spread of fast activity into this region; the slow waves occurring together with these clinical events were most likely not the primary electrical event corresponding to clinical expression.

Moreover, the neuropathological findings in our case were unusual. Similar astrocytic inclusions, immunopositive for filamin A (an actin-binding protein involved in neuronal migration), have been identified in cases of Aicardi syndrome (Van den Veyver *et al.*, 2004) and in some surgical resections from paediatric epileptic patients (Hazrati *et al.*, 2008) presenting with seizures in their first year of life and mild-to-moderate developmental delay. The clinical and pathophysiological significance of these inclusions remains unknown.

Finally, late-onset ES may be a common manifestation with variable cortical, often frontal, trigger zones. Therefore, in cases of late-onset ES, investigations should include a search for a focal trigger zone, even when scalp EEG abnormalities are not clearly localised. SEEG or electrocorticography should be used to seek

any focal rapid discharges preceding spasms; FDG-PET-MRI co-recording should be considered for guiding intracranial investigation. □

Acknowledgements.

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Disclosures.

None of the authors has any conflict of interest to disclose.

Legend for video sequence

At 22:22:53, a noise awoke the patient; a discharge of slow spike-and-waves appeared in a bilateral frontotemporal area, becoming faster and localised in left temporal area. At 22:23:53, she had a first spasm involving a sudden head flexion with adduction of upper limbs and lower limb flexion, lasting 0.5 seconds. These motor sequences were repeated (3-4 every 20 seconds) and were short and symmetric. At 22:27, they became asymmetric, the abduction movement being broader, more tonic on right limbs, and longer (lasting 2 seconds), and the patient had a hiccup. Consciousness was preserved and language was normal. The spasms stopped at 22:39, such that the cluster lasted 16 minutes. During the first events, EEG revealed a diffuse high-voltage sharp-and-slow-wave complex. The spasms then became asymmetric and more tonic, with a period of voltage attenuation following the slow-wave pattern. During the asymmetric spasm, the period of voltage attenuation tended to be diffuse, symmetric or asymmetric, longer and more evident over left central and temporal regions. The localisation of the slow-wave pattern was diffuse with a maximum peak over the vertex region.

Key words for video research on
www.epilepticdisorders.com

Syndrome: focal non-idiopathic frontal (FLE)

Etiology: brain malformation (not specified)

Phenomenology: spasm (epileptic); tonic posture; axial

Localization: frontal lobe (left)

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