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Electrical status epilepticus "invisible" to surface EEG in late-onset Rasmussen encephalitis

Jinane Fattouch[1], Carlo Di Bonaventura[1], Giancarlo Di Gennaro[2], Pier Paolo Quarato[2], Simona Petrucci[1], Mario Manfredi[1,2], Massimilano Prencipe[1], Vincenzo Esposito[2], Anna Teresa Giallonardo[1]

[1] Department of Neurological Sciences
[2] Neuromed Institute of Pozzilli (IS), University of Rome "La Sapienza", Italy

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ABSTRACT – Rasmussen's encephalitis (RE) is a chronic, progressive disease that typically occurs in childhood, rarely in adulthood. When it does occur in adulthood, it may be associated with atypical electro-clinical features, and neuroimaging alterations usually help diagnosis. Unlike childhood forms, in which epilepsia partialis continua is usually observed, the EEG pattern in adult variants may be aspecific. We describe a highly interesting case of late-onset RE in which an electrical status epilepticus was not detected by the surface EEG, but by a recording with subdural electrodes.

Key words: late-onset Rasmussen encephalitis, status epilepticus, subdural electrodes

Rasmussen's encephalitis (RE) is a chronic, progressive disease that typically appears in childhood and is usually characterized by intractable partial motor seizures, hemiparesis and cognitive impairment (Bien *et al.* 2005). Clinical features are often accompanied by typical neuroimaging findings and a fairly typical EEG pattern (Hart 2004). Although usually a childhood disease, there have been numerous reports of adult-onset RE, which could instead be characterized by atypical features (Hart *et al.* 1997). We describe a case of late-onset RE in which an electrical status epilepticus, not detected by the surface EEG, was documented in a recording with subdural electrodes.

Case report

The patient is a 39-year-old, right-handed woman whose birth and psychomotor development were normal. The patient was well until the age of 32, when she experienced brief simple partial seizures described as "tightness in the chest... a disgusting smell...shivering (she had goose pimples)... a feeling of suffocation ... anguish...", sometimes followed by loss of contact accompanied by oro-alimentary automatisms (chewing and swallowing). The seizure frequency gradually increased, eventually becoming refractory to antiepileptic drugs.

Interictal EEG recordings showed theta-delta slow waves and, when the

Correspondence:
C. Di Bonaventura
Epilepsy Unit,
Department of Neurological Sciences,
University of Rome "La Sapienza",
Viale dell'Università 30,
00185 Rome, Italy
<c_dibonaventura@yahoo.it>

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patient was in sleepiness, sharp wave activity located in the right fronto-temporal regions. At the follow-up MRI, serial scans between 1999 and 2003 revealed progressive focal hypo-atrophy, first involving the right mesial temporal structures and, later, all the homolateral fronto-temporal area *(figure 1)*; MRI spectroscopy study in the same region revealed a decreased N-acetyl-aspartate concentration. The neurological examination remained normal over time. When the patient was referred to our clinic, video-EEG monitoring documented three seizures characterized by ictal activity extensively involving the right fronto-temporal region, without a precisely-located focal onset. On the basis of the MRI, documented disease progression and, to a lesser extent, on the electro-clinical data, a presumptive diagnosis of RE was made and the patient underwent immunotherapy (first steroid, then intravenous gammaglobulin treatment), which did not however, reduce seizure frequency. Owing to the drug-resistant nature of the seizures, the patient underwent invasive monitoring with the implantation of subdural grid electrodes to more clearly define the epileptogenic zone. Depth recordings with subdural electrodes revealed: 1) an electrographic status with continuous rhythmic 1-1.5 Hz spike-and-wave activity located in the right fronto-dorsal

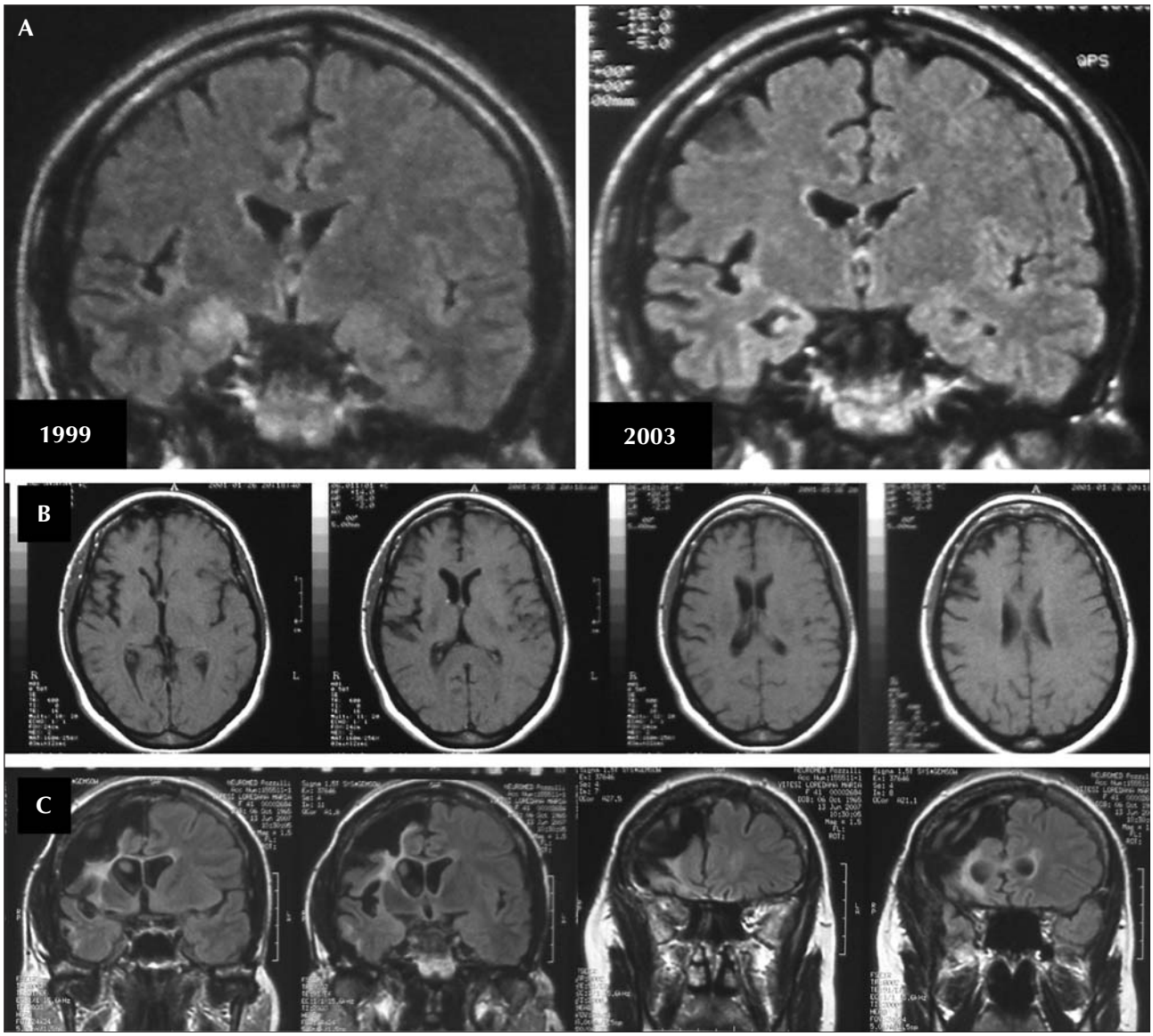

Figure 1. MRI images (**A**) coronal T2-weighted FLAIR images show a progressive, right hemispheric atrophy predominantly involving the temporal lobe (a hyperintensity in the right hippocampal region is also evident in the first scan), and the perisylvian regions; (**B**) axial T1-weighted images document the extensive involvement of frontal lobe and perysilvian region in pre-surgical evaluation; (**C**) post-surgical MRI scan: T2-weighted FLAIR images show a wide right fronto-dorsal corticectomy.

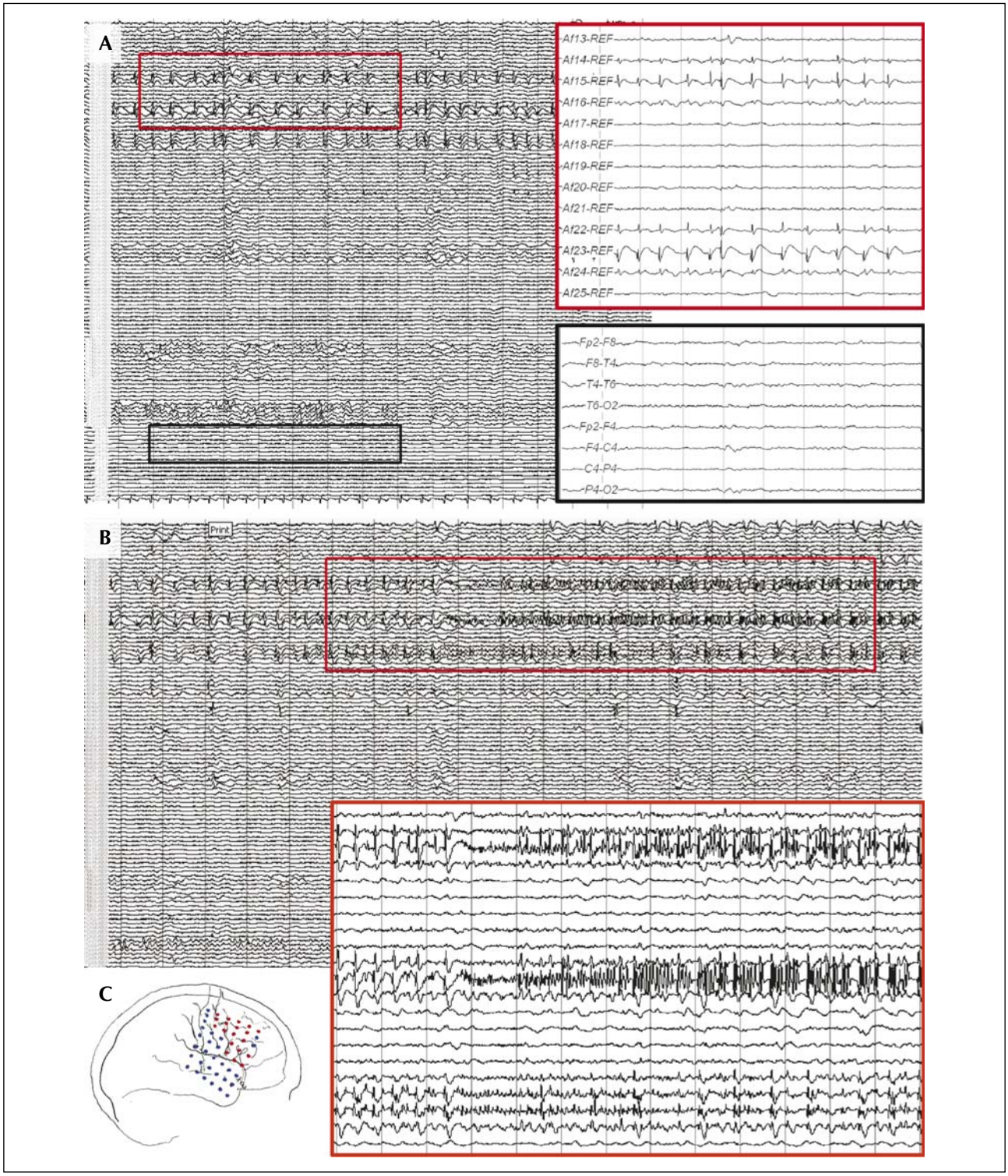

Figure 2. A) Continuous periodic epileptiform abnormalities configuring an electrical status epilepticus located in the right fronto-dorsal regions; panels show an enlargement of the EEG tracings: electrical status, which is well documented by the subdural grid (upper panel), is not detected by the corresponding surface recording (lower panel), which only shows slow theta-delta monomorphic activity. **B**) a seizure triggered by the aforementioned epileptic electrical activity, arising from the same fronto-dorsal regions and spreading to the homolateral temporal lobe and interemispheric structures; panel shows an enlargement of the corresponding EEG tracings. **C**) Schematic illustration of the subdural grid location: red points indicate electrodes corresponding to the subcontinuous ictal activity.

regions not detected by the concomitant surface EEG; 2) recurrent seizures triggered by the aforementioned epileptic activity, arising from the same fronto-dorsal regions and spreading to the homolateral temporal lobe and interemispheric structures *(figure 2)*. Based upon the findings of the invasive monitoring, the patient underwent a wide, right fronto-dorsal corticectomy. The histological study confirmed the diagnosis of Rasmussen encephalitis. Indeed, various histological specimens revealed findings that are typical of both the chronic (i.e. cortical neuronal loss with gliosis and spongiosis) and acute (i.e. neuronophagia, perivascular cuffs of lymphocytes and diffuse microglial hypercellularity) stages of the disease. Two years after the corticectomy, the patient is currently in Engel Class Ib.

Discussion

Although RE typically appears in childhood, there have been numerous reports of adult-onset RE (Villani *et al.* 2006). When compared with "typical" RE, the late-onset variant can occur with atypical electro-clinical and neuroradiological findings. Firstly, the ictal semeiology may include not only motor signs, but visual, olfactory and dysmnesic features, as well as loss of contact due to multilobar involvement not confined to the peri-rolandic region (Jaillon-Riviere *et al.* 2007) EEG interictal and ictal patterns appear to vary in both infancy/childhood and adulthood, though status epilepticus and subcontinuous epileptiform abnormalities rarely occur in the latter (Capovilla *et al.* 1997). As the lack of typical electro-clinical findings in adults often renders the diagnosis of RE more difficult, the diagnosis in such cases usually relies on MRI findings. Indeed, although the three typical alterations in RE (hemispheric atrophy, white matter signal hyperintensity and atrophy of the head of the caudate nucleus), rarely coexist in adult patients, progressive focal lobar atrophy may be crucial to recognizing this disease (Bien *et al.* 2002, Chiapparini *et al.* 2003).

In our patient, the EEG features were particularly worthy of note. Indeed, intracranial recordings through subdural grids revealed an asymptomatic electrographic status located in the right fronto-dorsal regions, which was not accompanied by any detectable changes on the surface EEG. Although it is known that the surface EEG may sometimes fail to detect epileptic activity, this is, to our knowledge, the first time this phenomenon has been well documented in late-onset RE.

In this patient, we may hypothesise that the recurrent electric status, in addition to the drug-resistant seizures, underlay the gradually worsening evolution of the patient's clinical condition. Indeed, sustained epileptic activity, even though asymptomatic and "externally invisible", may induce metabolic and haemodynamic changes underlying progressive cerebral focal atrophy.

This hypothesis is in accordance with widely accepted data pointing to the damage caused by a combination of progressive encephalitis and epileptic processes (Wellard *et al.* 2004). The case described in this report suggests that status epilepticus, which is believed to be rare in late-onset RE, is underestimated as a condition because it may be asymptomatic or may escape detection by surface EEG. □

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