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Rasmussen's encephalitis and SUDEP:
description of a difficult clinical case

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SUMMARY

PURPOSE: Rasmussen's encephalitis is a rare chronic neurological disorder characterized by unilateral inflammation of the cerebral cortex, drug-resistant epilepsy, and progressive neurological and cognitive deterioration. The 2005 European consensus on pathogenesis, diagnosis, and treatment of Rasmussen's encephalitis remains the accepted guideline for evaluative criteria (1). We describe the clinical picture of a patient with recurrent non convulsive and convulsive status epilepticus at focal onset starting when he was 38-year-old, who died 6 years later of SUDEP. The MRI showed asymmetric focal cortical atrophy with right hyperintense signal of the cortical-subcortical inferior frontal gyrus and atrophy of the ipsilateral caudate head. The EEG showed asymmetric slowing and right epileptiform activity. Because the patient died suddenly and unexpectedly at home, we could not make the autopsy but we considered for this case the diagnosis of Rasmussen's encephalitis

METHODS: A 44-year-old male with a 6 years history of recurrent non convulsive and convulsive focal status epilepticus was investigated in the course of 6 years, during the repeated hospitalizations, using videoEEG, brain MRI, DAT scan, neuropsychological evaluations, Neurolite SPECT, cerebrospinal fluid assays, including: 14-3-3 protein, T-Tau, P-Tau, beta-amyloid 1-42 peptide, Autoantibodies vs GluR3 peptide A and B.

RESULTS: EEG showed bilateral slowing with right parietal epileptiform activity, brain MRI showed asymmetric focal cortical atrophy with right hyperintense signal of the cortical-subcortical inferior frontal gyrus and atrophy of the ipsilateral caudate head, while DAT was normal and Neurolite SPECT showed hyperperfusion of the right parietal lobe. Neuropsychological examination was normal at the beginning but revealed progressive cognitive decline with impairment of praxis, constructive abilities, and slowing of the attentive and executive functions during the course of the years. The 14-3-3 protein test was negative, T-tau and P-Tau concentrations, CSF levels of the beta-amyloid 1-42 peptide were normal. The search of seric and CSF autoantibodies vs GluR3 peptide A and B was positive.

DISCUSSION: Because the patient died suddenly and unexpectedly at home we didn't make the autopsy, but we considered the diagnosis of Rasmussen's encephalitis on the basis of clinical presentation at the different stages and taking into account neuroimaging, EEG features and positivity of seric and CSF detection of autoantibodies against GluR3 peptide A and B.

CONCLUSIONS: the presence of recurrent focal status epilepticus, become drug-resistant during the years, associated with neurological and cognitive deterioration and with progressive severe brain asymmetric atrophy, at the MRI, could suggest the diagnosis of Rasmussen's encephalitis for our patient.

CLINICAL CASE

December 2008 (38 years)

A 38-year-old male shows recurrent clusters of seizures characterized by left head and eye deviation associated by motor inhibition lasting from 30 minutes to 6 hours >weekly after a change of antiepileptic treatment (introduction of zonisamide 300 mg/die in add on to valproate 2500 mg (LP 80,9 mcg/ml) and lamotrigine 400 mg/die (LP 12,2 mcg/ml). Ictal EEG *(Fig. 1)* doesn't show epileptiform discharge so that we suppose psychogenic seizures and we reduce the antiepileptic treatment (zonsamide ad lamotrigine) but when valproate was also decreased the patient has a generalized tonic-clonic seizure. Antiepileptic treatment was potentiated by adding carbamazepine 800/die mg and pregabalin 150/die mg to valproate 2500 mg/die. Recurrent clusters of seizures characterized by left head and eye deviation associated by motor inhibition continue daily/weekly without a clear epileptiform discharge at the EEG. MRI *(Fig. 2)* shows mild mainly frontal cortical atrophy.

Neurological evaluation shows some extrapyramidal signs (bradykinesia, camptocormic posture and gait, tremor). DaTSCAN *(Fig. 3)* was normal.

Neuropsychological evaluation shows some impairment in visual spatial function and in frontal executive functions with slow decision-making process. That clinical picture seems of uncertain origin: functional or organic. Neurolite SPECT (Fig.4) detects left parietal hypoperfusion. The patient was also followed by a psychiatrist without significant effect on the seizures frequency.

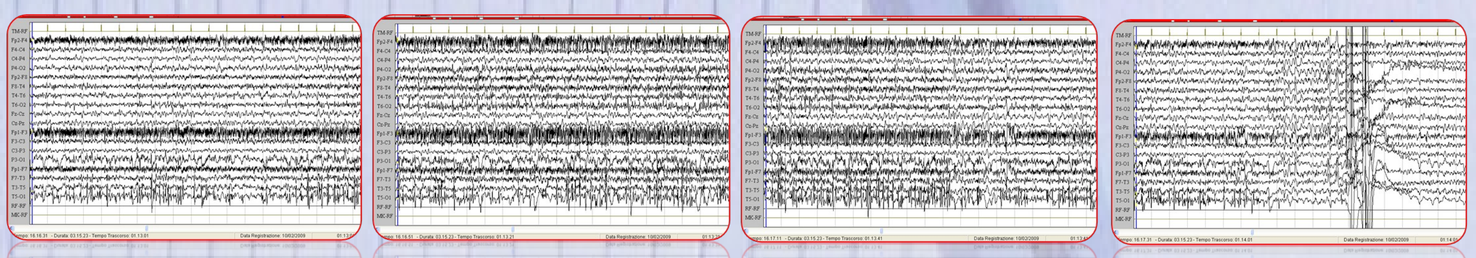

Fig.1 - Ictal EEG

Fig.2 – MRI 2008

Fig.3 - DaTSCAN

Fig.4 - Neurolite SPECT

July 2011 (40 years)

The patient was recovered because of fever and stuporous state with left or right eye and head tonic deviation associated with arms and legs tremor, loss of consciousness lasting from minutes to hours, often diazepam ev responsive, with daily frequency for 2 weeks.Ictal EEG show spikes and waves discharges on the right fronto-central derivations. MRI *(Fig. 5)* detects two areas of hyperintensity of signal in T2 and Flair localized in the right frontal gyrus and in the right cerebellum. CSF examination is normal. Neurological examination shows: slowing of speech, bilateral hand tremor, left arm and leg mild hyposthenia. Sonography of the supra-aortic trunks, echocardiography, blood tests for juvenile stroke, search for the most common mtDNA mutations revealed normal findings. Antiepileptic treatment was potentiated by adding oxcarbazepine 1200/die mg and clobazam 10 mg to pregabalin 150/die mg and valproate 2500 mg/die.

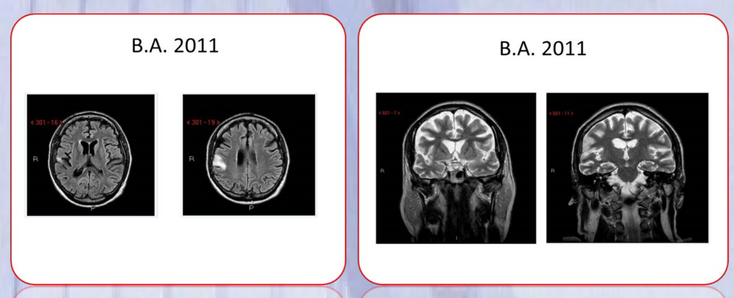

Fig.5 – MRI 2011

September 2011 (41 years)

The patient was recovered because of clusters of generalized tonic-clonic seizures every 10 minutes. Status epilepticus was interrupted by diazepam ev. Post-ictal EEG shows bilateral slow waves on alpha rhythm better organized on the left. Neurological examination shows: slowing of speech, impairment of eyes pursuit movement, mild left arm and leg hyposthenia, camptocormic posture and gait, tremor. MRI shows reduction of extension of the right frontal lesion and disappearance of the right cerebrellar lesion ("stroke like lesions"). Antiepileptic treatment was potentiated by adding diazepam 2 mg to clobazam 20 mg, oxcarbazepine 1200/die, pregabalin 150/die mg and valproate 2500 mg/die.

August 2012 (42 years)

The patient was recovered because of clusters of generalized tonic-clonic seizures every 10 minutes. Status epilepticus was interrupted by diazepam and midazolam followed by phenytoin ev. Postictal EEG shows delta waves associated with spike and waves on the right fronto-central derivations.

Neurological examination shows: slowing of speech, impairment of eyes pursuit movement, mild left arm and leg hyposthenia, camptocormic posture and ataxia, tremor. MRI *(Fig. 6)* shows mild alteration of signal in T2 and Flair on the right frontal gyrus and bilateral (right>left) cortical atrophy with ventricular dilatation. Antiepileptic treatment was potentiated by adding phenytoin 300 mg/die to clobazam 10 mg, oxcarbazepine 1200/die, pregabalin 150/die mg and valproate 2500 mg/die.

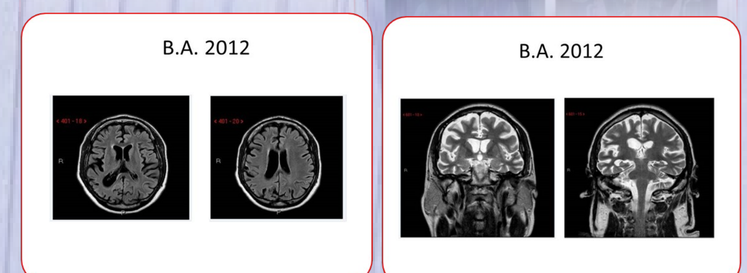

Fig. 6 MRI 2012

August 2013 (43 years)

The patient was recovered because of clusters of adversative tonic seizures (right eye and head deviation) with loss of consciousness.
Status epilepticus was interrupted by diazepam and midazolam followed by phenytoin ev.
Neurological evaluation shows: slowing of speech, impairment of eyes pursuit movement, mild left arm and leg hyposthenia, camptocormic posture and severe ataxia. Post-ictal EEG shows bilateral delta waves and spike and waves on theta rhythm. MRI *(Fig.7)* shows severe bilateral cortical atrophy mainly on the right side and increasing of ventricular dilatation.
Neuropsychological evaluation shows progression of cognitive impairment mainly in the parietal-occipital functions and marked slowing of decision-making process
Antiepileptic treatment was potentiated by adding diazepam 3 mg to phenytoin 350 mg/die, clobazam 20 mg, oxcarbazepine 1500/die and valproate 2000 mg/die.

Fig. 7 – MRI 2013

May 2014 (44 years)

The patient was recovered because of convulsive status epilepticus epilepticus at focal onset (right parietal onset). The convulsive status epilepticus was refractory to all therapy (diazepam, phenytoin, valproate, midazolam ev) and was finally interrupted by adding topiramate 800 mg/die in feeding tube. Ictal EEG *(Fig. 8)* shows right parietal spike and waves discharge. MRI *(Fig. 9)* shows progression of bilateral mainly right cortical-subcortical atrophy with atrophy of the ipsilateral caudate head.

Neurological evaluation shows slowing of speech, impairment of eyes pursuit movement, left arm and leg hyposthenia, inability to walk. OSAS of severe level (AHI di 80,3, SaO2 90-58,7%). CSF examination shows: The 14-3-3 protein test was negative, T-tau and P-Tau concentrations, CSF levels of the beta-amyloid 1-42 peptide were normal. The search of seric and CSF autoantibodies vs GluR3 peptide A and B was positive.

Antiepileptic treatment was potentiated by adding topiramate 600 mg/die to phenytoin 500 mg/die, diazepam 4 mg, clobazam 10 mg, oxcarbazepine 1800/die and valproate 4500 mg/die.

Demitted on July 2014

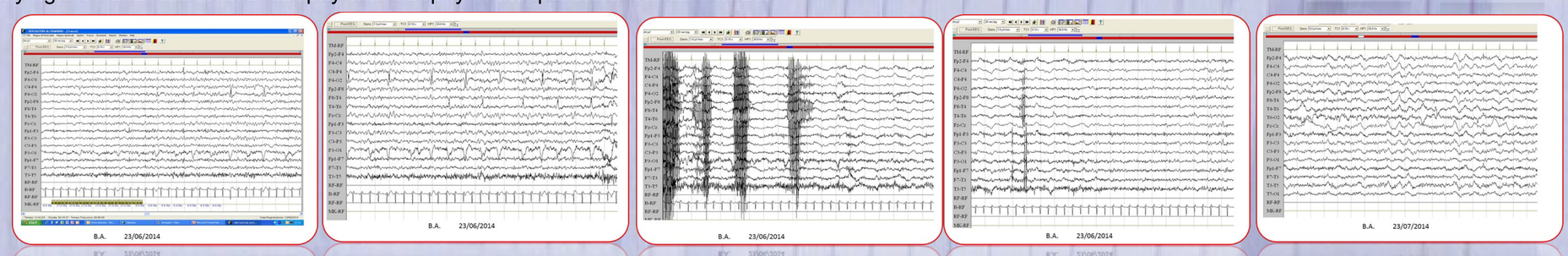

Fig. 8 – Ictal EEG

17 of August 2014 (44 years 11 months e 23 days)

The patient unexpectedly died at home not because of a seizure. Plasmatic levels of AED: Acido Valproate 82.2 µg/ml, Phenytoin 30.3 mcg/ml Oxcarbazepine 6.92 µg/ml, Topiramate 2.51 µg/ml

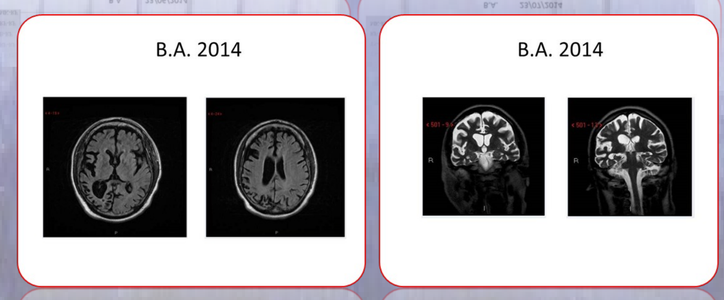

Fig. 9 MRI 2014

REFERENCES

1.Sophia Varadkar, Christian G Bien, Carol A Kruse, Frances E Jensen, Jan Bauer,
2.Carlos A Pardo, Angela Vincent, Gary W Mathern, J Helen Cross
Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances Lancet Neurol 2014; 13: 195–20