AUTOIMMUNE ENCEPHALITIS IN A SERIES OF PATIENTS WITH RAPIDLY PROGRESSIVE DEMENTIA: PRELIMINARY DATA FROM A PROSPECTIVE STUDY

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BACKGROUND

Autoimmune encephalitis represent one of the most important treatable cause of rapidly progressive dementia (RPD).
Few studies describe the incidence of autoimmune etiology in RPD and the clinical and paraclinical features of patients with autoimmune RPD.

We aim to report about a prospectively collected series of patients presenting with RPD, focusing on the subgroup of patients diagnosed with an autoimmune disease.

MATERIALS AND METHODS

From January 2016 to June 2017, we prospectively collected a series of **30 patients** with a diagnosis of RPD, referring to a Memory Clinic and to a Center specialized in Neurological Autoimmune Diseases.

Patients underwent neurological evaluation, MRI imaging, CSF analysis, electroencephalographic (EEG) study, neuropsychological evaluation, screening for onconeural and neuronal surface antibodies (NSAbs).

Patients were then classified in the subsequent subgroups (Table 1): 1) autoimmune neurodegenerative 2) prionic 3) others.

Characteristics of autoimmune subgroup are here reported, with diagnostic classification according to Graus 2016 (Box 1)

BOX – 1 Graus criteria for classificaion of autoimmune encephalitis

Diagnostic criteria for possible autoimmune encephalitis

Diagnosis can be made when all three of the following criteria have been met:
1.Subacute onset (rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms
2.At least one of the following:
- New focal CNS findings
- Seizures not explained by a previously known seizuredisorder
- CSF pleocytosis (white blood cell count of more thanfive cells per mm3)
- MRI features suggestive of encephalitis

1.Reasonable exclusion of alternative causes

Diagnostic criteria for definite autoimmune limbic encephalitis

Diagnosis can be made when all four of the following criteria have been met:
1.Subacute onset (rapid progression of less than 3 months) of working memory deficits, seizures, or psychiatric symptoms suggesting involvement of the limbic system
2.Bilateral brain abnormalities on T2-weighted fluid-attenuated inversion recovery MRI highly restricted to the medial temporal lobes
3.At least one of the following:
- CSF pleocytosis (white blood cell count of more than five cells per mm3)
- EEG with epileptic or slow-wave activity involving the temporal lobes

4. Reasonable exclusion of alternative causes

RESULTS

13/30 patients were diagnosed with autoimmune RPD (Table 1). Two patients met Graus' criteria for possible Autoimmune Encephalitis and were negative for neuronal antibodies. Eleven patients met criteria for limbic encephalitis with onconeural or surface neuronal antibodies associated. Notably one female harboured serum and CSF antibodies for Adenylite Kinase 5 (AK5) (Figure 1), a novel recent phenotype associated with prominent memory deficits.
Table 2 and Table 3 show clinical and paraclinical features respectively of the 13 patients.

Table 1

M/F	18/12
Mean age (range)	65,1 (21 – 84)
Autoimmune	**43,3% (13/30)**
Neurodegenerative	33,3% (10/30)
Prionic	16,7% (5/30)
Others	6,7% (2/30)

n. 2
Possible autoimmune encephalitis

n. 11
Definite limbic encephalitis
n.3 LGI1, 3 CASPR2, 2 Ma2, 1 Ak5

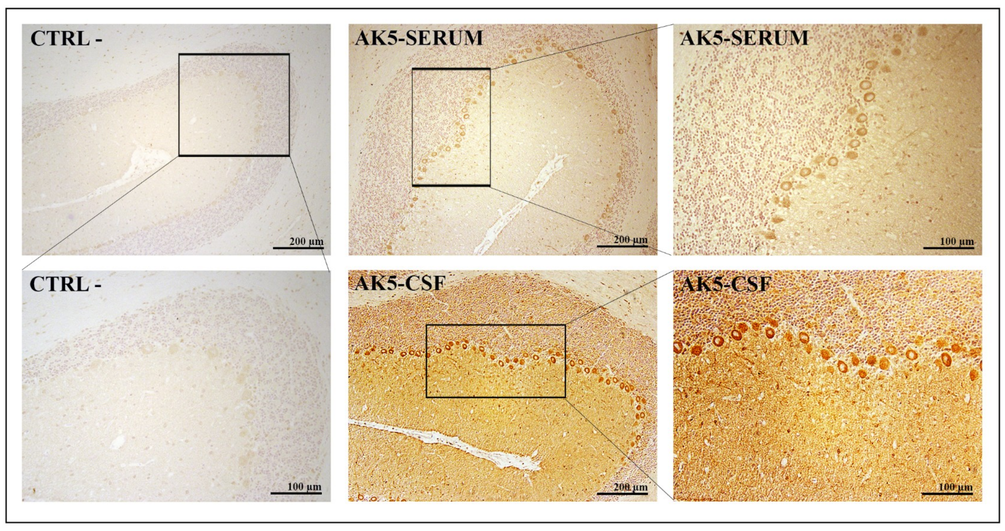

Figure 1: Immunohistochemistry on frozen rat cerebellum showing reactivity of serum and CSF with Purkinje and granular cells. AK5 antibodies were confirmed by a specific cell based assay

Table 2

Clinical features (Onset)	
Seizures	30,7% (4/13)
Cognitive deficits	76,9% (10/13)
Psychiatric symptoms	23,1% (3/13)
Clinical features (Peak)	
Seizures	53,8% (7/13)
Cognitive deficits	100% (13/13)
Psychiatric symptoms	69,2% (9/13)

15,4% (2/13) seizures alone
61,5% (8/13) cognitive deficits alone

Only one with faciobrachial distonic seizures

Memory, executive functions, visual-spatial abilities and visual-spatial memory

Table 3

Positive MRI	69,2% (9/13)
EEG	
Normal	30,7%(4/13)
Slow waves	15,4% (2/13)
Epileptic activity	53,8% (7/13)
Positive CSF	81,8% (9/11)
Paraneoplastic	15,4% (2/13)

Bilateral temporo-mesial hyperintensity

• 5/11 increased cells (mononuclear), mean 23,4 mm^3 (range 6-36)
• 8/11 increased protein
• 1/11 BOC

CONCLUSION

We confirm that autoimmune encephalitis represent an important cause of RPD. LE due to VGKC-complex abs was the predominant form. Therefore analysis of CSF to search for signs of inflammation and screening for neuronal antibodies are recommended in the diagnostic approach to RPD.

REFERENCES
Graus, F., Titulaer, M.J., Balu, R., Benseler, S., Bien, C.G., Cellucci, T., Cortese, I., Dale, R.C., Gelfand, J.M., Geschwind, M., et al. (2016). A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol *15*, 391–404
Geschwind, M.D., Shu, H., Haman, A., Sejvar, J.J., and Miller, B.L. (2008). Rapidly progressive dementia. Ann. Neurol. *64*, 97–108.