A case of PERM (Progressive Encephalomyelitis with Rigidity and Myoclonus) anti-GlyR positive

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Introduction: Progressive Encephalomyelitis with Rigidity and Myoclonus, (PERM) also called stiff-person syndrome plus, is similar to stiff-person syndrome with rigidity, stimulus-sensitive spasms, myoclonus, hyperekplexia and autonomic disturbance, but with additional brainstem or other neurological defects.
It has been historically associated with antiGAD antibodies. Since 2008, when a patient negative for antiGAD antibodies was found to have anti-glycine receptor antibodies (GlyR), further patients with PERM were investigated for them and correlation between these antibodies and PERM has been confirmed.

Materials and Methods: We report a case of a 74-year-old Caucasian man who first presented with severe dysphagia and hypophonia. His past medical history was unremarkable except for a progressive sleep disorder. Routine blood tests, neck and chest CT were all negative. Brain MRI showed small ischaemic lesions. Lanryngoscopy showed left vocal cord palsy. Patient received corticosteroids until full recovery of dysphagia and mild improvement of hypophonia. Eight months later he showed severe leg stiffness, jerks and paresthesias. Neurological evaluation revealed bilateral equinus foot and severe gait disturbance due to leg rigidity. CNS MRI and blood tests were unremarkable. After another course of steroids his symptoms improved, but he subsequently presented a relapse of his leg rigidity with painful cramps. ENG/EMG detected subcontinual motor activity, with lack of muscle relaxation in the gastrocnemii. Autoimmune work-up, including anti-GABA B and anti-GAD antibodies, resulted negative as well as oncomarkers (tables 1, 2, 3). After five months the patient complained severe deterioration of leg stiffness, dyplopia, dysphagia and dysphonia. Neurological evaluation revealed asymmetry of smiling, right eye esotropia, left deviation of protruted tongue, left curtain sign and severe leg stiffness. He repeated routine blood tests, and a CSF examination was performed, resulting all unremarkable. In suspicion of PERM we looked for anti-Glyα1R antibodies in both plasma and CSF . We initiated IVIg followed by corticosteroids.

Results and Discussion: almost complete regression of the symptoms was observed, with recovery of gait and swallowing. Anti-Glyα1R antibodies resulted positive at low titer in both plasma and CSF. Since 2008, when a patient with PERM was found to be positive to anti-Glyα1R, other similar patients have been described (1). GlyR is a pentameric gated ion channel and its activation by glycine leads to hyperpolarization of the membrane potential and reduced excitation (1). Its blockage by the anti-Glyα1R antibodies interfere with the mechanisms of motor and sensory excitation as well as with several other pathways, so that neurological signs appear.

Conclusions: anti-GlyR antibodies should be searched for in patients with brainstem dysfunction, hyperekplexia, stiffness, rigidity, myoclonus and spasms, due to the potential recovery after immunomodulating therapy, that must be initiated (1).

Table 1

Examination	Value	Normal ranges
INR	1.00	0.90-1.20
PTT	30.3 sec.	25-35 sec.
Fibrinogen	396 mg/dl	200-400 mg/dl
Anticardiolipine IgG	<3 GPLU/ml	0-15 GPLU/ml
Anticardiolipine IgM	<3 MPLU/ml	0-15
Lupus like anticoagulant (LAC)	1.1 RATIO	>2.0 present 1.5-2 mod. Present 1.2-1.5 weakly Present <1.2 absent
Anti Acetilcoline receptor	0.30 nmol/L	<0.25 negat 0.25-0.40 doubt > 0.40 positive
Anti-ENA antibodies profile		
nRNP/Sm	Negative	
SSA	Negative	
RO-52	Negative	
SSB(La)	Negative	
Scl 70	Negative	
Jo-1	Negative	
ANA	Negative	
Anti-DNA antibodies	Negative	
NSE (neuron-specific enolase)	8,4 ng/ml	4,7 – 14,7 ng/ml
Alpha-fetoprotein	1,3 ng/ml	0,0 – 8,1 ng/ml
CA125	8,4 U/ml	0 – 30,2 U/ml
CA15-3	17,3 U/ml	0 – 32,4 U/ml
Ca 19-9	8,73 U/ml	0 – 37 U/ml
CEA	1,03 ng/ml	0 – 5,0 ng/ml
PSA	0,58 ng/ml	0 – 4 ng/ml
TSH	1,144 microUI/ml	0,35 – 5,0 microUI/ml

Table 2

Examination	Value	Normal ranges
Anti-Ma1 antibodies	Negative	
Anti-Ma2/Ta antibodies	Negative	
Anti-CV2 (CRMP5) antibodies	Negative	
Anti-Yo antibodies	Negative	
Anti-HU antibodies	Negative	
Anti-Ri antibodies	Negative	
Anti-amphiphysin antibodies	Negative	
Anti-GABA B1 antibodies	Negative	
Reuma-TEST	0,9 IU/ml	0,0 – 20 IU/ml
Anti- GAD antibodies	0,4 U/ml	0,0 – 5,0 U/ml
Anti-neutrophil cytoplasmic antibodies (c-ANCA)	Negative	
Anti-neutrophil cytoplasmic antibodies (p-ANCA)	Negative	
Anti-MAG IgM	230,6 BTU	0,0 – 1.000 BTU
Anti-ganglioside antibodies IgG		
GM1 antibodies	Negative	
GM2 antibodies	Negative	
GM3 antibodies	Negative	
GD1a antibodies	Negative	
GD1b antibodies	Negative	
GT1b antibodies	Negative	
GQ1b antibodies	Negative	
Anti-ganglioside antibodies IgM		
GM1 antibodies	Negative	
GM2 antibodies	Negative	
GM3 antibodies	Negative	
GD1a antibodies	Negative	
GD1b antibodies	Negative	
GT1b antibodies	Negative	
GQ1b antibodies	Negative	
	Negative	

Table 3

Examination	Value	Normal ranges
Vitamin B12	209 pg/ml	120 – 970 pg/ml
Folic acid	2,1 ng/ml	1,5 – 16,9 ng/ml
Alpha-fetoprotein	3,44 ng/ml	0,0 – 6,0 ng/ml
CA125	19,3 U/ml	0 – 40,0 U/ml
CA15-3		
Ca 19-9	3,8 U/ml	0 – 37,0 U/ml

References
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