CHRONIC LYMPHOCYTIC INFLAMMATION WITH PONTINE PERIVASCULAR ENHANCEMENT RESPONSIVE TO STEROIDS (CLIPPERS): SPECTACULAR CLINICAL AND NEURORADIOLOGICAL SHRINKING IN A CASE WITH EXTENSIVE BRAIN INVOLVEMENT

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INTRODUCTION: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a rare disorder involving predominantly the pons, even if adjacent areas of central nervous system might be affected. Clinical and neuroradiological course may be progressively severe, prompting early diagnosis and treatment.

CASE REPORT: a 67 year-old-man was admitted for sub-acute onset of right arm weakness, dyplopia, distal four-limb paresthesias, gait instability, memory complaints and slowing; such symptoms had progressively appeared in the previous two months. Neurological examination revealed fourth left cranial nerve paresis, nystagmus, left-limb dysmetria, mild right arm weakness, ataxic gait; deep tendon reflexes were spared. Past medical history included asymptomatic carotid severe stenosis and mild hyperomocystinemia. Acetylsalicilc acid, atorvastatin and folinic acid were reported as usual therapy. No fever was detected; ECG, arterial blood pressure and routine blood exams were unremarkable. Five days before admission, brain magnetic resonance imaging (without contrast medium) had shown multiple areas of hyperintensity (using T2-FLAIR sequences) in medulla oblongata, pons, lower and middle cerebellar pedunculi (with left prevalence), midbrain, basal ganglia and temporo-mesial areas **(Fig.1)**; diffusion-weighted imaging had resulted negative. Repeated MRI evaluation showed enlargement of such areas, with "punctate" and "curvilinear" contrast enhancement **(Fig.2 - arrows)**; cervical spinal cord resulted normal. Cerebrospinal fluid analysis revealed mild pleyocitosis and hyperproteinorrachia; no oligoclonal IgG bands were detected. Extensive virological and reumathological laboratory evaluation resulted negative, as angiotensin converting enzyme, paraneoplastic markers, anti-neuronal autoantibody (including anti aquaporine-4 IgG); among blood lymphocyte subpopulations, a mild deficit of T-series was revealed. Digital subtractive angiography didn't reveal stenosis of the intracranial arteries; chest and abdomen CT scan were unremarkable. High-dose intravenous metylprednisone was administered for five days (with subsequent oral tapering), followed by dramatic clinical and neuroradiological improvement: at discharge, patient complained only mild distal arm paresthesias, neurologic examination was negative and MRI showed mild pontine abnormalities (on T2 FLAIR sequences - **Fig.3**), without contrast enhancement. Because of favorable course and the site of tiny alterations on MRI, brain biopsy was not performed. Diagnosis of CLIPPERS was hypothesized; going on with low-doses oral prednisone, neurological picture remained stable at a three-months follow-up.

DISCUSSION: CLIPPERS represents a rare disease deserving early diagnosis, because even in case of extensive and progressive brain involvement, response to steroids appears dramatic. Moreover, considering the risk of relapse, accurate long-term follow-up should be warranted.