Cerebellar degeneration syndrome associated to anti-CV2 antibodies and thymoma

D. Zaino, S. Casali*, S. Bocci*, G. Capoccitti*, L. Luzzi**, F. Giannini**

* Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy

**Department of Thoracic Surgery, University of Siena, Siena, Italy

BACKGROUND

Paraneoplastic cerebellar degeneration (PCD) is a rare neurological disorder associated with several cancers. Anti-CV2 antibodies (Ab) might be responsible of PCD.

CASE REPORT

· Femal, 74-year-old
· Medical hystory: cholecystectomy, diabetes mellitus type-2, mild renal failure, mild axonal sensorimotor polyneuropathy (ascribed to diabetes) and 2-years history of progressive ataxia
· Since some months: asthenia, gait instability, clumsiness of upper limbs, dysarthria and dysphagia
· Neurological examination: severe cerebellar gait ataxia, postural and acting tremor of hands with dysmetria, nystagmus, cerebellar dysarthria and dysphagia
· Brain MRI: unremarkable
·Genetic studies negative for Friedrich's ataxia and other adult-onset SCA.
·Total-body CT-scan (Fig.1): Anterior mediastinal mass with marked hypermetabolism at the total-body FDG-PET .
· RNS: Negative for neuromuscular junction disorders.
· Serum screening of onconeural Abs: Positivity of anti-CV2 and borderline value of anti-Ma2; positivity of Anti-AchR (Tab. 1)
· Surgery: Robot-assisted thymectomy.
· Histological examination: Thymoma (AB-type-WHO and stage IIa- Masaoka)
· Medical treatment: monthly IVIg (1.5 g/kg) inducing significant reduction of tremor and subjective improvement of limbs strength and dysarthria at 7 months follow up.

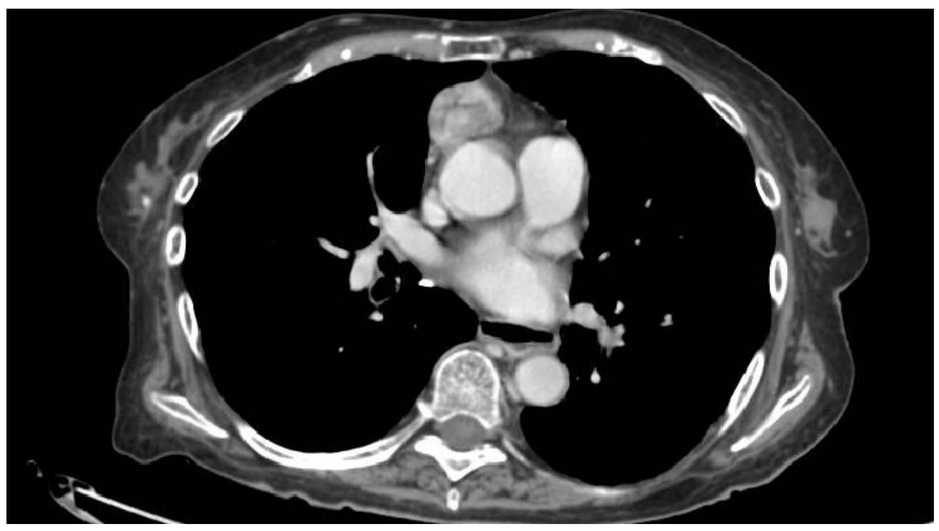

Fig.1 Total-body CT-scan showed thymoma.

Ab	Before surgery	After surgery (3 months)
Anti-CV2	+	+ (40)
Anti-sketetal muscle	+	+
Anti-ACHR	2.60 nmol/l	1.60 nmol/l
Anti-titin	unknown	+++ (97)

Tab. 1 Thymoma-related Ab values

DISCUSSION

Anti-CV2 Ab react with *collapsin response mediator protein* (CRMP5), a cytoplasmic antigen expressed by a subpopulation of oligodendrocytes in the brainstem, spinal cord and cerebellum. No specific tumors are related to anti-CV2 Ab. Small cell lung cancer, always expressing CRMP5, is the most frequent cancer associated to anti-CV2 (alone or with anti-Yo/anti-Hu). Up to 15% of patients with anti-CV2 present a thymoma. The most common paraneoplastic syndrome due to thymoma is myastenia gravis (MG), correlated with anti-AchR Ab. Conversely, detection of this Ab do not inevitably led to a myastenic clinical expression, as in our patient. Firstly reported in a patient with cerebellar ataxia, peripheral neuropathy, uveitis, optic neuritis and more rarely neuromyelitis optica have been described associated to anti-CV2 (Tab. 2). Since this onconeural Ab has never been found in idiopathic autoimmune conditions of CNS, therefore his detection is mandatory for the research of an occult cancer. In literature, only few cases concerning the follow-up of thymoma-related PDC showed a slow clinical improvement after-surgery without a further pharmacological therapy. Since any clinical improvement was observed three months after surgery, we decided to start periodic immunotherapy with IVIg. Four months later, a significant functional amelioration was noticed.

Clinical manifestations of paraneoplastic syndrome associated to *anti CV2-CRMP5*
Cerebellar ataxia
Chorea
Neuromyelitis Devic's like
Uveitis
Limbic encephalitis
Encephalomielitis
Paraneoplastic epilepsy
Sensory-motor neuropathy

Tab. 2 Major clinical features of anti-CV2 related syndromes

Camdessanché JP, Lassabliere F., Meyronnet D., Ferraud K, Absi L., Honnorat J., Antoine JC. Expression of the Onconeural CV2/CRMP5antigen in thymus and thymoma. J. Neuroimmunology 2006, 174:168-173.
Rogemond V., Honnorat J., Anti-CV2 Autoantibodies and Paraneoplastic Neurological Syndromes, Clinical Reviews in Allergy and Immunology, 2000, vol.19
Ducray F., Roos-Weil R., Garcia PY., Slesari J., Heinzlef O., Chatelain D., Toussaint P., Roullet E., Honnorat J. Devic's syndrome-like phenotype associated with thymoma and anti-CV2/CRMP5 antibodies. J. Neurol Neurosurg Psychiatry, 2007, 78(3): 325-7