Thymoma associated with an overlap of two paraneoplastic neurological syndromes: a case report

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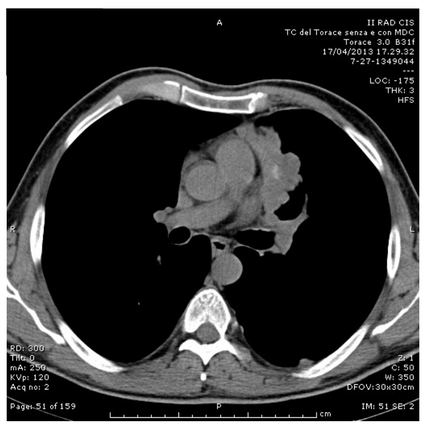
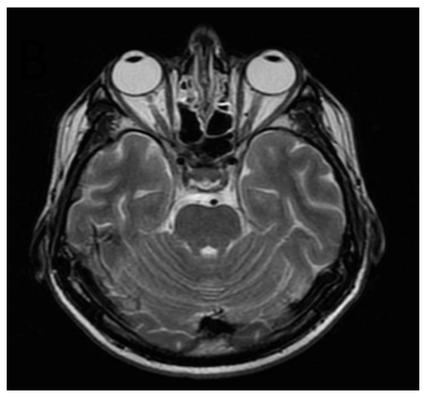
INTRODUCTION

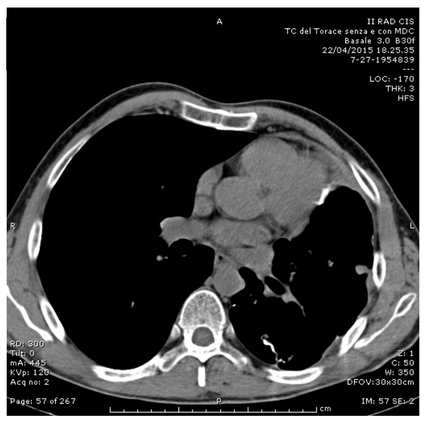
Paraneoplastic neurological syndromes (PNS) are disorders caused by immune responses directed against onconeuronal antigens of a neoplasia that crossreact with proteins expressed in the peripheral or central nervous system. Thymoma is often associated with myasthenia gravis while other PNS are rarely reported.
Here we report the case of a patient with thymoma, limbic encephalitis (LE) and neuromyotonia with occurrence of antibodies against AMPA receptor (AMPAR-Abs).

CASE REPORT

A 37 years old man came to our attention in March 2013 with a diagnosis of suspected thymoma with pleuropulmonary and lymph node implants. In 2010 a symptomatology characterized by back and cingular pain, weakness, severe hyperperspiration and mild fever occurred. After few months, fasciculations in legs occurred, together with memory loss and behavior disorders. In 2013, a chest CT-scan showed a solid mediastinal mass associated with a pleural thickening and a solid mass on the diaphragmatic pleura (figure A). Cytotoxic therapy was attempted, but was subsequently stopped because of infective complications. Brain MRI (figure B), EEG and dosage of AchR antibodies (0.10 nmoli/L) were normal. EMG showed the presence of multiple fasciculations, doublets, triplets and rare myokymia with a typical pattern of nerve hyperexcitability. On April 2013 the patient was hospitalized in our Division of Thoracic Surgery. In order to reduce PNS symptoms and to decrease the size of the thymic mass, as preparation for surgery, a treatment with high dosage of steroids (Prednisone 75 mg/die), intravenous immunoglobulins (IVIG) (0.4 g/kg/die for 5 days) and antiepileptic drugs (Carbamazepine 600 mg/die and Pregabalin 150 mg/die) was started. To reduce patient's confusion, anxiety and behavioral disorders low-dose benzodiazepines (Lorazepam) were used. On May 10, 2013 the patient underwent transternal extended thymectomy: the solid thymic mass infiltrated the pericardium and the left upper lung lobe. Multiple pleural lesions were also removed. Histology confirmed the suspected diagnosis of a thymoma B2-B3. Muscular twitching and hyperidrosis improved gradually until their disappearance. Clinical suspicion of a CNS neuronal surface antibody associated syndrome was confirmed by serological tests that showed the presence of AMPAR-Abs.
On February 2014 he developed a relapse of thymoma (figure C), treated with radiotherapy, and neurological symptoms appeared again, especially characterized by nerve hyperexcitability. On June 2014, he underwent thoracotomy for pleural and diaphragmatic implants of thymoma. A chest CT scan, performed in December 2014, revealed a pleural recurrence of thymoma treated with RT. A further abdominal relapse was surgically treated in March 2015. Actually, neurological symptoms are carefully controlled with pharmacological therapy (Phenytoin 300 mg/die, Prednisone 25 mg/die).







DISCUSSION AND CONCLUSIONS

In our case report, thymoma was associated with a PNS hard to classify: the positivity of AMPAR-Abs and the occurrence of memory loss and behavior disorders, even if MRI and EEG were negative, were suggestive of limbic encephalitis while nerve hyperexcitability and EMG findings were indicative of neuromyotonia. Surgical treatment of thymoma dramatically improved all the neurological conditions of the patient allowing the reduction of medical therapy. The association of steroids and IVIG increases the efficacy of thymectomy and represents an useful tool in the long-term control of autoimmune reactions triggered by thymic pathology. Diagnosis of PNS should be suspected in patients with sub-acute onset of nerve hyperexcitability. A prompt immunotherapy and a radical resection of the tumor are essential to obtain the best outcome.

	Syndrome	Cancer
NMDAR	Encephalitis	Ovarian teratoma (rare in children, present in 58% older than 18 years)
$GABA_BR$	Limbic encephalitis	SCLC (70%)
CASPR2	Morvan's syndrome	Thymoma (38%)
AMPAR	Limbic encephalitis	SCLC, breast, thymus (60%)
VGCC	PCD	SCLC (>95%)
mGluR5	Limbic encephalitis	Hodgkin's disease (two cases reported only)

Fig. 2: Antibodies against cell surface or synaptic antigens associated with paraneoplastic neurological syndromes. AMPAR, amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; CASPR2, contactin-associated protein 2; GABABR, γ-aminobutyric acid-B receptor; mGluR5, metabotropic glutamate receptor type 5; NMDAR, N-methyl-D-aspartate receptor; PCD, paraneoplastic cerebellar degeneration; SCLC, small-cell lung cancer; VGCC, voltage-gated calcium channel. From: Francesc Grausa and Josep Dalmau. Paraneoplastic neurological syndromes. Curr Opin Neurol. 2012 December ; 25(6): 795–801.

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