

Anti- Ma2–associated opsoclonus-ataxia syndrome

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Introduction

Opsoclonus is an ocular dyskinesia consisting of involuntary, chaotic, arrhythmic, and multidirectional saccadic ocular movements [1]. We describe a case associated with Anti-Ma2 antibodies.

Case report

A 56-year-old woman presented with a 6-month slowly progressive disorder characterized by abnormal gait and involuntary ocular movements. Her past medical history was remarkable for mixed anxiety-depressive disorder, subclinical Hashimoto's thyroiditis and chronic gastritis. She was a heavy smoker. She was under citalopram, propranolol, alprazolam, and esomeprazole.

On examination, she had mild ataxic gait and mild hypotonia of the limbs. Ocular examination revealed bilateral opsoclonus, eyelid flutter and intermittent exotropia.

Routine laboratory tests and brain MRI were normal. Laboratory testing for infections and autoimmune diseases were unremarkable. Thyroid hormones were within the normal values. Tumor markers were within the normal range except for thyroglobulin that was 107 ng/ml (normal range 0-50). A lumbar puncture was performed. CSF values of cells, proteins and glucose were within the normal values; search for malignant cells was negative.

To exclude systemic malignancy a whole body 18F-FDG PET/CT scan was performed, showing probably non-specific uptake in the tongue, in some small (<1-cm) cervical lymph nodes (SUV max 2.5) and diffusely increased uptake in the thyroid gland (SUV max 6).

We also carried out an extensive paraneoplastic workup including anti-Ri, anti-Hu, anti-Yo, anti MA2/TA, anti voltage-gated potassium channel, anti AMPA1-2, anti ANNA2, anti CV2, anti LGI1, anti-amphiphysin, and anti-NMDA receptor antibodies. Intravenous methylprednisolone, 1000mg daily for 5 days, was given, obtaining only a mild and partial exotropia improvement. One month later, we received the results of positive anti-Ma2 antibodies in the serum and the CSF.

Treatment was initiated with intravenous immunoglobulin (0,5g/kg for 5 days) and the opsoclonus rapidly improved. The effect lasted about 6 weeks.

At the moment, the patient is treated with IVIG every two months and is regularly screened for malignancy.

Discussion

In adults, opsoclonus has a paraneoplastic etiology in nearly 60% of cases. The most commonly found onconeural antibodies are anti-Ri and anti-Hu, while anti-Ma2 antibodies are usually associated with limbic encephalitis. There are very few case reports of paraneoplastic opsoclonus associated with anti-Ma2 antibodies, caused by lung cancer or gastric adenocarcinoma [2-3]. Paraneoplastic syndromes can antedate clinical manifestations of tumour by years and the underlying malignancy may be not detected although accurate screening.

References

1. A. Wong. An update on opsoclonus. *Curr Opin Neurol.* 2007 Feb;20(1):25-31
2. N. Mélé et al. Paraneoplastic opsoclonus and cerebellar ataxia related to anti-Ma2 antibody: a case report. *J Neurol.* 2016 Feb; 263(2): 405-6.
3. D. Biotti et al. Opsoclonus, limbic encephalitis, anti-Ma2 antibodies and gastric adenocarcinoma. *Eur J Neurol.* 2012 Dec;19(12):144-5

Table 1 Etiology of opsoclonus

Paraneoplastic

- Children – Neuroblastoma
- Adult – Lung, Breast, Thyroid, Stomach, Genital tract, Intracranial Tumors, Lymphoma

Parainfectious

- Meningitis, Streptococcal infection, HIV, EBV, CMV, Hepatitis, Scrub typhus, Borrelia, West Nile Virus

Toxic

- Toxins (OPC, Thallium, Toluene)
- Drugs (Cocaine, Lithium, Phenytoin, Amitriptyline)

Metabolic

- Hashimoto's thyroiditis
- Pregnancy

Miscellaneous

- Multiple sclerosis, Hydrocephalus, Thalamic bleed, Celiac disease, Sarcoidosis, Post stem cell transplantation

Table 2

Well-characterized onconeural antibodies, paraneoplastic syndromes (PNS), predominant associated tumours

Antibody	PNS	Tumours
Hu	PEM	SCLC, other
Yo	PCD	Ovary, breast
Ri	PEM, POM	Breast, SCLC
Amphiphysin	PEM, Stiff-person	Breast, SCLC
CRMP5	PEM, PCD, chorea, neuropathy	SCLC, thymoma
Ma2	PEM	Germ cell tumor, Lung, Breast, Lymphoma
Tr	PCD	Hodgkin lymphoma

PEM, paraneoplastic encephalomyelitis; PCD, paraneoplastic cerebellar degeneration; POM, paraneoplastic opsoclonus-myoclonus; SCLC, small cell lung cancer