Concurrent atypical paraneoplastic demyelinating polyneuropathy and neuromuscular junction defect in a patient with anti-VGCC antibodies

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❖ INTRODUCTION

Anti P/Qtype-voltage-gated calcium-channel antibodies (VGCC-Abs) are found in more than 90% of patients with Lambert Eaton syndrome (LES).
In some patients, anti-VGCC-Abs target both P/Q and N-type channels, but the clinical implications of such findings are uncertain.

❖ CASE REPORT November 2015

We report a case of a 68-year-old patient with a neuroendocrine cancer who developed an atypical subacute polyneuropathy followed by a neuromuscular junction defect, with antibodies targeting both the P/Q and N-type VGCC.

CLINICAL FEATURES

subacute numbness at the extremities with progressive gait impairment

ELECTROPHYSIOLOGICAL STUDY → demyelinating sensory-motor polyneuropathy

CSF ANALYSIS → pleocytosis (25 cells/mm3)
mild blood-brain-barrier damage
unique to CSF oligoclonal IgG bands

BLOOD TESTS → Negative:
systemic autoimmunity
anti-Borrelia Burgdorferi Abs
anti-HIV Abs
anti-nerve and onconeural Abs

ONCOLOGICAL SCREENING

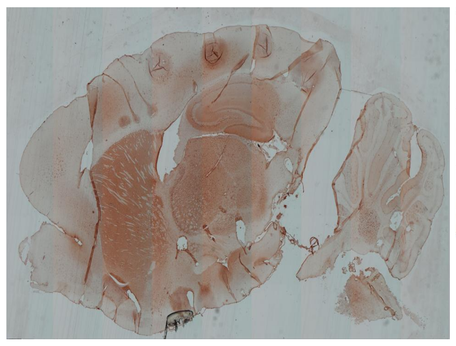
Total body CT: **left adrenal mass**
Total body FDG-PET: **ilar, left adrenal high metabolic tissue**.

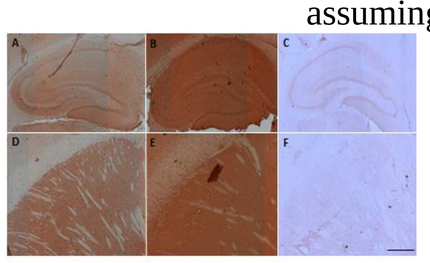
Duodenal ecoendoscopic biopsy: **neuroendocrine cancer.**

chemotherapy with **cisplatin** and **ethoposide**
+
high dose intravenous Methylprednisolone

Serum and CSF samples were tested with **immunohistochemistry (IHC)** on rat brain optimized for **surface neuronal antigens** that revealed a **staining pattern involving hippocampus, globus pallidus and striatum**

assuming an immune-mediated origin of the disorder





Immunohistochemistry on rat brain sagittal slices, 7 microns. Brown: peroxydase staining using ABC-kit on byotinilated goat anti-human secondary antibody. Autoantibodies in patient's cerebrospinal fluid (CSF, 1:2) provide a 'neuropilar' staining involving the hippocampus (A) and the striatum (D). A similar staining, with differences in the distribution, can be observed using a positive control for LGI1 (serum, 1:200), a neuronal surface protein (B-E). No staining is obtained using a control CSF (C,F).

The patient presented poor response
in addition, **intravenous Immunoglobulin** were administered, without benefit.

❖ CLINICAL COURSE May 2016

The patient developed intense fatigue, weakness and ptosis, especially during the evening.
At the neurological examination: proximal weakness in all limbs and a convergent strabismus in the right eye after muscular exercise
TBTC demonstrated a reduction of the tumour →

ELECTROPHYSIOLOGICAL STUDY
BLOOD TESTS

repetitive stimulation test : negative
anti-acetylcholine receptor antibodies test: negative

The patient was tested with a specific radioimmunoassay for P/Q-type-VGCC-Abs that resulted positive

The IHC staining was retrospectively evaluated and found to be compatible with N-type-VGCC-Abs

❖TREATMENT RESPONSE

The patient started treatment with **Rituximab (1000 mg every 15 days, 2 cycles)** and symptomatic therapy with amifampridine.
One month later the last cycle of Rituximab, the neurological examination showed a **complete recovery of the proximal weakness**, with a stabilization of the remaining neurological signs and symptoms.

❖ CONCLUSION

A **N-Type-VGCC-Abs** have been reported in a **minority of patients with LES**, usually in co-occurrence with P/Q.
In our case, this unusual serologic finding was associated with an **atypical paraneoplastic syndrome** combining **demyelinating polyneuropathy** and **neuromuscular junction defect.**
Whether N-type-VGCC-abs could have a diagnostic value in paraneoplastic disorders needs to be further explored.

P/Q- and N-type calcium-channel antibodies: oncological, neurological, and serological accompaniments, Nicholas L. Zalewski, et al., Muscle Nerve 54: 220–227, 2016