LONG-LASTING RESPONSE TO CYCLOPHOSPHAMIDE IN A PATIENT WITH ANTI-CONTACTIN-1 ANTIBODY POSITIVE CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND MEMBRANOUS GLOMERULONEPHRITIS.

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Background
Anti-contactin-1 (CNTN1) antibodies of the IgG4 isotype have been recently detected in a subgroup of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) showing acute/subacute onset of severe sensorimotor polyneuropathy, early axonal damage and poor response to intravenous immunoglobulin (IVIg) and corticoststeroids. The anti-CNTN1 antibody pathogenic mechanism seems to be related to the physical interaction with CNTN1-neurofascin 155 (NF155) complex at paranodes, leading to loss of nodal integrity. Treatment of these patients is challenging. We report a patient with anti-CNTN1 antibody-positive CIDP and membranous glomerulonephritis (MGN) showing a long-lasting response to cyclophosphamide.

Case Report
Male, 70 yo, Caucasian, no relevant past medical history

2004
Neurological symptoms and signs:
Pins-and-needles sensation at lower limbs progressing to upper limbs, walking difficulties progressing within a month
Proximal and distal muscle weakness (3-4 MRC)
Absent DTR, “stoking&glove” pattern of hypoesthesia, LL impaired vibratory sense and SK ;sensory ataxia; gait with double support
CSF:
CSF protein: 142 mg/dL, cell count: 1
EMG:
Demyelinating polyneuropathy
Sural nerve biopsy:
Diffuse loss of myelinated fibers

Diagnosis ACUTE POLYRADICULONEURITIS
Treatment IvIg
Outcome No clinical and functional improvement

Subsequent clinical course:
worsening of lower limb weakness + ankles swelling
Blood test:
anemia, low serum albumin, proteinuria (up to 10 g/24h)
Kidney biopsy:
consistent with MGN

Diagnosis NEPHROTIC SYNDROME
Treatment Prednisone 50 mg/die
Outcome Improvement of kidney function, neurological function substantially unchanged

2005
Neurological symptoms and signs:
substantially unchanged

MRI:
mild enlargement of spinal nerve roots (Gd not administered due to kidney failure)

Blood analysis:
CBC, ESR, ANA, ANCA, FR, serum and urine immunoelectrophoresis, anti-ganglioside antibodies: negative

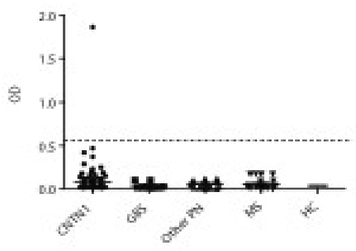
CSF:
albumin: 83 mg/dL, CSF cell count: <2

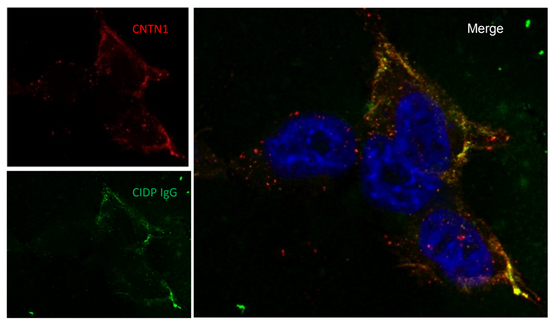
Kidney biopsy:
confirms pathologic features of MGN stage I, with subepithelial deposits of immune complexes and complement deposition (C3). No evidence of vasculitis or amyloid deposits

Diagnosis CIDP + ANCA-NEGATIVE MGN

Treatment 1g iv cyclophosphamide monthly for 6 months; slow prednisone tapering
Outcome Normalization of muscle strength and partial improvement of sensory ataxia; unassisted gait; normalized renal function

2016
Subsequent neurological course:
stable neurological and kidney function; no further immunosuppressive treatment required
Neurological examination:
normal muscle strength, weak DTR, hand finger and distal LL hypoesthesia, LL impaired toes vibratory sense and SK, slight sensory ataxia (unassisted gait)





Conclusions
The clinical features of our patient fit with the mostly reported ones in patients with anti-CNTN1 antibody positive CIDP. As recently reviewed, CIDP has rarely been reported in association with MGN. CNTN1 protein is expressed at low levels in kidney and might represent a shared antigen target with peripheral nervous tissue. However, in the only other patient reported with anti-CNTN1 antibody positive CIDP and MGN, binding assays on mouse kidney sections did not show increased reactivity with respect to normal controls. Despite all limitations of a single case observation, our report suggests that cyclophosphamide could be considered an effective therapy in anti-CNTN1 antibody-associated CIDP and MGN.

References
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