Peripheral Autoimmune Neuropathy Assessed Using Corneal In Vivo Confocal Microscopy

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**Background:** Corneal nerves can be examined using in vivo confocal microscopy (IVCM). This new technique permits sequential observation of the corneal subbasal nerve plexus and detects early signs of diabetic peripheral neuropathy.

**Objective:** To describe a patient with autoimmune peripheral neuropathy followed up using corneal IVCM.

**Design:** Case report.

**Setting:** Clinic of neurology, Geneva, Switzerland.

**Patient:** A 56-year-old man with peripheral neuropathy diagnosed as anti–myelin-associated glycoprotein neuropathy. His symptoms initially worsened despite the administration of intravenous immunoglobulins and plasma exchange. Evolution was eventually favorable after rituximab and corticosteroids were given. At 1-year follow-up, clinical recovery was almost complete, and the patient was stable according to the results of clinical and electrophysiologic assessments.

**Main Outcome Measure:** Corneal nerve measurement by IVCM.

**Results:** Examination of corneal nerves using IVCM at 2 different times during the patient’s clinical evolution (peak disease and recovery phase) demonstrated histologic signs that correlated with the results of clinical and electrophysiologic assessments.

**Conclusion:** This observation supports the hypothesis that corneal IVCM could also be helpful for the early detection or follow-up of autoimmune peripheral neuropathy.

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**Report of a Case**

Across a 2-month period, a 56-year-old man developed progressive ascending sensory loss in both legs, associated with distal weakness. On hospital admission, neurologic examination of the lower limbs revealed distal and symmetrical weakness (grade 4 on the Medical Research Council scale) associated with alteration of touch and pain sensations. Tendon jerks were absent. The remaining results of his neurologic examination were normal.

Results of routine laboratory blood tests and cerebrospinal fluid examination were normal. Immunologic tests revealed a paraproteinemia IgM kappa (monoclonal gammopathy of undetermined significance) associated with anti-MAG antibodies to 7916 arbitrary units (N < 1000). Paraneoplastic antibodies (amphipysin, CV2/CRMP5, GAD, HU, Ri, and Yo) and anti-ganglioside antibodies (GM1, GM2, GD1a, GD1b, and GQ1b) were absent. Results of serologic testing were negative (human immuno deficiency virus, hepatitis B and C, Borrelia burgdorferi, syphilis, and Campylobacter jejuni) or were not suggestive of an acute infection (herpes virus types 1-6). Findings from spinal magnetic resonance imaging and thoracic computed tomography were normal. Bone marrow biopsy results were normal except for mild polyclonal plasmacytosis.

Despite the initiation of intravenous immunoglobulin therapy and, 1 month later,
plasma exchange, the clinical course was marked by rapid progression of distal lower limb weakness and sensory ataxia, which necessitated assistance with walking. Electroneuromyography of the lower limbs at this stage showed reduced amplitudes, increased latencies, severe temporal dispersion of distal motor responses with marked slowing of nerve conduction velocities, and disappearance of F waves.

The patient had no personal or family history of eye disease and no history of contact lens wear, ocular trauma or surgery, or systemic diseases that might have affected the cornea. Results of an ophthalmic evaluation, including visual acuity and anterior segment, fundus, and corneal sensitivity using cotton-wool stimulus all over the corneal surface, were clinically normal.

Corneal IVCM was performed using a Heidelberg Retina Tomograph II Rostock Cornea Module (Heidelberg Engineering GmbH, Dossenheim, Germany). After the application of topical anesthesia (oxybuprocaine, 0.4%) (Novartis Pharma Schweiz AG, Bern, Switzerland), Lacryvisc gel (Alcon Laboratories Inc, Hünenberg, Zug, Switzerland) was applied before aligning the

Figure. Corneal nerve examination by means of in vivo confocal microscopy (left eye; bar = 50 µm). A, Basal epithelial nerve bundles are normal in our patient (arrows). B, Stromal nerves in a control patient with typically linear morphologic features (arrow). C, Stromal nerves are thickened and tortuous during clinical worsening (arrows). D, One year after escalation of therapy, including rituximab dosage, the stromal nerves are thinner and less tortuous (arrows).
The cornea is one of the most densely innervated parts of the human body. The nerve bundles lose their perineurium at the limbus and continue centrally and anteriorly in the cornea surrounded by Schwann cell sheaths. The case reported herein illustrates an anti-MAG neuropathy requiring polyimmunosuppressive therapy eventually associated with a favorable clinical evolution.

In conclusion, we believe that corneal IVCM, a noninvasive surrogate marker of nerve fiber abnormalities, may be useful for assessing peripheral autoimmune demyelinating conditions such as anti-MAG neuropathy. This new technique might help physicians detect autoimmune neuropathy earlier and follow disease progression or response to therapeutic intervention by means of repeated assessment.

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