Course of disease and response to treatment

Patient 1 was admitted in 09/2017 with suspected GBS and became tetraplegic and almost locked-in within two months. He was resuscitated once, presumably as a result of autonomic failure. NCS showed prolonged DML and reduced NCV, SNAP and CMAP and spontaneous activity was recorded during the course of disease. Sural nerve biopsy revealed axonal loss, no signs of demyelination (Supplemental Figure 2 <http://links.lww.com/NXI/A134> ). Treatment with IVIG, glucocorticoids, plasma exchanges and rituximab did not lead to a major improvement although anti-NF titers decreased to 1:100 but strong paranodal binding to murine teased fibers persisted. The patient died due to sepsis in 07/2018.

Patient 2 first reported gait ataxia and distal hypesthesia in 06/2014. An anti-NF-155 titer of 1:1,000 was retrospectively detected in a serum sample from 07/2014. The patient developed progressive tetraparesis in 10/2014, resulting in tetraplegia and almost locked-in syndrome in 11/2014. Serum from 01/2015 revealed an increased anti-NF-155 titer of 1:5,000. IVIG, glucocorticoids, repetitive plasma exchanges and an experimental course of abatacept did not show any effect and the patient was tetraplegic and ventilated for 1.5 years. First improvement was reported in 11/2015 after another treatment with glucocorticoids and weaning of mechanical ventilation was successfully performed in 05/2016. In 01/2017 some movement of the wrist was possible again (MRC 1-2) and oculomotor palsy slowly improved. The patient did not get any further treatment and recovered. In 10/2018, the patient could sit in a wheel-chair and move it with his feet. Proximal strength was assessed with MRC 2-3, distal strength 3-4. Cranial nerve involvement was completely regressive. He was able to live independently with assistance for transfers. Improvement is still ongoing. No anti-NF autoantibodies were detectable anymore.

Patient 3 was categorized as GBS. Symptoms started with tingling of both hands. On the next day, tingling included both feet and the patient developed rapidly progressive tetraparesis, resulting in almost tetraplegia within a few days. CSF was normal. NCS showed moderate reduction of CMAP and SNAP and reduced F wave persistence, but normal NCV and DML. EMG recorded some spontaneous activity as a correlate of mild axonal damage. In combination with the clinical presentation of almost tetraplegia, distal partial CB (resulting in reduced CMAP) and proximal partial CB (as a correlate of reduced F wave persistence) can be assumed. Plasma exchange was performed and the patient fully recovered within several weeks.

Patient 4 was diagnosed with CIDP in 12/2015, suffering from tingling feet, gait ataxia and tetraparesis. He became almost wheel-chair bound in 2017. Disabling tremor and severe autonomic symptoms were apparent. Anti-NF-155 titers were 1:6,000 in 2017. In spite of plasma exchange and rituximab, anti-NF155 titers increased to 1:10,000 in 2018 and the patient showed only mild improvement.

Patient 5 had been suffering from progressive action, postural and intention tremor since his late childhood. He reported progressive impairment of fine motor skills, particularly during sports and drawing, over the years. These symptoms led to neurological consultation in 2017 when additional mild gait ataxia and absence of deep tendon reflexes, but no obvious sensorimotor deficits were documented. In 2018, mild distal paresis and reduced vibration sensation were found. CSF showed markedly raised protein levels (4400mg/l) with normal white cell count. NCS showed features of severe demyelinating neuropathy with prolonged DML, significant reduction of NCV, CMAP and SNAP, and spontaneous activity in the EMG as a sign of axonal damage. NCS values were deteriorating despite IVIG treatment. Sural nerve biopsy did not unveil any demyelinating features, but signs of advanced (secondary) axonal damage. The patient reported mild, but only temporary improvement of tremor after the first plasma exchange in 10/2018 and moderate improvement after therapy with rituximab in 2019.

Patient 6 presented with slowly progressive distal-symmetric sensorimotor peripheral neuropathy. Symptoms started with severe back pain in 2004 (not surely related to neuropathy), followed by tingling of the feet in 2006. Sensory deficits in the hands, and more rapidly progressive tetraparesis and neuropathic pain occurred at the end of 2007 and the patient was wheelchair-bound nine months later. NCS showed signs of demyelinating neuropathy, CSF protein was elevated. IVIG was not effective.