**Supplemantary file 1**

Description of the clinical course, neuroimaging findings and outcome of three children with MOG- encephalitis

Patient 1

The first child was born at term after an uneventful pregnancy and had a normal development when she presented with severe headache for three weeks to the emergency room of a local hospital in July 2015 at the age of 14 years (Patient 1, Table 1). In addition, the parents noted tiredness with a poor attention span and absent mindedness. At first presentation she had no signs of infection. On the second day at the hospital she developed fever of 38.5°C, increased headaches, and two focal seizures affecting the left arm with secondary generalization followed by a hemiparesis lasting for eight weeks. CSF studies showed an elevated cell count of 256 WCC/µl. Work-up for bacterial and viral pathogens for suspected meningoencephalitis in stool, throat swab, blood and CSF including HCV- PCR were all negative. The EEG revealed a continuous right sided delta/sub-delta slowing without any embedded spike-waves. MRI of the brain performed four days after admission showed signal changes in the temporal-parietal right cortical grey matter without contrast enhancement (Figure 1 A-D). The girl was treated with antibiotic and antiviral medications in addition to phenobarbital and referred in stable condition to a rehabilitation unit for six weeks.

Two days after discharge from the rehabilitation unit she developed left-sided focal seizures and was admitted to hospital. A lumbar puncture showed an elevated cell count of 32 WCC/µl. This time the MRI of the brain revealed T2 signal changes in different areas including the deep white matter, midbrain, pons as well as the cerebellar peduncles (images not shown). Autoantibody testing revealed serum MOG abs with a titer of 1:100 (Euroimmun) in addition to positive OCBs. She was treated with high-dose IVMP 1g/daily for three days and discharged in a healthy condition. Four weeks later she developed sudden onset of memory problems, aggression, sleeping problems, and social withdrawal. The third MRI of the brain showed a new and large T2 signal alteration in the pons with contrast enhancement (Figure 1E, F). In addition to serum MOG abs, anti-NMDAR abs were detected in serum and CSF. Treatment with IVIG 2g/kg/cycle and RTX 375 mg/m2 body surface area was administered leading to substantial and ongoing improvement for the following 2.5 years. Repeat MRIs of the brain showed resolution of lesions. Testing for serum NMDAR abs was repeated 12 months later and reported as being negative.

In October of 2018 she was admitted to the local hospital with dizziness, a tendency to fall to the left side combined with a sudden loss of hearing of the left ear. Brain imaging showed a new infratentorial lesion (Figure G, H). Serum MOG ab levels were 1:320. The acute episode was treated with IVMP and led to complete recovery. A maintenance therapy with SCIG of 0.5g/kg/bodyweight/month was started. So far in the last 12 months no new episodes have occurred.

In July 2015 a serum sample was sent for virological studies to the MERIN project, an epidemiological study of the state of Lower-Saxony, Germany, on the incidence of viral encephalitis in children. We contacted the study coordinator in June 2019 and were given a portion of the remaining sample. Retesting with a live CBA revealed an elevated MOG ab titer of 1:640 of the July 2015 sample indicating that the initial episode had been a MOG- encephalitis followed by further demyelinating episodes in addition to a NMDAR-encephalitis overlap syndrome four months after the initial episode. The serum sample from July 2015 was negative for NMDAR abs. CSF samples from this episode were not available.

*Patient 2*

The second child was a previously healthy 12-year-old boy who developed high temperature (>38.50 C) and gastroenteritis with frequent watery stools prior to admission (Patient 2, Table 1). One week later his general condition worsened. He refused to drink and his parents noted that he became more tired associated with mental status changes. He was not orientated to place and time, could not speak in full sentences and appeared confused. He was not able to walk alone.

His neurological examination revealed no focal neurological signs apart from mild meningism without signs of increased cranial pressure. CSF analysis showed 21 WCC/µl. HSV- and tick-borne encephalitis -PCR in CSF were negative. Serological studies in serum and CSF did not reveal any signs of Lyme neuroborreliosis, adenovirus nor enterovirus infection. Throat swab and stool samples tested for different pathogens including enterovirus were reported as normal.

Autoantibody studies against neuronal surface antigens in CSF and serum were all negative. Serum MOG abs tested with a live CBA were positive with 1:320. EEG recording showed a generalized slowing with high- amplitude delta and sub-delta waves.

The initial MRI of the brain was characterized by widespread swelling of the cortical areas and deep gray matter structures in particular of the putamen and increased signal intensity on FLAIR sequences (Figure 2 A, B).

The patient was started on IVMP and given a first dose of IVIG, when he showed worsening of his general condition again with increased somnolence. Due to presumed generalized swelling of the cortical regions the patient was transferred to a pediatric intensive care unit. With a second cycle of IVMP over five days and IVIG he showed signs of improvement and was transferred ten days later back to our hospital with still marked weakness of his upper and lower limbs. He received a third IVMP pulse followed by an oral steroid taper over the following weeks. MRI of the brain was repeated after seven days and showed an improvement of the cortical and deep gray matter alterations but a new demyelinating lesion in the pons (Figure 2 C-F) explaining his inability to move arm and legs. Nevertheless, the patient showed a remarkable recovery in the following two weeks with physiotherapy. At the time of discharge five weeks later, he was able to walk alone with good cognitive capacities while waiting for his rehabilitation placement.

*Patient 3*

The third child was a previously healthy 16-year-old competitive rower who presented to the emergency room with a six-day history of severe right-sided headache (Patient 3, Table 1). His teachers noted that his personality had changed over the last days. He was described as withdrawn, tired and not responding to questions in his usual manner. He started to play with simple toys and lost his ability to walk safely on his own. The main finding in the initial neurological examination was impairment in orientation in time and space. He was somnolent and could only follow simple commands, his speech was dysarthric. EEG recording in awake state showed slowing with continuous high-amplitude delta and theta waves over the right cerebral hemisphere but no spike-wave activity. In the first brain MRI FLAIR signal changes in combination with diffusion-restriction were detected in both hippocampi (Figure 3 A-D). CSF cell count was elevated with 44 WCC/µl with an elevated total protein of 122 mg/dl. No additional OCBs in the CSF were found. HSV- and enterovirus-PCR in CSF were negative. Serological studies in serum and CSF did not reveal any signs of Lyme neuroborreliosis or varicella infection.

Autoantibody studies against neuronal surface antigens in CSF and serum were all negative. Serum MOG abs were positive with a titer of 1:640. Apart from standard treatment he was started on IVMP 1g/daily for five days followed by prednisolone taper over eight weeks. After ten days he had recovered completely and was discharged in good health. He was last seen in the clinic 10 months later. Follow-up MRI of the brain was reported as normal. MOG abs levels declined to 1:80 (>1:160 cut-off).