Recurrent meningoencephalitis in a T cell dysregulated patient – A case report

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Case presentation
We present a 57-year-old male with an eleven-month history of recurrent episodes of meningoencephalitis.

- **Initial symptoms**: diarrhea, fever and cephalgia
- **Initial diagnostics**: no neurological deficit; no abnormalities on first cerebral and spinal MRI; CSF pleocytosis with 95 cells/μl and negative test results for common infectious triggers
- **Disease course**: recurrent episodes of cephalgia, fever and fatigue (for more details, see figure 1), later with a mild neurocognitive disorder and fine motor skill disorder in the right hand
- **Treatment and Outcome**: Symptoms relieved after empirical antibiotic and antiviral treatment, but also spontaneously. Treatment with immunoglobulins and oral prednisone was insufficient. Complete regression of MRI lesions was observed while treated with high-dose steroids combined with interferon beta.

Results
- **CSF/brain biopsy**: sequential lumbar puncture with a pleocytosis ranging from 5 to 65 cells/μl (figure 1), positive PCR for human parechovirus (3.9 months post symptom-onset); negative results for paraneoplastic and autoimmune antibodies in CSF and serum; brain biopsy and metagenomics analyses revealed no additional etiological information.
- **Serum**: Detection of a T cell dysregulation; autoantibodies against type I interferon omega (figure 3).
- **MRI**: Multiple follow-up MRIs revealed fulminating, bihemispheric hyperintense fluid-attenuated inversion recovery (FLAIR) lesions, predominantly in the fronto-temporo-parietal regions (figure 2). MRI lesions correlated with the clinical course.
- **Negative results** for differential diagnosis including infectious, rheumatologic, vascular, metabolic disorders, and neoplastic diseases.

![Graphical case overview](figure1.png)

**Figure 1.** Graphical case overview including clinical data (fever, headache), serological data (sNfL, CSF cell count and total protein), and treatment

![Longitudinal radiological course](figure2.png)

**Figure 2.** Longitudinal radiological course: (a) 3.8 months, (b) 4.8 months, (c) 5.2 months, (d) 6.3 months, (e) 8 months, (f) 9.5 months, (g) 10.4 months post symptom-onset.

Discussion
Human parechovirus, detected in the CSF of the patient, is known to cause gastrointestinal and respiratory infections. It can, in rare cases, also lead to encephalitis in children. The patient presented with highly neutralizing autoantibodies against interferon omega, known in the context of severe COVID-infection, combined with a T cell dysregulation in the peripheral blood, causing a partial immune defect in this individual, resulting in a possible infection of the central nervous system. The hypothesis of an ongoing chronic infection with relapses approximately every three weeks is contradicted by repetitive negative results, even in the metagenomics analyses, and the spontaneous recoveries. Interestingly, complete recovery of the FLAIR hyperintense lesions (figure 2g) and an increase in the time interval to the next relapse (figure 1) was observed while treated with high-dose steroids combined with interferon beta.

Conclusion
We report a rare case of adult recurrent meningoencephalitis, suspected to have a viral origin, accompanied by a dysregulation of the immune system. Immunosuppressive treatment with high-dose cortisone and interferon beta led to a recovery of FLAIR hyperintense lesions. This supports the hypothesis of either ongoing seronegative autoimmune encephalitis or an interferon pathway-related immunodeficiency that triggers meningoencephalitis following harmless infections.