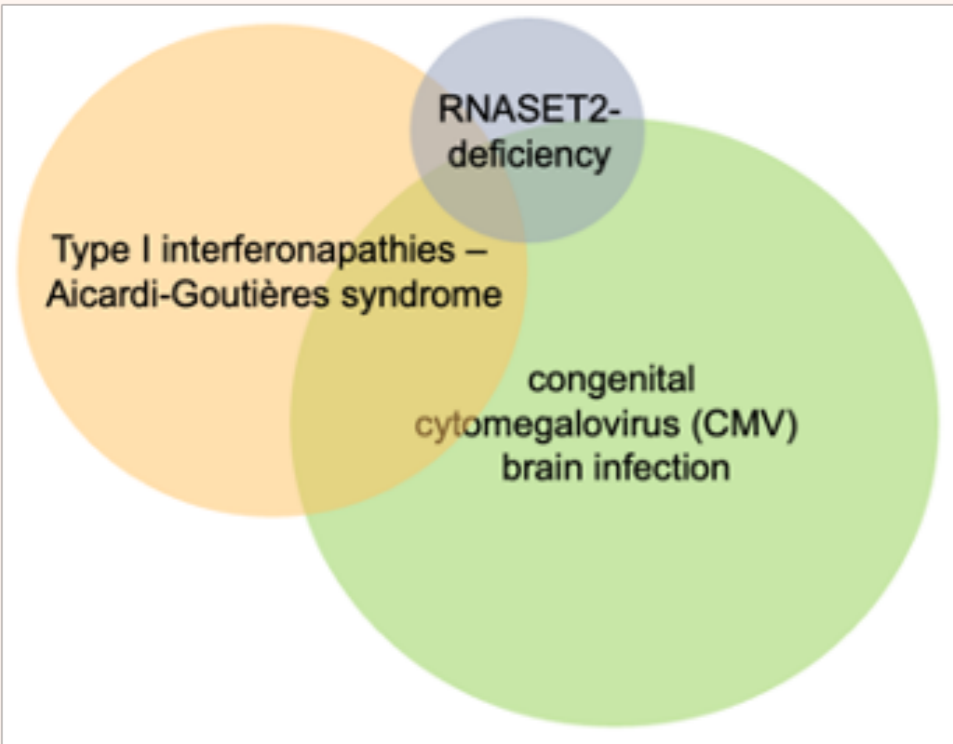


Type-I-Interferonopathies: Neurology meets Rheumatology – Phenotype description and treatment approach for RNASET2-deficient cystic leukoencephalopathy

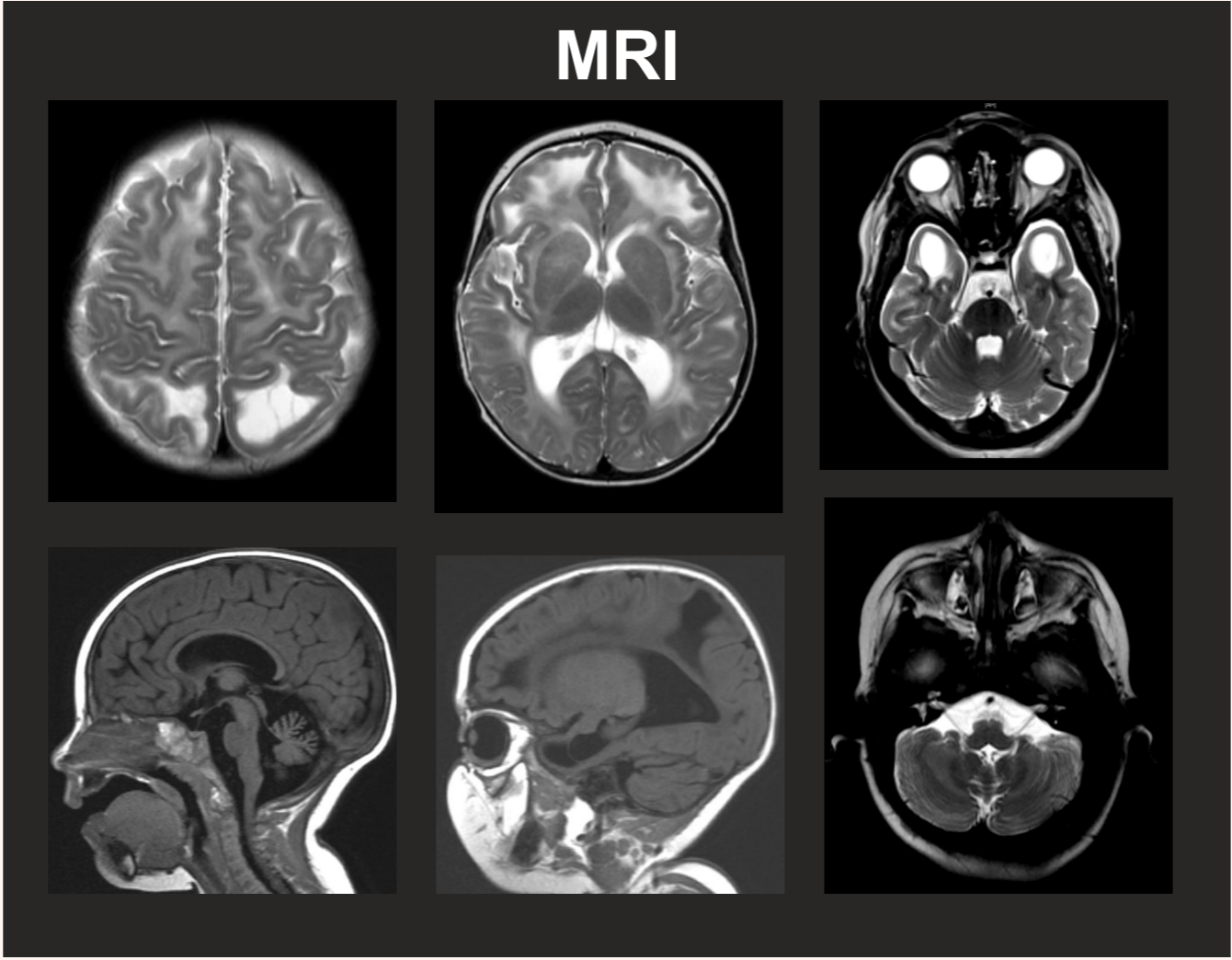
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Phenotype description

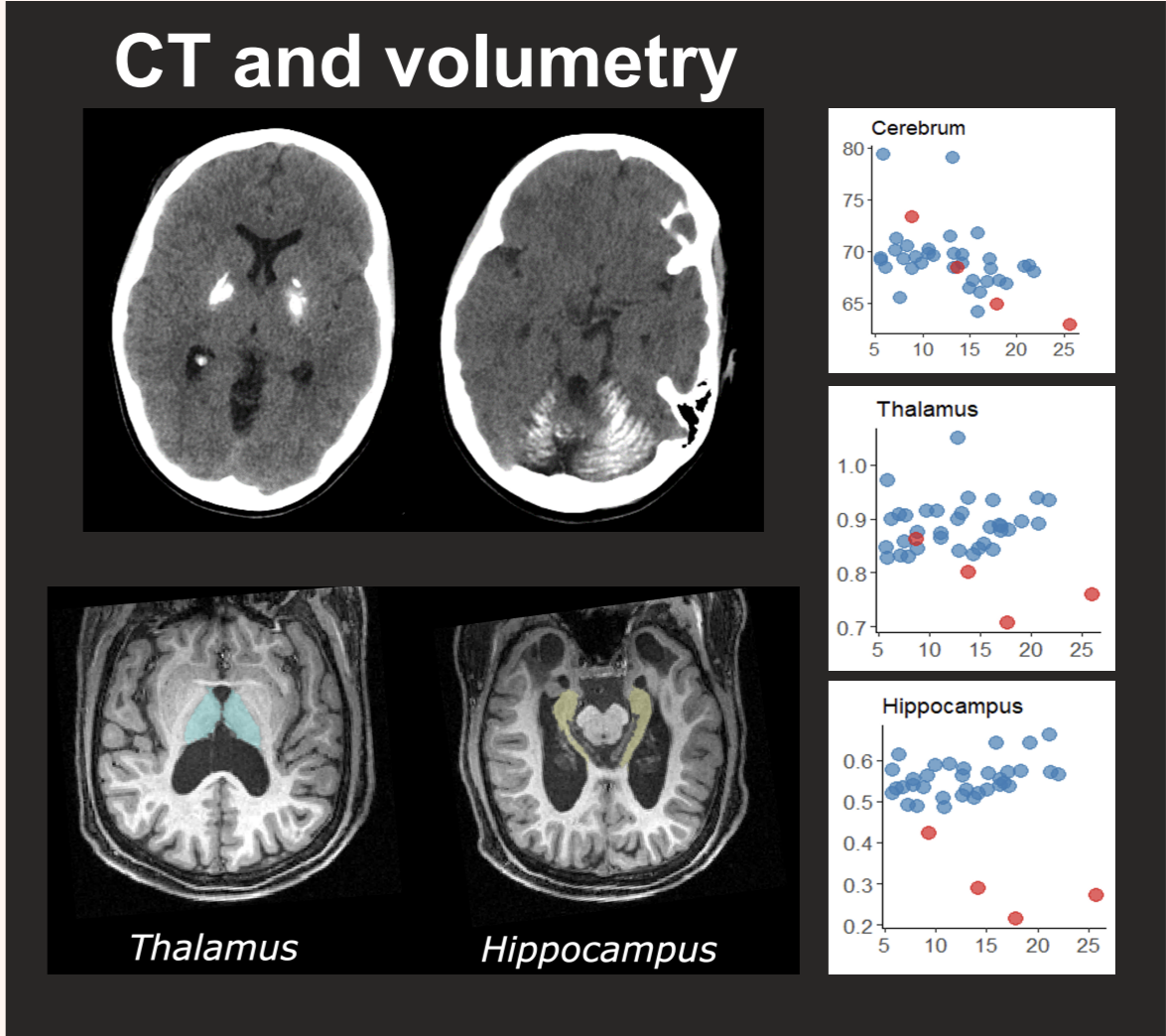
A cohort of 19 patients from all over the world with this ultra-rare disease underwent detailed phenotypic analysis.



RNASET2 deficiency shares clinical features with Aicardi-Goutières syndrome and congenital CMV infection, establishing it as a model disease for interferon-mediated neuroinflammation.

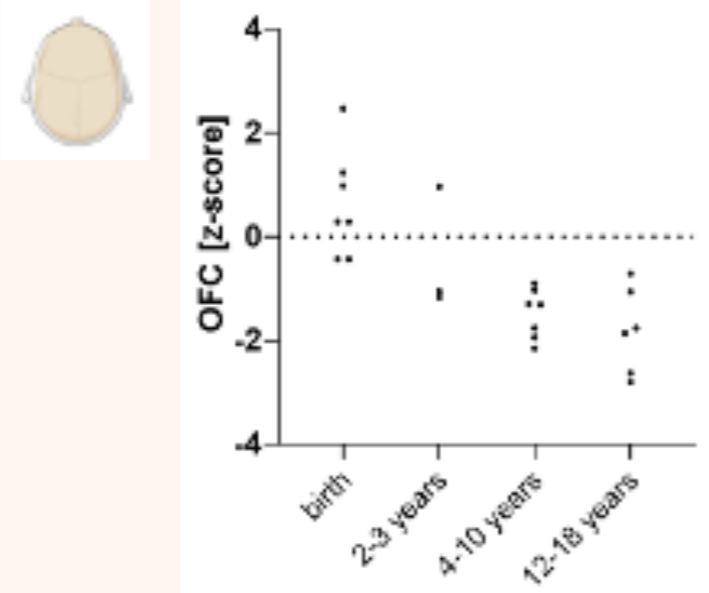
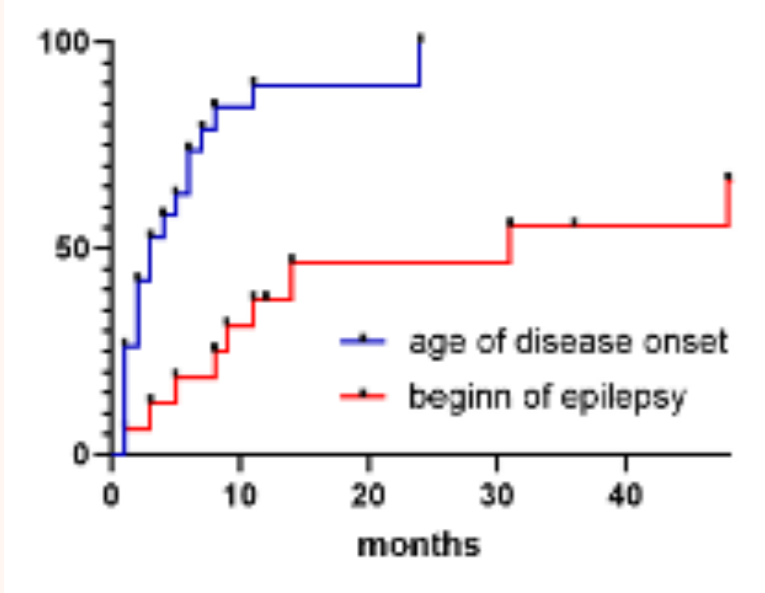


Typical MRI findings in RNASET2 disease include occipital, frontal, and temporopolar cysts, diffuse supra- and infratentorial white matter alterations, and pronounced cerebellar atrophy.



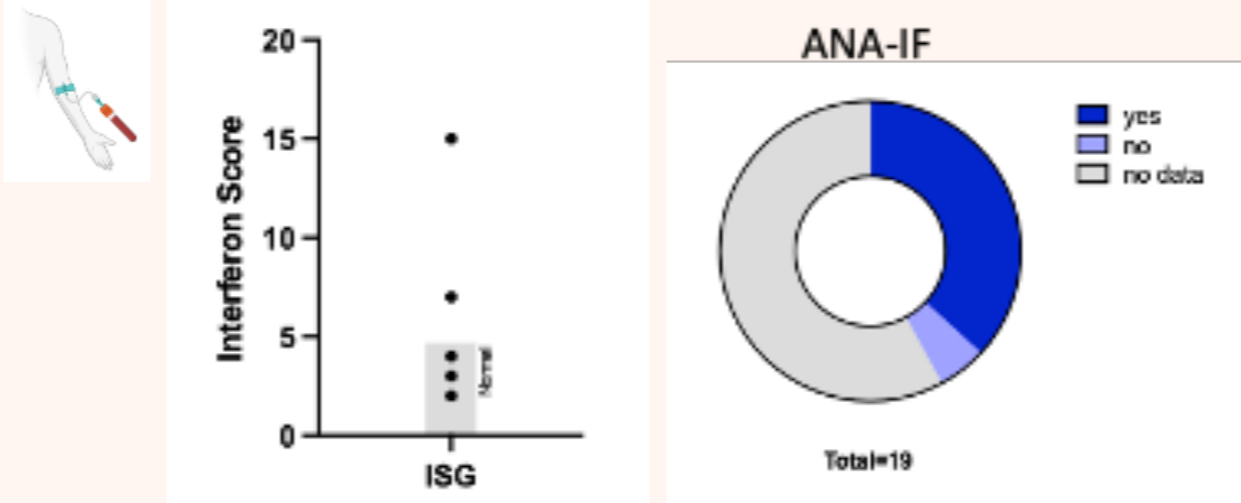
CT images show calcifications in the basal ganglia and cerebellum. Volumetric analysis reveals pronounced thalamic and hippocampal atrophy. The

Clinal features



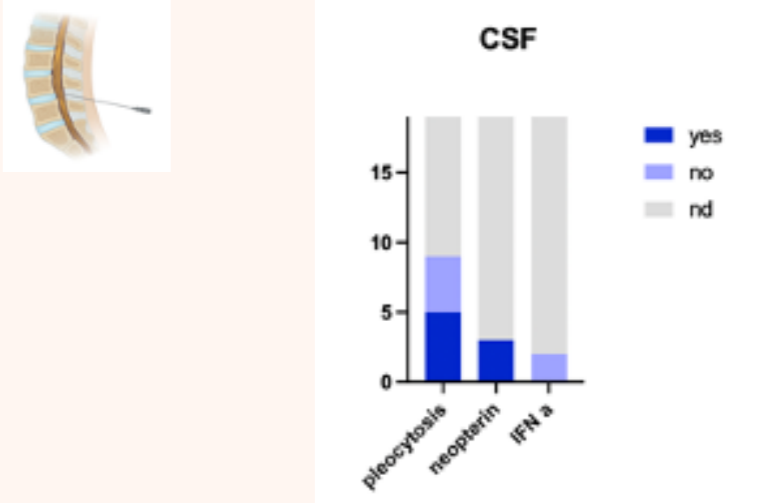
RNASET2-deficient patients exhibit muscular hypotonia in the first year of life, followed by severe psychomotor impairment, spasticity, epileptic seizures, and progressive microcephaly.

Blood values



In blood, the interferon score is inconsistently elevated. Most patients exhibit paraclinical signs of autoimmunity (ANA-IF).

CSF values



In the CSF, half of the patients exhibit pleocytosis. Direct IFN-α measurements are normal, but all examined patients show elevated neopterin levels as an indirect marker of interferon signaling.

Tofacitinib treatment

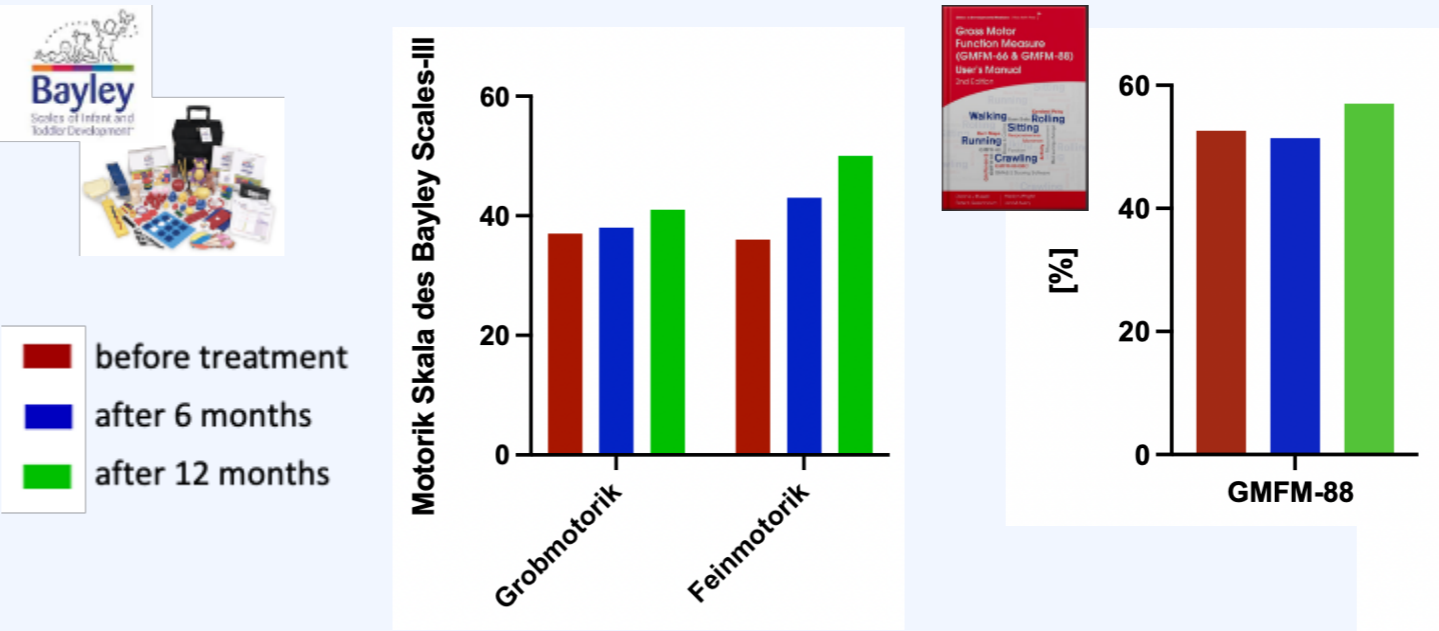
Dosing and timing



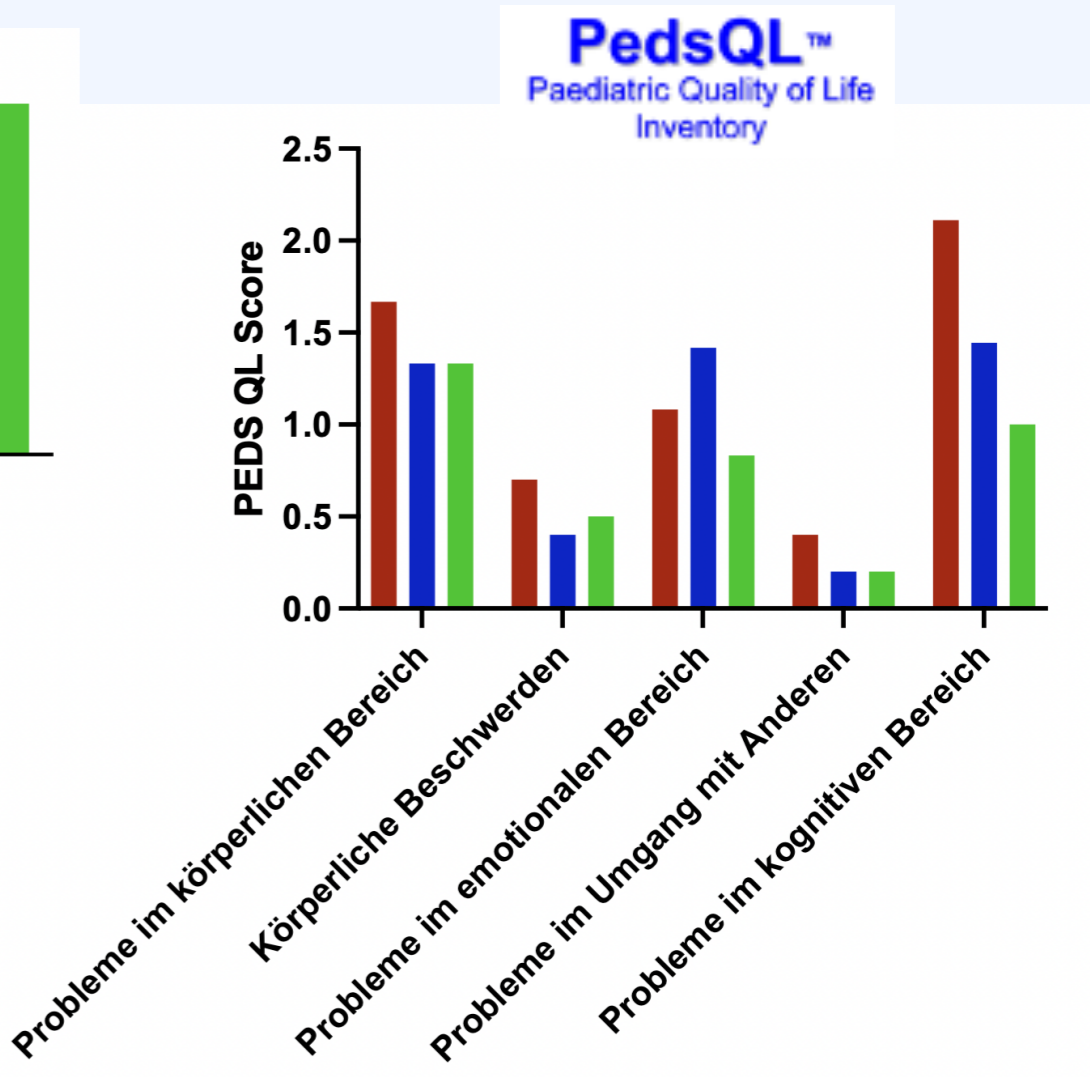
Course of the 12 Months:
No safety issues in the laboratory
Hypersalivation has improved
Mother and kindergarten report increased "energy"
A total of 4-5 upper respiratory infections, with one requiring antibiotics

DFG / Germany's Excellence Strategy
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DFG research grants Ga354/16-1

Clinical outcome

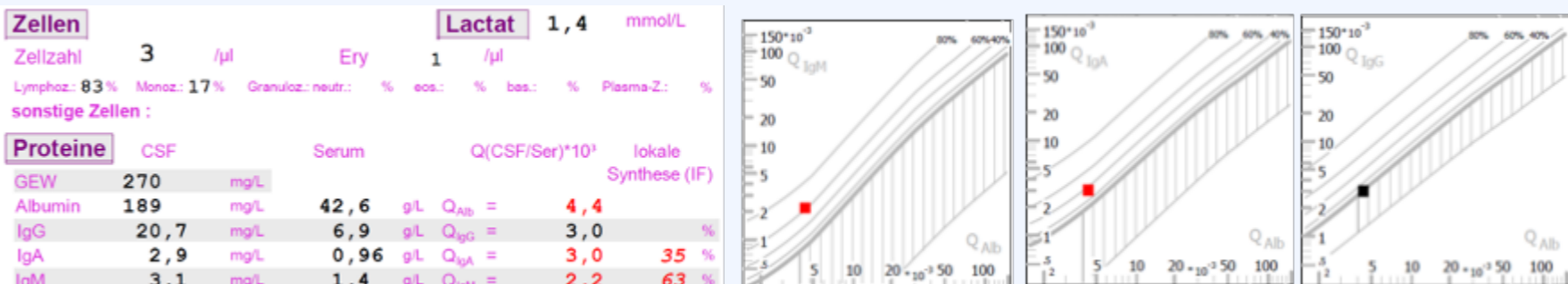


After 12 months of treatment, the patient showed greater improvement in fine motor skills than in gross motor skills. Quality of life improved across all subdomains, with the most notable gains in cognition.



Laboratory values

Zeitpunkt	Neopterin i. L.	ANA-IF	ds-DNA-AK
vor Behandlung	>28 µg/l	1:320	111 IU/ml
nach 6 Monaten		1:1000	58 IU/ml
nach 12 Monaten	26,4 µg/l	1:1000	40 IU/ml



The interferon score improves under treatment with tofacitinib but remains elevated. While ANA-IF remains high, double-stranded DNA antibodies decrease rapidly. In the CNS, intrathecal immunoglobulin synthesis persists, although neopterin levels decrease after 12 months of treatment.