

Recurrent fever, headache, abdominal pain, and aphthous lesions in a 7-year-old boy

Maria Fasshauer^{1,2}, Franziska Jaenicke^{1,2}, Marie Gerisch^{1,2}, Sophia Schroeder^{1,2}, Isabell Schumann³, Christine Wolf⁴, Catharina Schuetz^{4,5}, Min Ae Lee-Kirsch^{4,5}

1St. Georg Hospital Leipzig, Center for Pediatric and Adolescent Medicine, Leipzig, Germany

2ImmunoDeficiencyCenter Leipzig (IDCL), St. Georg Hospital Leipzig, Leipzig, Germany

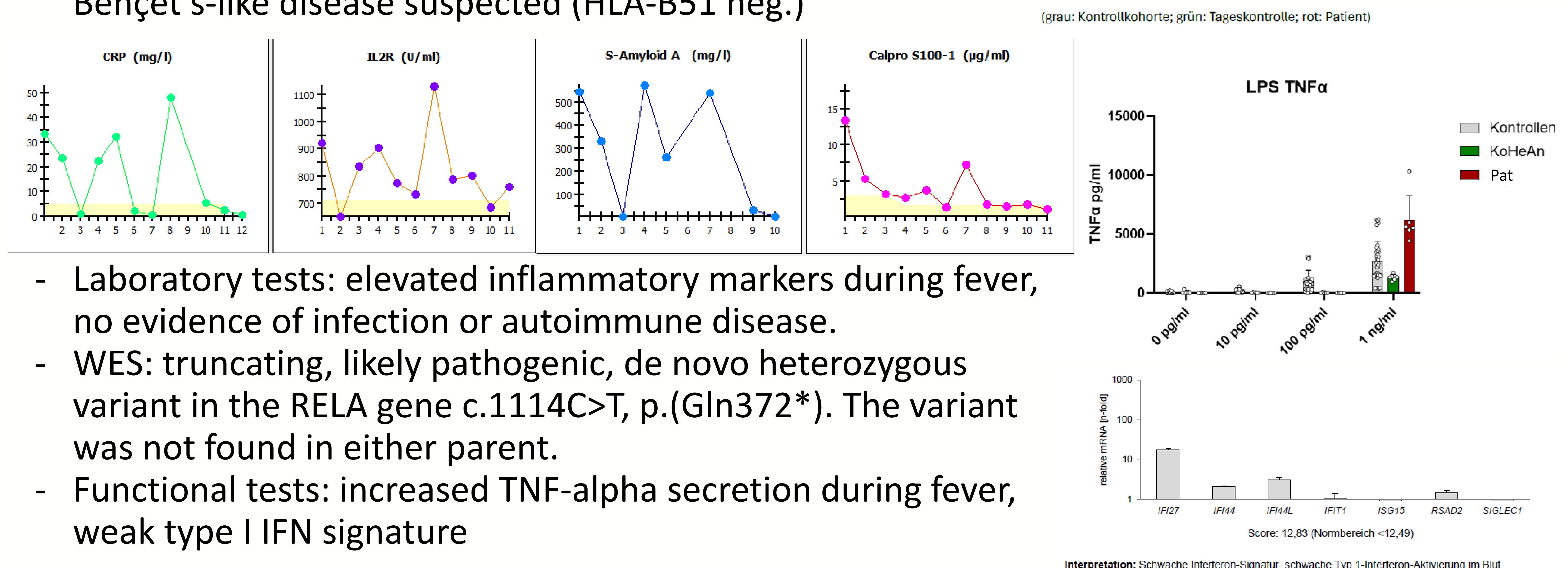
3Institute of Human Genetics, University of Leipzig Medical Center, Leipzig, Germany

4Department of Pediatrics, Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

5University Center for Rare Diseases, Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Case report:

- 7-year-old boy of caucasian, non-consanguineous, healthy parents
- Recurrent, self-limiting fever (starting age 18 months), occurring every 2 - 4 weeks, lasting 2 - 4 days, accompanied by oral aphthous lesions, episodic headache, and abdominal pain (without diarrhea or vomiting), and flu-like limb pain. No lymphadenopathy, skin, muscle or joint involvement.
- First presentation for immunologic-rheumatologic evaluation at age of 6 years and Behçet's-like disease suspected (HLA-B51 neg.)



- Laboratory tests: elevated inflammatory markers during fever, no evidence of infection or autoimmune disease.
- WES: truncating, likely pathogenic, de novo heterozygous variant in the RELA gene c.1114C>T, p.(Gln372*). The variant was not found in either parent.
- Functional tests: increased TNF-alpha secretion during fever, weak type I IFN signature

Diagnosis: RELA-associated disease (RELAD)

RELA encodes a subunit of the NF-κB transcription factor complex, which is critical for immune regulation and inflammatory responses. RELA haploinsufficiency is a recently identified monogenic cause of early-onset autoinflammatory disease resembling Behçet's disease.

- Therapy: initially single doses of prednisone (1.5 mg/kg) at beginning febrile episode -prompt resolution, intervals shortened to 1-2 weeks
- With detection of increased TNF-alpha secretion, compassionate treatment with a tumor necrosis factor (TNF) inhibitor (etanercept) was started and until now remission of disease is observed.

Summary: RELA-associated inflammatory disease should be considered in patients with early-onset Behçet's -like disease or other autoinflammatory syndromes. Early genetic diagnosis facilitates access to targeted treatment and has the potential to prevent long-term complications.

References

No conflict of interest. No funding.
Email: maria.fasshauer@sanktgeorg.de

www.sanktgeorg.de

Badran, Y.R. et al. J. Exp. Med. 2017
Adeeb, F., E.R. et al. Arthritis Rheumatol. 2021
Lecerf, K., D.C. et al. Rheumatology (Oxford). 2022