STAT 1 Immunodeficiency and HSV-1 Associated Encephalitis

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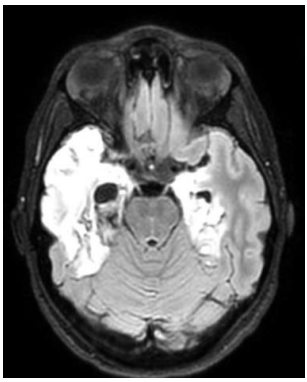
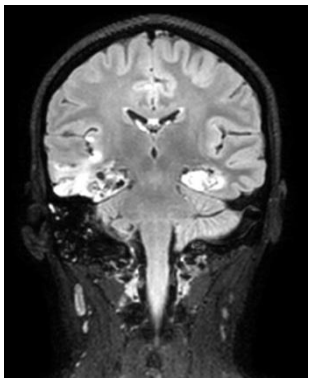
Introduction: pathogenic variants in Signal Transducer and Activator of Transcription 1 gene (STAT1) are a rare cause of primary immunodeficiency with susceptibility to several infections, often affecting the central nervous system (CNS). To the best of our knowledge, Herpes Simplex Virus (HSV) encephalitis in patients with primary immunodeficiency due to STAT1 variants has not been reported so far.

Case description : A 17-year-old female with a known history of primary immunodeficiency due to a STAT1 presented to the Emergency Department with **fever, confusional episodes, and drowsiness**.

Brain CT scan showed no remarkable findings. Her neurological status rapidly **deteriorated** to mutism and unresponsiveness, requiring sedation and orotracheal intubation. **She was transferred to the intensive care unit (ICU)**.

Cerebrospinal fluid (CSF) analysis revealed polymorphonuclear pleocytosis (70 cells/ÃµL, 89% neutrophils) and mildly elevated glucose level (4.3 mmol/L) with a **positive HSV-1 DNA PCR**. Anticonvulsant prophylactic therapy with levetiracetam and lacosamide was therefore initiated, along with antiviral therapy with acyclovir. **Initial brain MRI revealed bilateral signal alterations and restricted diffusion in the hippocampus, parahippocampus, amygdala, and posterior cingulate regions, along with right temporal pole and insular involvement, suggestive of HSV encephalitis.**

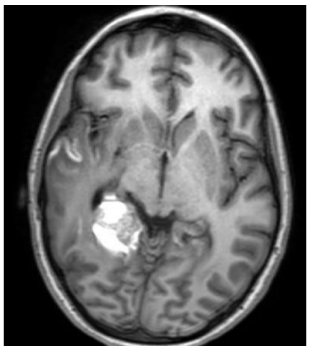




Over three weeks, progressive improvement was observed, allowing for extubation and transfer to the neurology department. Upon transfer, the patient was alert with a tendency to drowsiness, disoriented to time and person, and exhibited fluctuating attention.

Examination revealed no sensory-motor deficits in all four limbs; however, widespread hypotonia in all four limbs was noted.

Follow-up MRI demonstrated a worsening of previous findings, characterized by **hemorrhagic transformation, increased swelling, and the emergence of widespread pseudo-laminar necrosis within the affected regions.**The electroencephalogram showed evidence of epileptiform activity with an almost periodic pattern in the fronto-centro-temporal region, with a certain predominance on the left (periodic discharges + spikes). Clinically, no sensory- motor deficits were observed; however, the patient



Experienced significant neurocognitive sequelae, including **deficits in executive functions, working memory, selective attention, anomic latencies, and an abulia attitude**. Following a period in a **neurorehabilitation** facility with improvement observed across all rehabilitative domains (particularly memory), though a significant difficulty in initiating actions persisted, **suggestive of a pattern consistent with ideational apraxia**.

Conclusions: To our knowledge, this is the only case report of herpetic encephalitis in a patient with STAT1 variants. CNS infections, including HSV encephalitis, should be strongly considered in the differential diagnosis of sudden consciousness deterioration in patients affected by primary immunodeficiency due to STAT1 variants. A neuroradiological and neurophysiological follow up should be performed to identify neurological sequelae in order to referring patients for ad hoc rehabilitation.

Bibliography:

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