

# Atypical Pediatric HSV-1 Encephalitis Following Initially Negative CSF Testing and Antiviral Re-initiation

## 1 Presentation

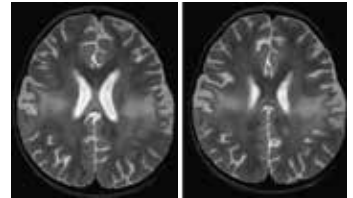
A previously healthy, fully vaccinated 21-month-old girl presented with acute bilateral facial twitching, tongue fasciculations, and confusion without fever.



## 2 Clinical Workup

Initial CSF analysis showed mild pleocytosis, while brain MRI revealed bilateral perirolandic diffusion restriction and thalamic T2/FLAIR hyperintensity, raising concern for autoimmune encephalitis, infection, or genetic/metabolic encephalopathy. BioFire multiplex syndromic panel and CSF mNGS performed at an outside laboratory were both negative for HSV, and dedicated HSV PCR was not initially performed. The patient was treated for presumed autoimmune encephalitis with IVIG, pulse corticosteroids, and later plasma exchange, while empiric acyclovir was discontinued following negative CSF testing.

**Brain MRI demonstrating evolving perirolandic cortical injury with cortical thinning, encephalomalacia, and thalamic abnormalities consistent with evolving meningoencephalitis.**



## 3 Delve Detect

After clinical and radiographic progression, the patient was subsequently transferred to UCSF. Delve Detect CSF mNGS performed on CSF collected 16 days after initial presentation identified HSV-1.

**4,889**

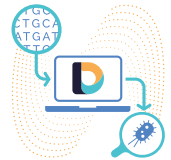
Unique DNA reads for HSV-1

**19 Million**

Total sequencing reads

**88.1%**

Viral genome coverage



## 4 Clinical Impact

Following mNGS detection of HSV-1, infection was confirmed by dedicated HSV PCR, supporting a revised diagnosis of primary HSV encephalitis with possible secondary autoimmune encephalitis. Acyclovir was re-initiated for a 21-day treatment course along with plasma exchange, followed by suppressive antiviral therapy after documented CSF HSV PCR clearance. The patient gradually improved clinically.



## 5 Delve Insights

This case highlights the potential value of CSF mNGS in pediatric patients with atypical or diagnostically challenging CNS presentations, particularly when initial microbiologic testing is negative or incomplete. Broad pathogen detection enabled identification of HSV-1 despite prior negative syndromic panel and outside mNGS testing, supporting timely antiviral re-initiation and appropriate refinement of immunomodulatory therapy.

