delvedetect
CEREBROSPINAL FLUID

Delve Detect CSF - immunocompromised adolescent - Cache Valley virus

CSF mNGS Guided Experimental Antiviral Therapy and Detection of Disease Recurrence in Cache Valley Virus Meningoencephalitis

PATIENT PRESENTATION

Initial clinical presentation and symptoms

A 16-year-old male developed progressive dysarthria, aphasia, dysphagia, motor apraxia, ataxia, hearing impairment, and cognitive decline following an upper respiratory illness. Despite extensive evaluation, his neurologic disease progressed over more than two years with repeated hospitalizations and worsening neuroimaging findings.

Patient profile

16-year-old male with IKZF1-associated combined immunodeficiency and history of immune thrombocytopenia. The clinical course was characterized by chronic progressive meningoencephalitis in the setting of impaired immunity.

DIAGNOSTIC WORKUP

Pre-Delve Detect diagnostic work-up

Extensive infectious, autoimmune, metabolic, genetic, and neurodegenerative evaluations were unrevealing despite persistent CSF lymphocytic pleocytosis and progressive cerebral/cerebellar atrophy. CSF mNGS performed through UCSF collaborators established the diagnosis of Cache Valley virus meningoencephalitis and prompted experimental antiviral therapy with molnupiravir. After apparent CSF viral clearance and discontinuation of therapy, the patient experienced renewed neurologic decline, raising concern for recurrent active CNS infection versus progression from established neurologic injury.

HOW mNGS CHANGED THE CLINICAL COURSE

Delve Detect results

Date of Delve collection: July 2025

Turnaround time: 29.1 hours from sample receipt to result

Pathogen detected: Cache Valley virus, 6 unique reads

Key interpretation: Recurrent Cache Valley virus detected following prior treatment-associated CSF clearance, supporting recurrent CNS infection after antiviral discontinuation.

Impact on diagnosis

CSF mNGS established the diagnosis of an exceptionally rare neuroinvasive arboviral infection after extensive conventional testing was unrevealing. Subsequent mNGS demonstrated treatment-associated viral clearance. Delve Detect CSF later confirmed recurrent Cache Valley virus in the setting of clinical deterioration, supporting recurrence rather than neurologic progression alone. This functioned as a rule-in of recurrent active CNS infection.

TREATMENT IMPACT

Treatment and patient outcome

Initial mNGS diagnosis prompted initiation of experimental molnupiravir therapy, with subsequent CSF viral clearance. After clinical deterioration following antiviral discontinuation, Delve Detect identified recurrent Cache Valley virus and supported re-initiation of molnupiravir. Despite treatment, the patient continued to decline, ultimately entered hospice care, and passed away.

TIMELINE

Feb-Jun 2023 — Progressive neurologic decline despite extensive diagnostic evaluation.

May 2024 — CSF mNGS through UCSF identifies Cache Valley virus.

July 2024 — Experimental molnupiravir initiated.

April 2025 — CSF mNGS (UCSF) negative for Cache Valley virus; antiviral therapy discontinued.

July 2025 — Neurologic deterioration recurs; Delve Detect CSF returns in 29.1 hours and detects recurrent Cache Valley virus (6 unique reads).

Aug-Dec 2025 — Molnupiravir restarted; patient ultimately progresses despite therapy and passes away after hospice enrollment.

Delve insight: This case demonstrates the value of CSF mNGS throughout the clinical journey - establishing the diagnosis of a rare neuroinvasive virus, documenting treatment-associated viral clearance, and detecting recurrent infection following antiviral discontinuation. Together, these findings informed key treatment decisions during a prolonged and diagnostically challenging illness.

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