

Rapid Identification of Dual CNS Infection with *Aspergillus terreus* and VZV in an Immunocompromised Host Leading to Antiviral Initiation and Clarification of Antifungal Therapy

1 Presentation

A 37-year-old woman with aggressive glioblastoma and leptomeningeal spread on high-dose corticosteroids and bevacizumab presented with 2 days of fever and acute altered mental status. On examination, she was lethargic, non-verbal, with diminished right-sided breath sounds.



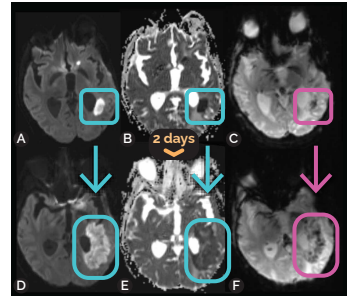
2 Clinical Workup

On presentation, the patient was found to have *Streptococcus pneumoniae* bacteremia with necrotizing right lower lobe pneumonia. Brain MRI revealed rapidly progressive diffusion-restricting CNS lesions, while CSF demonstrated pleocytosis and elevated protein with negative Gram stain and culture. Serum fungal markers, including β -D-glucan >500 pg/mL and positive galactomannan, were strongly supportive of invasive fungal disease, prompting empiric voriconazole and caspofungin.

- **CSF:** 120–161 WBC/ μ L (90% PMNs), protein 90 mg/dL; Gram stain/culture negative
- **Serum:** β -D-glucan >500 pg/mL; galactomannan positive
- **Empiric therapy:** voriconazole + caspofungin for suspected disseminated fungal infection

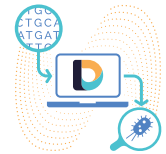
Figure A–C. Initial brain MRI demonstrating multifocal diffusion-restricting lesions, including a representative left parietal lesion.

Figure D–F. Follow-up MRI obtained 2 days later demonstrated marked interval progression in the extent and number of diffusion-restricting lesions, concerning for an aggressive invasive fungal process.



3 Delve Detect

The differential diagnosis included septic emboli and invasive fungal infection. Delve Detect CSF identified both *Aspergillus terreus* and Varicella-Zoster Virus (VZV), with elevated fungal biomass and substantial VZV signal despite negative CSF cultures and ongoing antifungal therapy, providing species-level fungal identification alongside detection of an unexpected viral co-infection.



4 Clinical Impact

Delve Detect identified a dual CNS infection rather than a single causative organism and supported diagnosis of invasive mold disease. The unexpected VZV finding prompted repeat clinical evaluation, during which a groin rash was identified and subsequently confirmed as VZV-positive by PCR. mNGS results directly led to initiation of acyclovir while clarifying ongoing antifungal therapy. Results were delivered within ~30 hours of sample receipt and informed clinical management in an immunocompromised patient with rapidly progressive disease.



5 Delve Insights

Early CSF mNGS testing can provide critical value in immunocompromised patients with diagnostically complex CNS presentations. Broad pathogen detection enabled identification of an otherwise unrecognized viral co-infection while also providing species-level fungal identification to support antifungal selection. Earlier integration of Delve Detect CSF can help shorten diagnostic uncertainty and accelerate targeted treatment decisions.

