

A Case of Fatal Neuroinvasive Astrovirus VA1 Encephalitis in a Child With High-Risk B-ALL

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Background on Astrovirus

Clinical presentation

- In immunocompetent patients: Self-limited gastroenteritis
- In immunocompromised patients: Neuroinvasive infection with severe neurologic morbidity and mortality

Diagnosis

- RT-PCR or metagenomic next-generation sequencing (mNGS)
- Often delayed

Reported empiric treatments

- Intravenous immunoglobulin (IVIG), corticosteroids, ribavirin, interferon- α , and nitazoxanide

Management and prognostication

- Uncertain due to the rarity of cases and limited clinical data

Objectives

To recognize, diagnose, and manage neuroinvasive astrovirus infection in children with hematologic malignancies

Methods

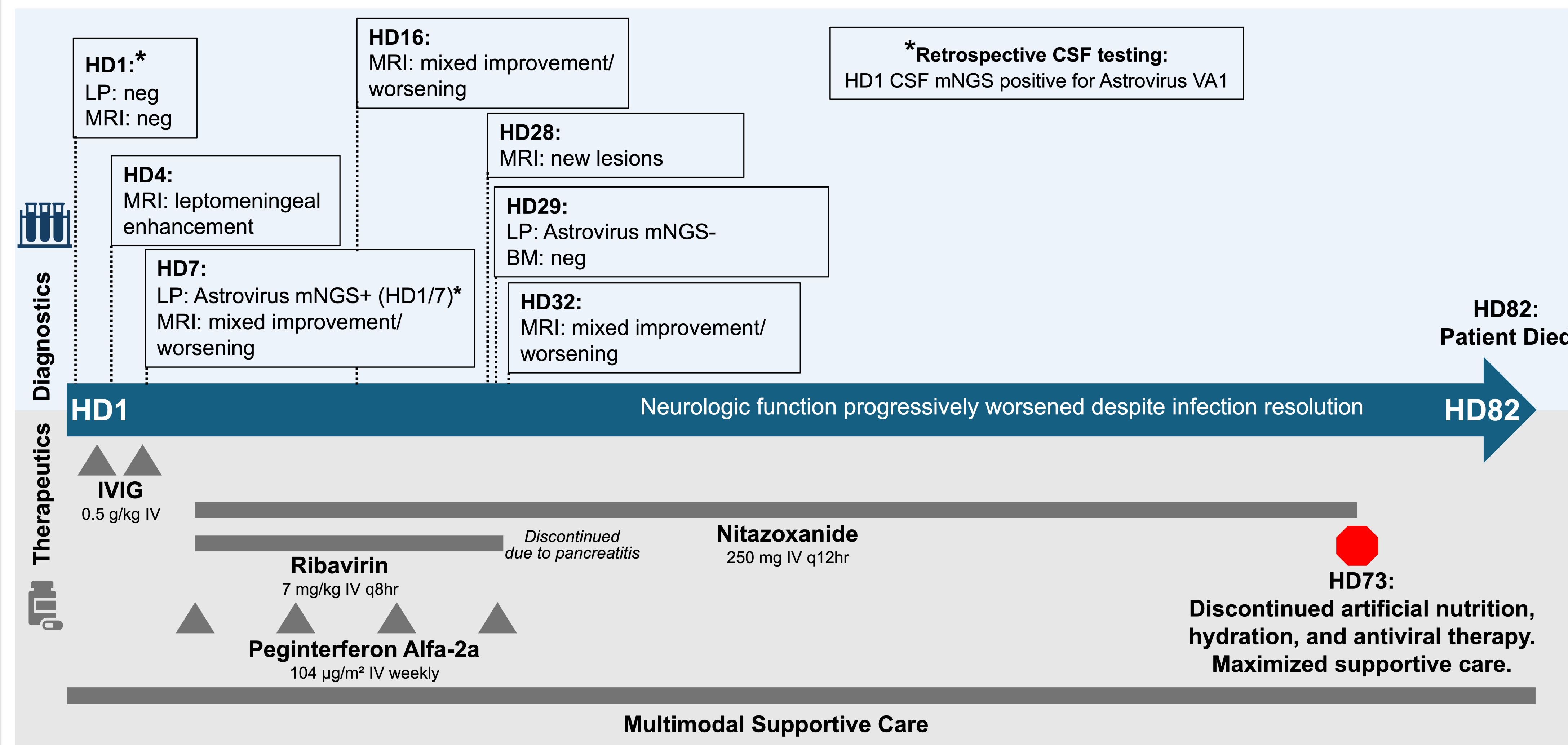
Case report, with parental consent

Initial Presentation

- A 4 yo M with high-risk B-cell acute lymphoblastic leukemia (B-ALL) and *IKZF-1* deletion presented with 3 days of somnolence, ataxia and encephalopathy
- 10 months in complete remission, treating as per very-high-risk arm of DFCI 16-001 with plus two blinatumomab blocks
- No prior infectious complications
- Labs at presentation: neutropenia (1070 cells/ul), lymphopenia (1020 cells/ul), and hypogammaglobulinemia (IgG 41 mg/dl)

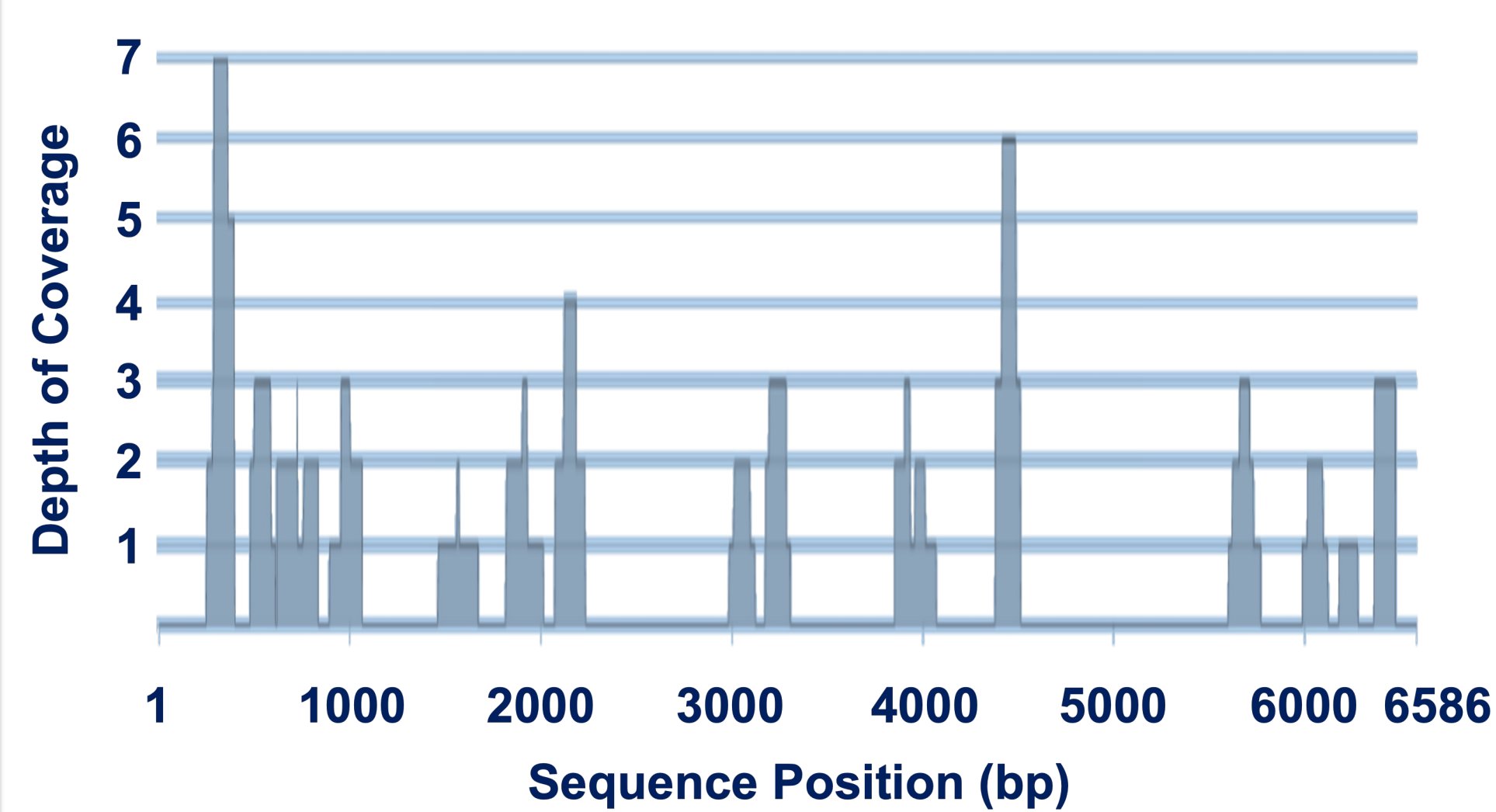
Diagnosis: Neuroinvasive Astrovirus Infection

Patient Course of Illness



Key diagnostics, therapeutics and clinical events; HD=hospital day, LP=lumbar puncture, MRI=magnetic resonance imaging, BM=bone marrow biopsy, CSF=cerebrospinal fluid

HD1 Astrovirus VA1 mNGS

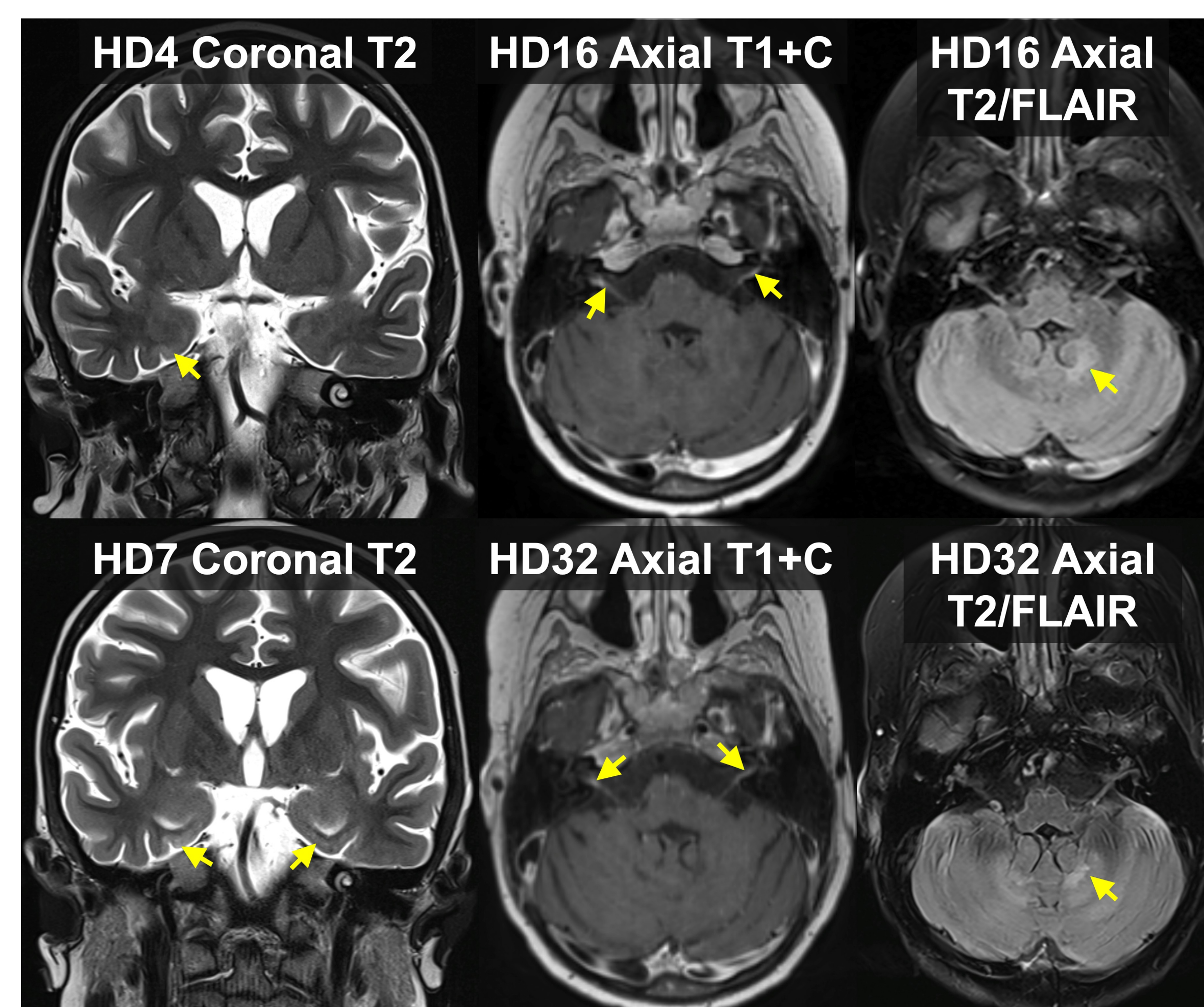


Coverage map of retrospective HD1 sample to Astrovirus VA1; bp=base pairs

Reads	50
Sequence Length	6586 bp
Covered Bases	2359 bp
% Coverage	35.8%

Sample parameters

Brain MRIs



Serial brain MRIs with right hippocampal T2 hyperintensity, variable perivascular and cranial nerve enhancement, and overall progression

Applications to Practice

Early recognition and detection

- When to suspect and test for astrovirus or other less common causes of encephalitis
- Early use of mNGS in patients with hematologic malignancy presenting with unexplained encephalitis or other infectious signs

Multidisciplinary care

- Coordination with oncology, infectious disease, and supportive care teams for comprehensive management

Managing rare complications

- Standard frameworks to guide goals-of-care discussions for uncertain prognoses

Sharing expertise

- Expansion of institutional and multi-center case reporting to characterize epidemiology, management strategies, and outcomes of rare infections

Areas for Future Research

Targeted astrovirus treatments

- Develop effective treatments for astrovirus, as currently no established therapies or clinical trials exist

Impact of immunotherapies on infections

- Understand how frontline immunotherapies like blinatumomab influence susceptibility to infections

Role of IgG in infection risk

- Establish evidence-based guidelines for IgG monitoring and repletion

Role of vaccines

- Evaluate modified vaccination strategies to improve infectious outcomes in patients receiving immunotherapies
- Ongoing astrovirus vaccine development

