Variability in the Evaluation and Management of Children with Suspected Encephalitis by Pediatric Infectious Disease Providers

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Background

Encephalitis may lead to severe neurological abnormalities and extreme morbidity in survivors.[1] Unfortunately, a large number of pathogens may cause this illness, many of which are challenging to diagnose and are without effective therapies.[2-4] Additionally, the signs and symptoms of non-infectious causes of encephalitis may overlap with infectious causes, further complicating attempts at effective diagnosis.[5] Since the publication of the most recent Infectious Disease Society of America (IDSA) guidelines addressing encephalitis in 2008,[4] multiple changes in the diagnosis and epidemiology of pediatric encephalitis have occurred. Metagenomic next-generation sequencing[6] (mNGS) of the cerebrospinal fluid (CSF) and multi-plex polymerase chain reaction[7] (PCR) testing have increasingly entered clinical practice. Autochthonous transmission of neurotropic tropical viruses has occurred in several U.S. states as well (e.g. Chikungunya virus).[8] In addition, clinicians are increasingly appreciating the emerging burden of disease caused by autoimmune encephalitides.[9] These developments have greatly changed the diagnostic approach for encephalitis. In an effort to determine how clinicians are adapting to these changes, we surveyed pediatric infectious disease physicians through use of the Infectious Disease Society of America's Emerging Infections Network to characterize their approach to several evolving clinical issues related to the management of pediatric encephalitis.

Objectives

1.) Characterize the approach utilized by pediatric Infectious disease physicians towards the use of newer diagnostic modalities (mNGS and multi-plex PCR) in the evaluation of children with encephalitis.

2.) Assess the frequency and comfort level with which pediatric infectious disease providers manage autoimmune encephalitis

3.) Characterize the criteria utilized by pediatric infectious disease providers prior to instituting immunomodulatory therapy in a child with suspected encephalitis

4.) Determine the frequency with which pediatric infectious disease physicians would screen for autochthonous tropical viral pathogens in a child with suspected encephalitis

Methods

An 11-question, confidential, web-based survey link was distributed to 370 pediatric infectious disease physician members of the Emerging Infections Network (EIN) of the IDSA and remained open between January 29th through February 17th, 2020 (http://www.int-med.uiowa.edu/Research/EIN/PedsEncephalitisquery.pdf). Non-responders were sent two reminders approximately one week apart. Only responses from providers who cared for children with suspected encephalitis were analyzed. Respondents were characterized by region of the country in which they practiced, years of experience following fellowship, place of employment and their primary hospital type. The survey assessed respondents' approaches to the use of multi-plex PCR and mNGS testing in the CSF, their likelihood of testing for autochthonous tropical viral pathogens in the United States in a hypothetical scenario, their role and comfort level in evaluating and caring for children with auto-immune encephalitides, as well as criteria for initiating immunomodulatory agents in a child with suspected encephalitis.

Results

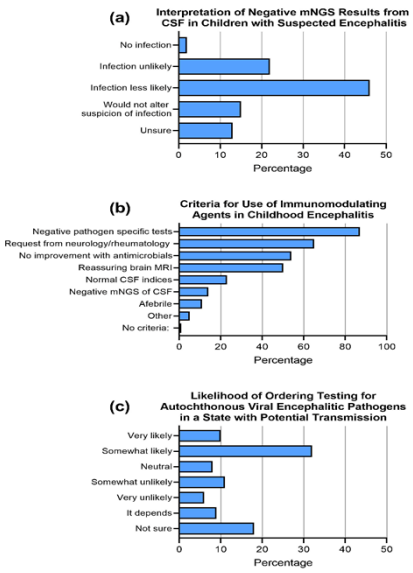
Table 1 Characteristics of 222 Respondents to an Emerging Infections Network Survey Assessing the Evaluation and Management of Pediatric Encephalitis

Variable	#/(%) of Respondents
Region of the Country	
New England	8 (4%)
Mid Atlantic	27 (12%)
East North Central	41 (18%)
West North Central	20 (9%)
South Atlantic	35 (16%)
East South Central	23 (10%)
West South Central	12 (5%)
Mountain	12 (5%)
Pacific	41 (18%)
Canada	3 (1%)
Experience Since ID Fellowship	
<5 years	55 (25%)
5-14 years	77 (35%)
15-24 years	41 (18%)
≥25 years	49 (22%)
Employment	
Hospital/clinic	61 (27%)
Private/group practice	15 (7%)
University medical school	144 (65%)
VA/Military	0 (0%)
Primary Hospital Type	
Community	13 (6%)
Non-university teaching	58 (26%)
University	144 (65%)
VA Hospital or Department of Defense	2 (1%)
City/county	5 (2%)

Table 2 Approach to Encephalitis Management among 196 Respondents Caring for Children with Encephalitis

Topic	#/% of Respondents
Multi-Plex PCR Testing	
No institutional restrictions	109 (56%)
Not used	39 (20%)
Use in initial evaluation	110 (56%)
Use of pathogen-specific confirmatory testing with initial use	71 (36%)
Require exclusion of likely diagnoses with standard testing before use	60 (31%)
Require exclusion of likely diagnoses with standard testing and child not improving before use	25 (13%)
Metagenomic Next-Generation Sequencing	
Used at least once	92 (47%)
Unaware of the test	22 (11%)
Require exclusion of likely diagnoses with standard testing before use	145 (74%)
Require exclusion of likely diagnoses with standard testing and child not improving before use	93 (47%)
Uncertain how best to use mNGS	25 (13%)
Management of Autoimmune Encephalitis	
Pediatric infectious disease service primarily responsible	65 (33%)
Feel comfortable diagnosing the condition	107 (55%)
Criteria Prior to Use of Immunomodulatory Agents	
Negative results from pathogen-specific testing	170 (87%)
Lack of fevers	21 (11%)
Normal CSF indices	45 (23%)
Reassuring MRI findings (e.g. lack of necrosis, enhancement)	98 (50%)

Figure 1 Approaches to the Interpretation of Negative CSF mNGS Results (a), Use of Immunomodulating Agents (b) and Testing for Autochthonous Tropical Viral Pathogens (c) in Children with Encephalitis



Discussion

We noted variability in the evaluation and management of children with suspected encephalitis by pediatric infectious disease physicians. The manner in which newer diagnostic modalities (e.g. mNGS and multi-plex PCR testing of CSF) were implemented varied greatly. Roughly half of providers had used mNGS testing of CSF, though disagreement existed as to the optimal timing and interpretation of results. Notably, negative results from mNGS testing were interpreted with differing levels of confidence.

Our survey also highlights the large role infectious disease physicians play in the evaluation of auto-immune encephalitis, as well as their lack of comfort with this diagnosis. Similarly, the criteria used to guide the initiation of immunomodulatory agents in children with suspected encephalitis varied tremendously.

Clinical management guidelines for encephalitis, last published in 2008,[4] should be updated to address the uncertainties we identified, primarily the use of newer diagnostic modalities and the evaluation and management of auto-immune encephalitides.

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