Does a Standardized Multi-disciplinary Approach Improve Outcomes for Children with NMDA Receptor Antibody Encephalitis? A Preliminary Assessment of a Single Center Experience

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Objectives

- To describe a consensus-driven and standardized approach to pediatric NMDA receptor antibody encephalitis (NMDAR) at a tertiary care hospital.
- To determine differences in outcome after initiating a consensus-driven approach.

Background

- NMDAR is a potentially devastating neuronal autoimmune condition affecting children and young adults. Mostly unrecognized prior to 2007.
- **The classic clinical phenotype includes**: encephalopathy, neurocognitive deficits, behavioral changes, seizures, and abnormal movements.
- Earlier diagnosis, and utilization of rituximab or cyclophosphamide in refractory cases may decrease relapse rates and neurologic morbidity.[1]
- Consensus regarding timing of immunotherapy and the role of rheumatologists in pediatric NMDAR has not been reached.

Methods

- A task force composed of neurology, rheumatology, critical care medicine, and transfusion medicine clinicians was charged with standardizing NMDAR care after struggling with initial cases (Initial cohort January 2009-July 2012).
- There were 3 face to face meetings in 2012. A best care practice was designed after review of the literature and BRAINWORKS' protocol, review of meeting minutes, and adjudication of action items (Figure 1).[2,3]
- The Pediatric Cerebral Performance Scale (PCPC) was agreed upon as an inpatient measure of neurologic status.[4]
- Task force members agreed upon therapeutic plasma exchange (TPE) criteria and timing of rituximab administration in children refractory to initial interventions.

Methods (cont.)

- Data for all children with at least 2 clinical NMDAR features and a positive antibody test at a commercial lab (CSF or serum) was reviewed after IRB approval.
- We describe initial presentations, interventions, and neurologic outcomes for all children during the review period (2009-2014).
- Modified Rankin scores (mRS) were calculated from the last clinic note. A good outcome was determined as either no deficits (0) or mild deficits with no disability (1) at follow-up as per Titulaer et al.[1]
- Descriptive statistics are presented due to the small sample size of our cohort (medians, ranges).

Results

Table 1: Demographics, Total cohort 2009-2014 (N=13)

Median Age at Presentation (years)	10 (range 3-17)
Gender, F (%)	9 (70%)
Ethnicity/Race, N (%) Hispanic African –American	 10 (77%) 3 (23%)
Time from disease onset to initial treatment (median days, range)	16 (range 2-90)

- Children had **all** the clinical features at presentation except for 2 patients who were encephalopathic and had one additional feature (seizure or movement disorder).
- There were no significant differences in age **or** time to diagnosis in the two cohorts (median time to treatment was < 30 days in both).
- Only one patient (11 yr old F) had an associated immature ovarian teratoma (picked up by intra-abdominal imaging).
- All patients were initially treated with methylprednisolone and IVIg.

Figure 1: TCH Standardized Treatment Protocol (7/2012-current)[5]

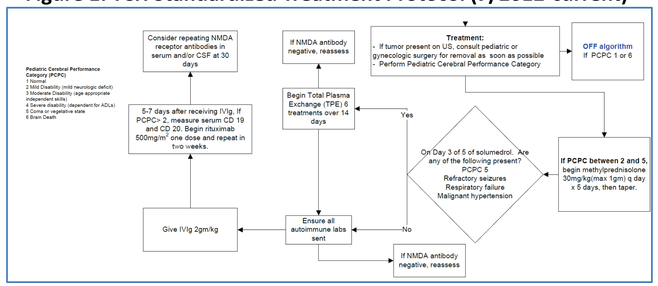

Table 2: Treatment and Outcomes

	Initial Cohort (N=6)	Standardized Care Cohort (N=7)
Time from onset to treatment, (d)	15 (range 9 -90)	22.5 (range 2-49)
ICU admission, N (%)	1 (17%)	3 (43%)
Rituximab usage , N (%) Time from 1st line tx, days	1 (17%) 10	6 (86%) 14 (range 12-24)
TPE use, N (%)	2 (33%)	1 (14%)
Follow-up period (months)	20.5 (range 7-33)	10 (range 4-12)
Relapse/flare rate, N (%)	4 (67%)	0%
Good outcome (mRS 0-1), N (%)	2 (33%)	5 (71%)

- Relapses in the initial cohort were all during the first 12 months after initial Tx.
- **INITIAL COHORT**: Two patients received mycophenolate after 1st line Tx. Cyclophosphamide was used in one adolescent who did not improve after rituximab.
- **STANDARDIZED COHORT**: All patients received 2-4 months of IVIg after the initial hospital discharge. No patients in this group were maintained on mycophenolate.

Conclusions

- There have been no relapses or flares in children treated with a standardized care regimen that includes early use of rituximab.
- Neurologic outcomes appear more robust in children treated with a standardized approach. Most with mild cognitive deficits at follow up.
- Differences in relapse rates and outcomes cannot be accounted for by any differences in age, time to treatment, or severity of disease (ICU stay).
- It is not apparent whether low relapse rates in the standardized treatment cohort patients receiving rituximab will be sustained with a longer follow-up.

Limitations and Future Directions

- There has been a short follow-up for most children in the more recent standardized care cohort.
- Formal neuropsychology testing data is only available for a handful of patients and was not assessed in this review.
- Length of stay data was not reviewed as a rehabilitation unit at our institution opened in 2012 (admitting 6 of 7 patients in the recent cohort).
- The institutional task force aims to address best care practices for psychiatric, neuropsychological and rehabilitation services.

References

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5. TCH NMDAR Algorithm http://connect2depts.texaschildrens.org/depts/1/nursing/EvidenceBasedOutcomesCenter/Documents/BelowREDLine/NMDArEncephalitis.pdf