NMDA R Encephalitis management: to be aggressive or cautious, investigating a standardized treatment regimen

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Introduction

- N-methyl-D-aspartate receptor (NMDA R) encephalitis is the most common paraneoplastic encephalitis and second most common autoimmune encephalitis.
- This syndrome is characterized by memory deficits, psychiatric symptoms, decreased consciousness, hypoventilation and frequently is associated with underlying malignancy, most commonly ovarian teratoma.
- We present two cases of NMDA encephalitis that received two different treatments and their response and outcomes.

Presentations

Case 1

- 39 year old left-handed woman with subacute presentation of fatigue and progressive encephalopathy.
- Vivid dreams and witnessed GTC seizure
- Initially treated as if had HSV encephalitis, acyclovir IV
- HR >150-170s, focal motor seizure with secondary generalization
- Nonverbal, alert and following simple commands, normal tone, diffusely hyperreflexic
- Spiked a fever, Non-interactive, tremulous and catatonic

Case 2

- 20 year old right-handed woman admitted for progressive encephalitis and myelopathy
- Febrile to 102.6 F, treated initially for suspected pyelonephritis
- Progressive numbness in legs
- Alert, awake, responding to external stimuli, tracks but is lethargic, orofacial dyskinesias, unable to perform commands, decreased tone, hyporeflexic except R ankle; nonsustained clonus and upgoing greater toe, no withdrawal from noxious stimulation

Testing	Case 1 (39 yo F)	Case 2 (20 yo F)
MRI brain	Normal	Abnormal T2 signal **in inferior vermis, inferior 4th ventricle, superior cerebellum, posterior hippocampi, Leptomeningeal enhancement**
MRI spine	N/A	Vague abnormal cord signal is suspected to be present extending from the **C2 through the C6-C7** and **T2 to T4, Patchy abnormal enhancement**
CSF	W: **145 (99% L**), R: 0, P: 53, G: 53, **OCBs: 7, IgG synthesis: 8.3**	W: **1166 (91% L),** R: 0, **P: 287**, G: 50
CSF 2nd	W: **231 (97% L),** R: 0, P: 37, G: 64, **OCBs: 12, IgG synthesis: 10.7, IgG index: 1.04**	W: **315 (98%L**), R: 0, P: 50, G: 63**, OCBs: 12, IgG index: 0.77,** IgG synthesis rate 0.2
Miscellaneous	HSV CSF PCR Neg, HSV Serum positive	AQP-4, MOG: Negative
EEG	Generalized rhythmic delta activity (GRDA), frontally predominant	Frontally maximal high-voltage beta activity superimposed on frontally maximal delta waves consistent with **'extreme delta brush**.'
Serum Encephalopathy Panel	NMDA+	NMDA+
CSF Encephalopathy Panel	Negative	NMDA+,GFAP+
Tumor screen	CT C/A/P negative	MRI pelvis, ovarian U/S: ovarian simple cyst

Reference ranges: IgG index: 0.28-0.66, IgG synthesis rate: ≤ 8 mg/d, OCBS (oligoclonal bands): 0-1
GFAP: Glial Fibrillary Acidic Protein

Treatment and Outcomes

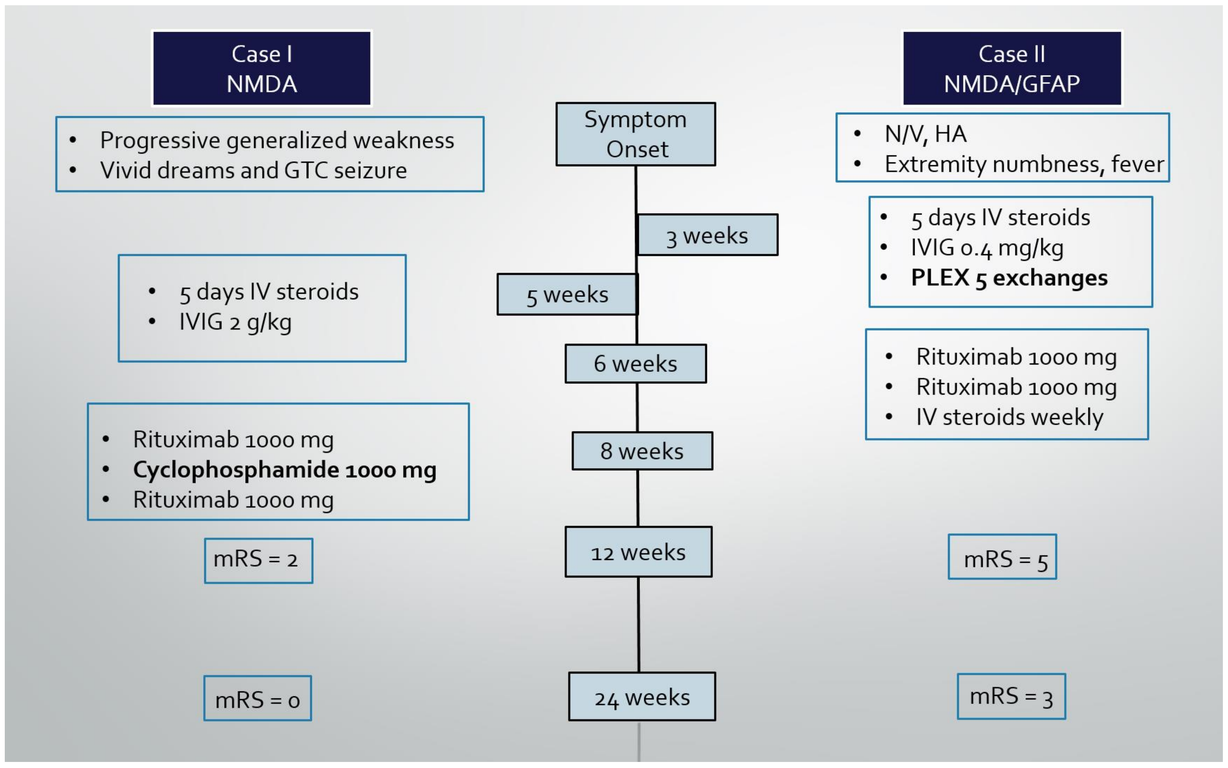

Figure 1. Comparison of treatments
mRS: modified Rankin Scale

Proposed Treatment Algorithm

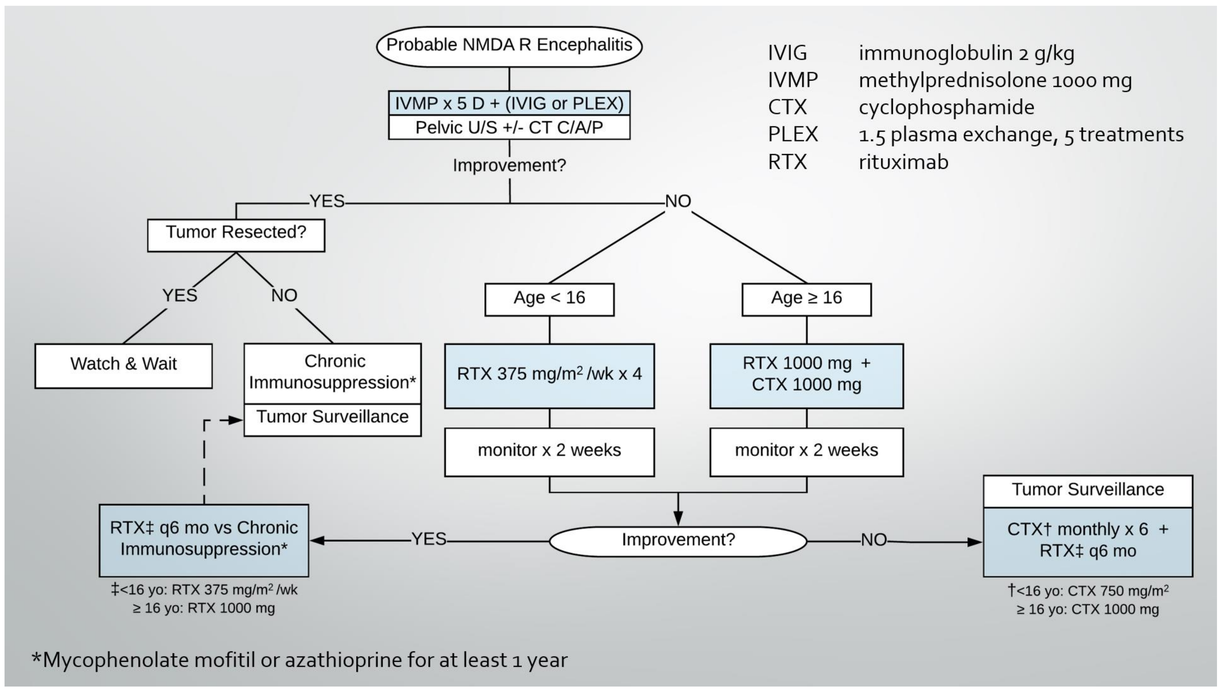

Figure 2. Proposed treatment algorithm
Adapted from diagrams from Titulauer, Florance-Ryan and Dalmau

Conclusions

- There are associated autoimmune overlaps
- Although it is important to be cautious when using immunosuppression as there are many potential adverse effects, NMDA R encephalitis is an aggressive disease entity and aggressive therapy is warranted.
- Treatment is not standardized however frequently PLEX, IVIG, methylprednisolone used initially
  - Rituximab and cyclophosphamide 2nd line
- Earlier treatment purports a better prognosis
- Duration of therapy is not known, relapse risk ~12% in 2 years
- Multicenter prospective studies are needed to evaluate efficacy of treatments

References

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