

# New-Onset Refractory Status Epilepticus (NORSE)

Marta Melis<sup>1</sup>, M. Mizrahi<sup>2</sup>, JY Yoo<sup>3</sup>, M. Fields<sup>3</sup>, L. Marcuse<sup>3</sup>, M. Puligheddu<sup>1</sup>, F. Marrosu<sup>1</sup>, SA. Meyer<sup>2</sup>

<sup>1</sup>Università degli studi di Cagliari; <sup>2</sup>Icahn School of Medicine at Mount Sinai, Departments of Neurology and Neurosurgery, New York, NY, United States; <sup>3</sup>Icahn School of Medicine at Mount Sinai, Department of Neurology, New York, NY, United States



**Background:** New-onset refractory status epilepticus (NORSE) is a recently described entity (1) defined as refractory status epilepticus presenting de novo without an obvious cause despite extensive investigation. Infectious and immunological mechanisms have been suggested, although no clear etiology has been identified. We describe 2 index patients with NORSE admitted to the Mount Sinai Hospital Neurological Intensive Care Unit (NSICU)

**MD:**  
21yo, M, Turkish  
No past medical history

- ✓ 20/12/14 nausea, abdominal pain, respiratory symptoms
- ✓ 22/12/14 confused, nonsensical language, unresponsive.
- GTCs and CSE:** L2P iv, PHN iv
- NSICU:** Right sided SE → LEV iv, LAC iv → MDZ iv- Intubated
- NSICU:** L facial twitching, coma. EEG: R focal SE/Gen SE.
- MDZ drip** → Burst suppression. **Stop MDZ** → SE → PHB

**Outcome:** seizures were super refractory to multiple AEDs and anesthetics. He has remained comatose during the entire hospital course.

✓ 06/06/15 Family decided to transfer his care

**TREATMENT:** VPA, CBZ, TPA, VGB, PTB, Ketamine, Propofol, FBM, ECT, Ketogenic diet, PLEX, Steroids, IVIG, Vanco, CFT, Acyclovir



**JM:**  
25yo, F, Asian  
No past medical history

- ✓ 19/02/15 fevers, myalgias and reduced food intake
- ✓ 21/02/15 lethargic, noted to have 2 GTCs at home

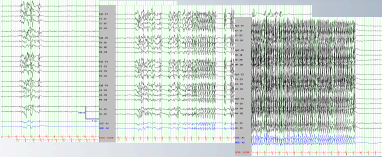
**GTC on EMS arrival and SE:** D2P iv and PHN iv  
Transferred to NSICU: 2 GTCs → LEV iv, VPA iv, MDZ iv- Intubated

**NSICU:** 2x GTC and subclinical NCSE. EEG: Generalized SE → PHB

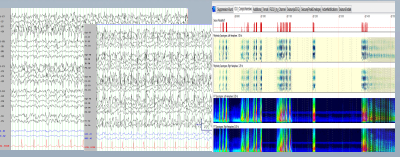
**Outcome:** seizures were super refractory to multiple AEDs and anesthetics. She became acidemic and went to multisystem organ failure. AEDs were discontinued.

✓ 04/03/15 Patient went into cardiac arrest

**TREATMENT:** LAC, OXC, CBZ, Ketamine, Propofol, Hypothermia Steroids, Vanco, CFT, Acyclovir



Generalized Seizures out of burst suppression pattern



Seizures and QEEG showing SE while in burst suppression

## SUGGESTED TESTS FOR NORSE DIAGNOSIS

Modified from Gall R.E. Seizure 22 (2013) 217-220

<b>Infectious</b>	HSV I, HSV II, VZV, EBV, HHV6, St. Louis Encephalitis virus, Western Equine Encephalitis virus, West Nile virus, Eastern Equine Encephalitis, Measles virus, <b>Enterovirus</b> , Adenovirus, Influenza A, Influenza B, Chlamydia species, Mycoplasma Pneumoniae, HIV, RPR-VDRL, Lyme serology, CMV, JC virus, Mycobacterium TB, Toxoplasma serology, Ehrlichia, Cryptococcus Neoformans, Bartonella, Fungal culture, prion disease, Rocky Mountain Spotted fever, Tularemia, Babesiosis
<b>Toxicological</b>	Marijuana, benzodiazepines, amphetamines, cocaine, LSD, Heroin, PCP, ecstasy, marine toxins, occupational and iatrogenic drug history, heavy metals
<b>Immunologic al/ Paraneoplas tic</b>	ANA, anti-thyroid antibodies, anti-dsDNA, ANCA, Jo-1, Ro, La, Scl-70, Rheumatoid factor, ESR, C-reactive protein, serum ACE level, CSF immunoelectrophoresis, <b>anti-GluR3, anti GluR1/2, anti-GAD65, anti-VGKC antibody (Casp2, LGI1), anti-GABA B, anti-GABA A, mGluR5, anti-DPPX, Anti-Hu, Ma2, CV2/CRMP5, anti-amphiphysin, anti -NMDA</b>
<b>Neoplastic</b>	CXR, CT thorax, abdomen, pelvis, whole body PET, bone marrow biopsy, CSF cytology, CSF flow cytometry

**MD**

- ✓ Head CT neg
- ✓ MRI neg
- ✓ CT total body neg

**CSF:** gluc 70; prot 39; WBC 6 (Ly); RBC 4

**Brain Biopsy:** non-specific findings. Possible involvement of small/medium blood vessels but no evidence of active vasculitis..

**JM**

- ✓ Head CT neg
- ✓ No MRI (unstable)
- ✓ No CT total body

**CSF:** gluc 96, protein 73 (>100) RBC 2, WBC 4 (Ly)

**NEGATIVE**

### Infectious panel:

Adenovirus, HSV1-2, VZV, CMV, EBV, Enterovirus, HHV6, HIV, Borrelia PCR/ Ab, Cryptococcus, West Nile Ab, anti Rabies test serum, Mycoplasma IgG serum/PCR CSF, HBV/ HCV serum

**NEGATIVE**

**NEGATIVE**

### Immunological panel:

Autoimmune serology, anti VGKC, anti NMDA, Celiac serology, anti Yo, anti-Hu, anti-Ri, anti-PCA2, anti-amphiphysin, anti CV2/CRMP5, anti Tr, ANNA 3, anti AGNA

**NEGATIVE**

**Conclusions:** Recent papers (2,3) identified common features among NORSE patients: young age, a mild prodrome, non-specific labs and imaging findings, severe prognosis. The two case reports share a similar evolution and no clear cause despite an extensive investigation, defining NORSE as a rare but homogeneous syndrome. Our experience stresses the need to establish appropriate diagnostic tests and management for NORSE patients.

## Bibliography:

- 1) Wilder-Smith EP et al., The NORSE (new-onset refractory status epilepticus) syndrome: defining a disease entity. Ann Acad Med Singapore 2005;34:417-20
- 2) Gall CR et al., Five cases of new onset refractory status epilepticus (NORSE) syndrome: outcomes with early immunotherapy. Seizure 22 (2013) 217-220
- 3) Gaspard N et al., New-onset refractory status epilepticus: Etiology, clinical features, and outcome Neurology 2015;85:1-10