

# Anti-NMDA-receptor encephalitis: two cases with atypical course and good response to early immunotherapy

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## Case report 1

### 60 years-old woman

- Temporo-spatial disorientation and decreased level of consciousness
- Within 2 days tachycardia and tachypnea with resulting cardiac and respiratory failure
- Respiration and hemodynamic support in Intensive Care Unit

**Blood analysis:** PCR 1,67 mg/dl; WBC  $12,14 \times 10^3/\text{mmc}$ .

Infectious disease work-up for principal neurotropic agents: negative.

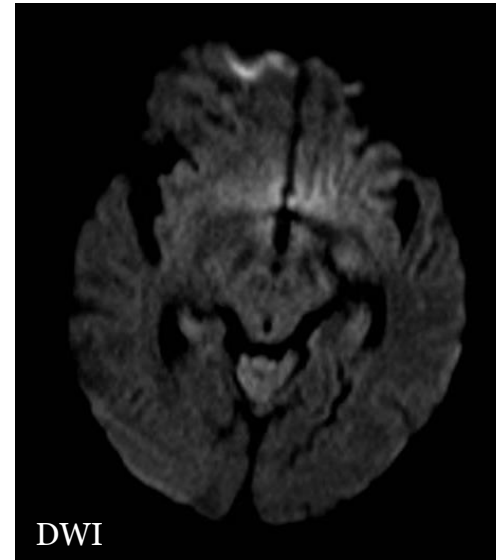
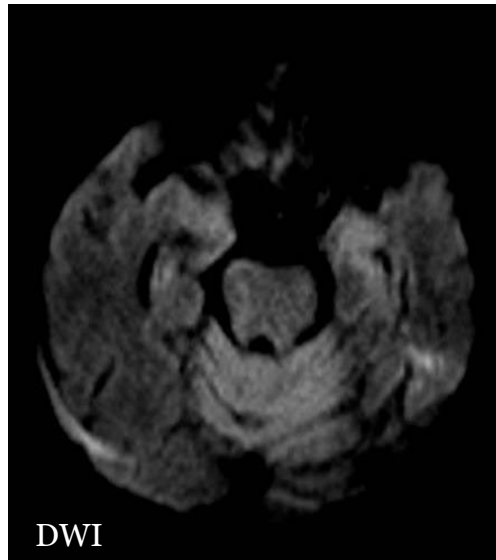
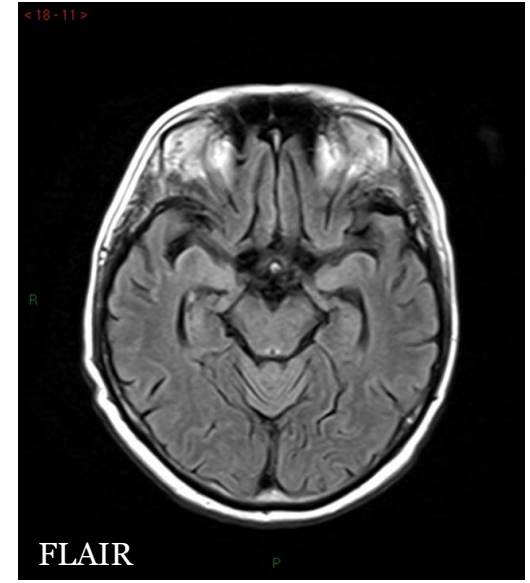
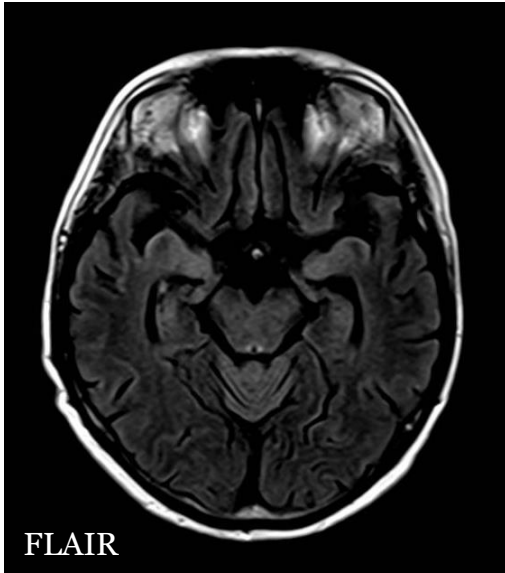
**CSF analysis:** normal for protein, IgG, glucose, WBC.

PCR for principal neutropic agents: negative.

**EEG:** diffuse slowing of brain biorhythms, more evident in the right frontal region with large delta components.

**ANTI-NEURONAL AND ANTI-SURFACE ANTIBODIES TESTING:** positive for anti-NMDAR antibodies in serum.

**BRAIN MRI:** hyperintensity of bilateral hippocampal cortex and fronto-temporal mesial lobes compatible with inflammatory/infectious disease.

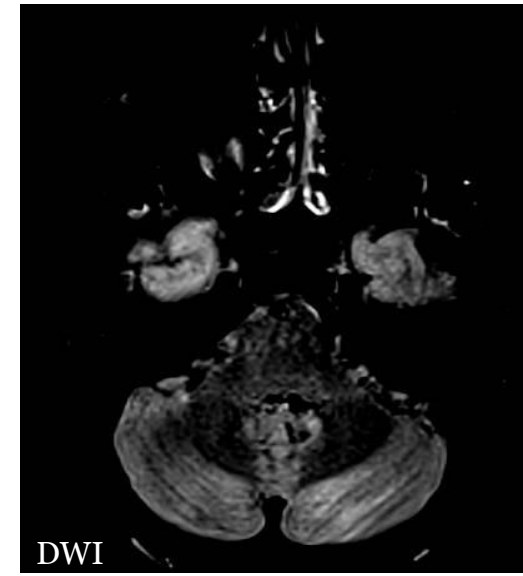
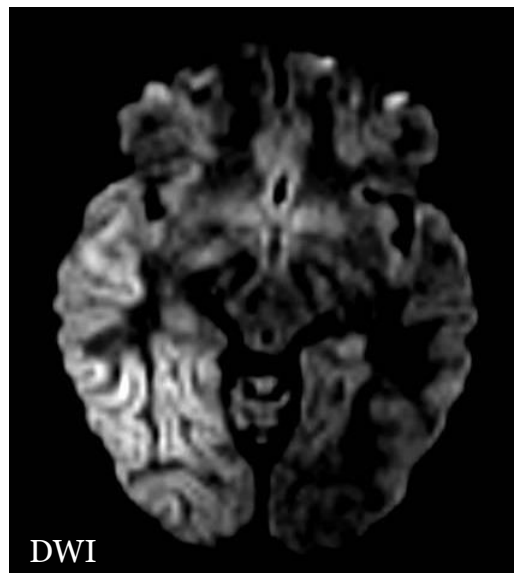
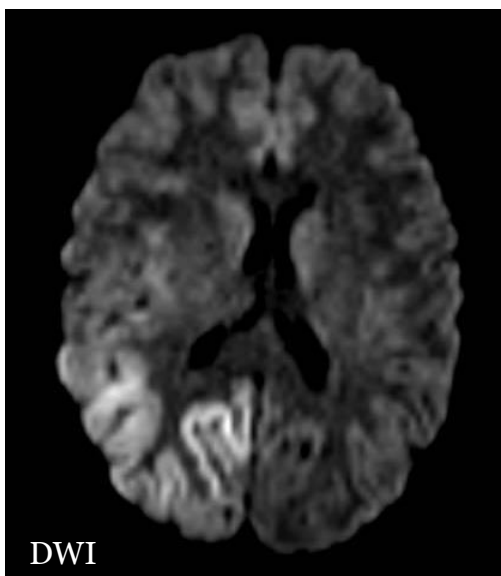
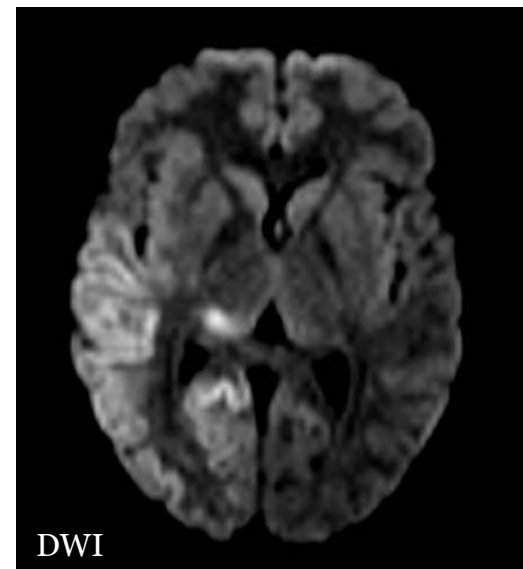
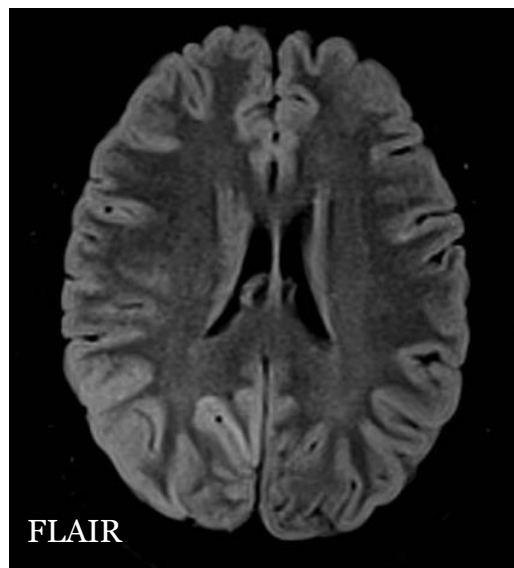
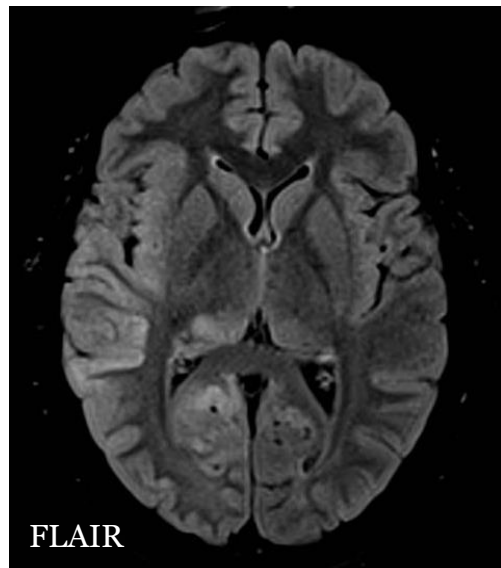




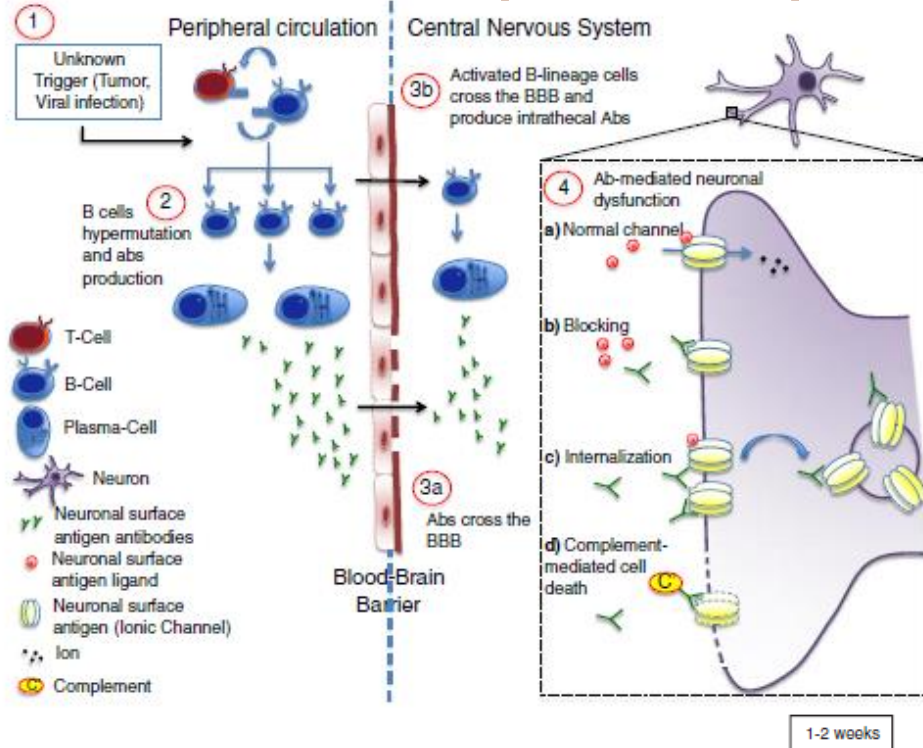
**EEG:** focal slowing in the right temporal region; delta activity (1-3 Hz) with superimposed rhythmic beta activities (20-30 Hz) constitutes the typical pattern of **EXTREME DELTA BRUSH**.

**ANTI-NEURONAL AND ANTI-SURFACE ANTIBODIES TESTING:** positive for anti-NMDAR antibodies in serum and negative in CSF.

**BRAIN MRI:** T2/FLAIR hyperintensity of right thalamus and occipital-temporal-parietal lobes and left cerebellar cortex compatible with inflammatory/infectious alterations.



# Anti-NMDA-receptor encephalitis

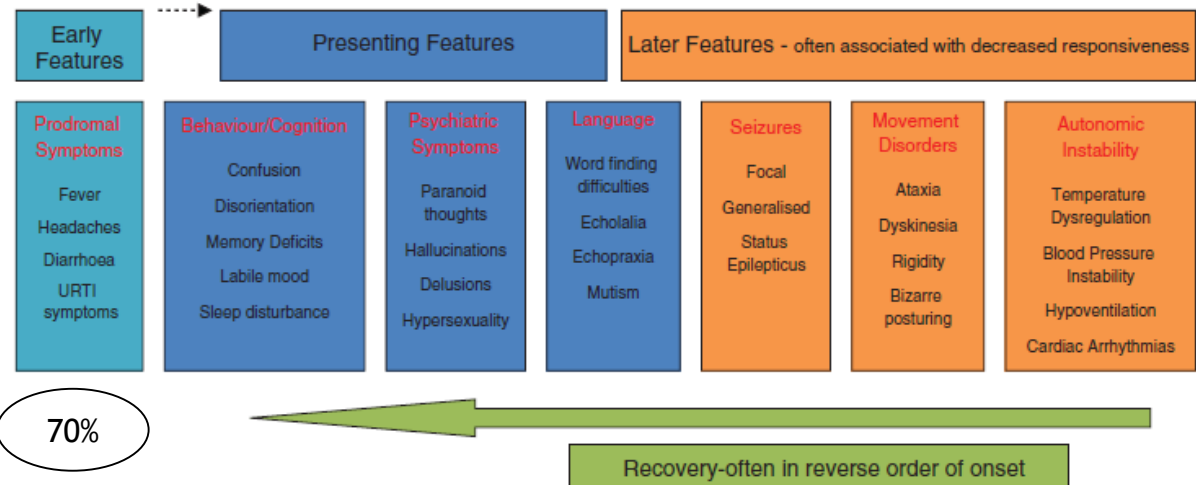


## Paraneoplastic etiology

Type of tumor depends on sex and age

- Female sex, 12-45y: ovarian teratoma (58%)
- Female sex, >45y: ovarian carcinoma (23%)
- Male sex or children <12y: 6%

“Anti-NMDA-Receptor Encephalitis: From Bench to Clinic”, Venkatesan et al., 2017





# Anti-NMDA-receptor encephalitis

## A clinical approach to diagnosis of autoimmune encephalitis

Francesc Graus, Maarten J Titulaer, Ramani Balu, Susanne Benseler, Christian G Bien, Tania Cellucci, Irene Cortese, Russell C Dale, Jeffrey M Gelfand, Michael Geschwind, Carol A Glaser, Jerome Honnorat, Romana Höftberger, Takahiro Iizuka, Sarosh R Irani, Eric Lancaster, Frank Leypoldt, Harald Prüss, Alexander Rae-Grant, Markus Reindl, Myrna R Rosenfeld, Kevin Rostásy, Albert Saiz, Arun Venkatesan, Angela Vincent, Klaus-Peter Wandinger, Patrick Waters, Josep Dalmau

## Diagnosis

### Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies

Josep Dalmau, \*Amy J Gleichman, \*Ethan G Hughes, Jeffrey E Rossi, Xiaoyu Peng, Meizan Lai, Scott K Dessain, Myrna R Rosenfeld, Rita Balice-Gordon, David R Lynch

#### CSF analysis altered in about 90% of patients

Pleocytosis >5 cells/mm<sup>3</sup> (90%)

Oligoclonal bands (60%)

#### Brain MRI normal in up to 60% of patients

T2/FLAIR and DWI images alterations of cerebral cortex, hippocampus, cerebellum, corpus callosum, basal ganglia, periventricular white matter.

Aspecific, mild and transient alterations

#### EEG altered in about 90% of patients

Diffuse ed aspecific slowing

Epileptic activity (10%)

Extreme delta brush (16-33%)

#### Anti-NMDAR antibody testing in serum and liquor

### Panel 4: Diagnostic criteria for anti-NMDA receptor encephalitis

#### Probable anti-NMDA receptor encephalitis\*

Diagnosis can be made when all three of the following criteria have been met:

- 1 Rapid onset (less than 3 months) of at least four of the six following major groups of symptoms:
  - Abnormal (psychiatric) behaviour or cognitive dysfunction
  - Speech dysfunction (pressured speech, verbal reduction, mutism)
  - Seizures
  - Movement disorder, dyskinesias, or rigidity/abnormal postures
  - Decreased level of consciousness
  - Autonomic dysfunction or central hypoventilation
- 2 At least one of the following laboratory study results:
  - Abnormal EEG (focal or diffuse slow or disorganised activity, epileptic activity, or extreme delta brush)
  - CSF with pleocytosis or oligoclonal bands
- 3 Reasonable exclusion of other disorders (appendix)

Diagnosis can also be made in the presence of three of the above groups of symptoms accompanied by a systemic teratoma

#### Definite anti-NMDA receptor encephalitis\*

Diagnosis can be made in the presence of one or more of the six major groups of symptoms and IgG anti-GluN1 antibodies,† after reasonable exclusion of other disorders (appendix)

## ONCOLOGICAL SCREENING

- Serum neoplastic markers
- Peripheral blood smear
- Mammary and gynecological ultrasound
- Gastro- and colonoscopy
- Pelvic MRI
- Total body CT

# Treatment

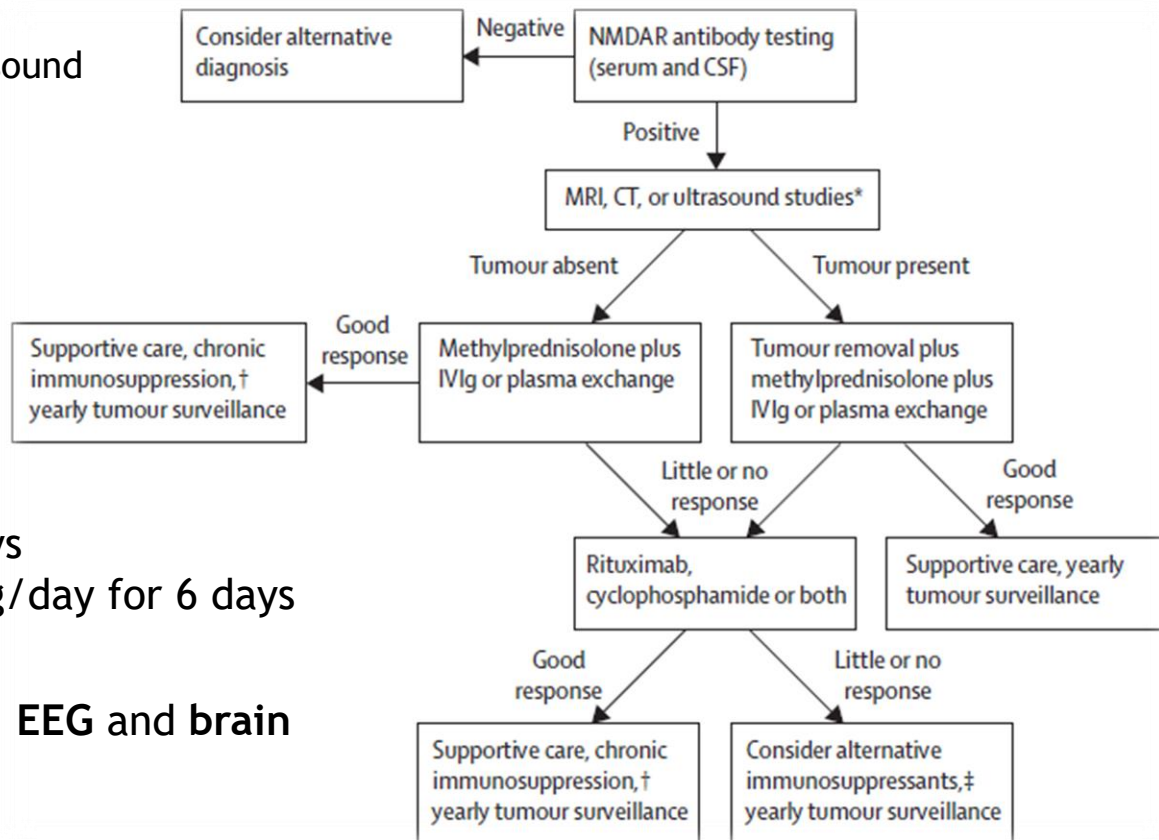
## FIRST LINE IMMUNOTHERAPY

- CASE 1: IVIG 25g/day for 5 days
- CASE 2: Methylprednisolone 1g/day for 6 days plus IVIG 25g/day for 6 days

Clear improvement of **symptoms**, **EEG** and **brain MRI** alterations.

## SECOND LINE IMMUNOTHERAPY

- CASE 2: Rituximab 375mg/m<sup>2</sup>/week for 4 weeks



**Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis**

*Josep Dalmau, Eric Lancaster, Eugenia Martinez-Hernandez, Myrna R Rosenfeld, Rita Balice-Gordon*



## Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study



*Maarten J Titulaer, Lindsey McCracken, Inigo Gabilondo, Thais Armangué, Carol Glaser, Takahiro Iizuka, Lawrence S Honig, Susanne M Benseler, Izumi Kawachi, Eugenia Martinez-Hernandez, Esther Aguilar, Núria Gresa-Arribas, Nicole Ryan-Florange, Abiguel Torrents, Albert Saiz, Myrna R Rosenfeld, Rita Balice-Gordon, Francesc Graus, Josep Dalmau*



- ✓ Anti-NMDAR encephalitis usually begins with **prominent psychiatric symptoms** followed by great constellation of neurological dysfunctions (cognitive deficits, seizures, movement disorders, autonomic instability); however a **broad variability of clinical course** may be evident.
- ✓ **CSF analysis** is altered in about 90% of patients; **brain MRI** is negative in up to 60% of patients; **anti-NMDAR antibodies testing** in serum and CSF is mandatory for the diagnosis
- ✓ **Early immunotherapy** is strongly associated with good outcome and fewer relapses: up to 53% of patients experience improvement within 4 weeks, evaluated through the **modified Rankin Scale**
- ✓ **Second line immunotherapy** is indicated in cases with absent or not detected tumor and with poor response to first line immunotherapy ( $mRS \geq 3$ ): this therapy represents an **independent positive predictive factor** for relapses
- ✓ Indications for **chronic immunosuppression** and its duration remain uncertain

# Thanks for your attention

