Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

Case vignette

A 23-year-old woman, with no medical history, had an uncomplicated episode of gastroenteritis with fever, which resolved spontaneously. Two weeks later, she presented with speech difficulties, hypophonia, anxiety, and tremulous eye and head movement followed by increasing gait instability. Neurological examination revealed severe psychomotor slowing, apathy, hypomimia, bilateral facial paresis, opsoclonus, myoclonic jerks of the head and the trunk, static and kinetic ataxia, as well as a right-sided hemiparesis. Tendon reflexes were normal. There was no inflammatory parameter on the routine blood test. The CSF examination showed mild lymphocytic pleocytosis (29 leukocytes/µl, 4% plasmocytes), normal protein and glucose concentrations, and intrathecal IgG synthesis with oligoclonal bands. Brain magnetic resonance imaging results were normal. EEG showed generalized slowing of activity with left-sided predominance and no epileptiform discharges (figure 1).

MCQ

1. *At this stage, which diagnosis is the least probable?*

A Viral encephalitis
B Bacterial encephalitis
C Acute disseminated encephalomyelitis
D Miller-Fisher syndrome
E Autoimmune encephalitis

2. *Among these additional examinations, which one would you* not *choose?*

A Thoraco-abdominal CT
B Total body PET-CT
C Cerebral biopsy
D Toxic and metabolic screening
E Antineuronal antibodies

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The patient's condition worsened rapidly with development of pseudobulbar paresis and rigid tetraparesis. Infectious, toxic, and metabolic workup results were negative. A second electroencephalography showed more marked diffuse slowing (figure 2).

The patient was initially treated for probable viral or autoimmune encephalitis with acyclovir and a high dose of intravenous methylprednisolone. Her condition continued to worsen to almost an akinetic mutism; she became incontinent and needed tube feeding, but she had no respiratory difficulties. The PCR for herpes was negative. Plasma exchange was started with the suspicion of autoimmune or paraneoplastic encephalitis. Because of a systemic hypotension, it was decided to switch to intravenous immunoglobulins (IvIg). A slow clinical improvement was observed after the first days of IvIg, consistent with improvement of background EEG activity (figure 3).

MCQ

3. *Immunologic workup revealed the presence of antibodies. Which one?*

A Anti-Yo
B Anti-Hu
C Anti-AChR
D Anti-NMDAR
E Anti-VGKC

Diagnosis

Immunologic workup revealed the presence of antibodies to NR1/NR2 heteromers of N-Methyl-D-Aspartate receptors, confirming the diagnosis of anti-NMDAR encephalitis.

MCQ

4. *Concerning anti-NMDAR encephalitis, which of the following sentences is* false*?*

A A limbic symptomatology is less frequent than with anti-VGKC antibodies
B This encephalitis is non-paraneoplastic in about 40% of cases
C The commonly associated tumour is the ovarian teratoma
D Like anti-VGKC, the answer to immunotherapy seems to be better than with other paraneoplastic antibodies
E Antibodies bind to intraneuronal antigens

Figure 1 Awake EEG, montage II (double banana), 20 sec per page: generalized slowing with left-sided predominance; eyelids movement's artefacts in frontal areas on eyes closure *(yeux fermés)* who disappeared on eyes opening *(yeux ouverts)*.

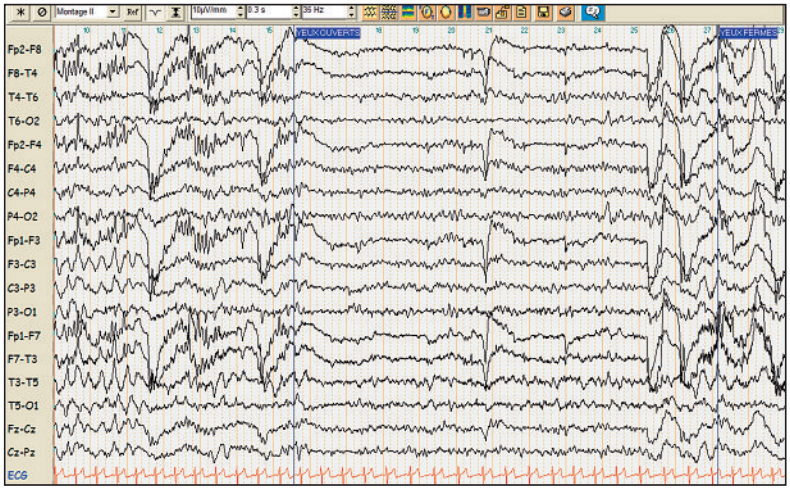


Figure 2 More diffuse and marked generalized slowing (same EEG parameters than figure 1).

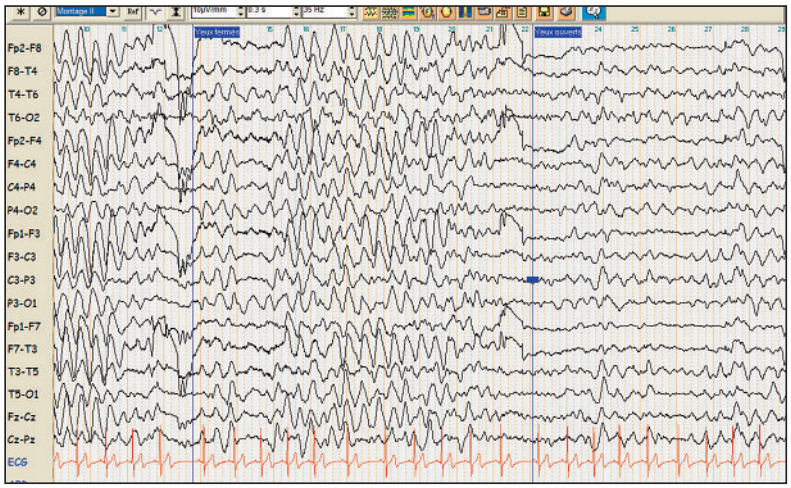
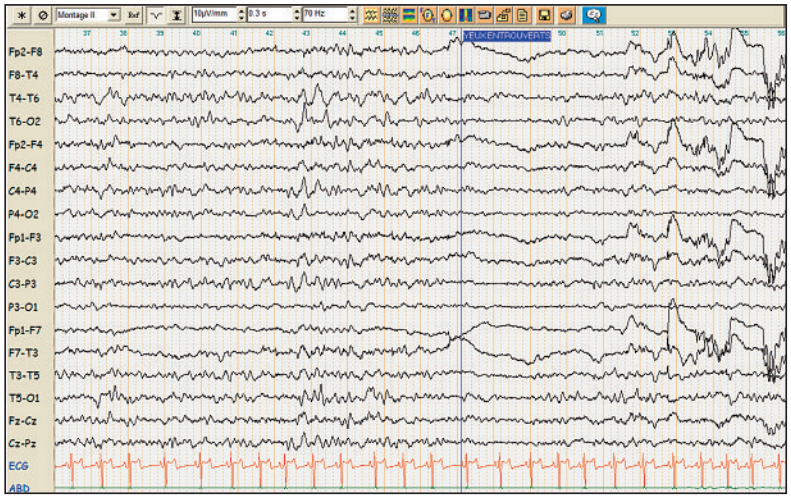


Figure 3 Persistent generalized but less marked slowing (theta rhythm rather than delta) and more reactivity (same EEG parameters than figure 1 and 2).



Comments

There are some particularities in our clinical case [1], considering anti-NMDAR encephalitis:

- The opsoclonus-myoclonus syndrome is more often described in children with neuroblastoma; in adults, anti-Ri antibodies are sometimes found.
- Antibodies were identified only in the CSF. Usually, they are found either only in the serum [2], either in the serum and the CSF. A normal CSF without intrathecal synthesis or oligoclonal bands, may be seen in antibodies-mediated encephalitis.
- Our patient didn't have seizures or hypoventilation, as described respectively in 3/4 and 2/3 of patients in the largest case series [3].
- No tumour was found so far. Her clinical status improved in three months, with residual signs of frontal lobe dysfunction. However, she is still under regularly oncologic screening.

Suggested reading

Tuzun E, Dalmau J. Limbic encephalitis and variants: classification, diagnosis and Treatment. Neurologist 2007;13:261–71.
Dalmau J, Rosenfeld MR. Paraneoplastic syndromes of the CNS. Lancet Neurol 2008;7:327–40.
Graus F, Saiz A, Dalmau J. Antibodies and neuronal autoimmune disorders of the CNS. J Neurol 2010;257:509–17.

References

1 Kurian M, Lalive PH, Dalmau JO, Horvath J. Opsoclonus-myoclonus syndrome in anti-N-methyl-D-aspartate receptor encephalitis. Arch Neurol. 2010;67(1):118–121.
2 Vincent A, Bien CG. Anti-NMDA-receptor encephalitis: a cause of psychiatric, seizure, and movement disorders in young adults. Lancet Neurol 2008;7:1074–5.
3 Dalmau J, Gleichman AF et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008;7:1091–98.

Answers to MCQ

1. D
2. C
3. D
4. E