J Neurol (2010) 257:1568–1569
DOI 10.1007/s00415-010-5546-z

LETTER TO THE EDITORS

Abnormal multifocal cerebral blood flow on Tc-99m HMPAO SPECT in a patient with anti-NMDA-receptor encephalitis

Verónica Llorens · Iñigo Gabilondo · Juan Carlos Gómez-Esteban · Marta Agundez · Mar Mendibe · Juan Carlos Bergara · Roberto Ciordia · Albert Saiz · Juan J. Zarranz

Received: 20 February 2010 / Revised: 10 March 2010 / Accepted: 12 March 2010 / Published online: 30 March 2010

Dear Sirs,

Anti-*N*-methyl-D-aspartate receptor (NMDA-R) encephalitis has been related with teratomas of the ovary in young women. However, this syndrome is non-paraneoplastic in about 40% of patients, particularly in the youngest patients [1, 3]. This encephalitis is associated with antibodies against the NMDA-R NR1 and NR2 subunits. The clinical picture includes movement disorders (dystonia, orolingual dyskinesias, chewing movements, myoclonias,…), decreased level of consciousness, seizures, central hypoventilation and autonomic disturbances. Frequently it is preceded by psychiatric symptoms such as changes of mood, behavior and personality, or acute psychosis.

Brain MRI is normal or with mild changes in most patients. To date, scarce data from functional neuroimaging studies [4] or MR spectroscopy are available. Few neuropathological cases have been described [2, 6, 7].

V. Llorens
Department of Nuclear Medicine, Hospital of Cruces, Baracaldo, Spain

I. Gabilondo · J. C. Gómez-Esteban (✉) · M. Agundez · M. Mendibe · R. Ciordia · J. J. Zarranz
Service of Neurology, Hospital of Cruces, Baracaldo 48903, Vizcaya, Spain
e-mail: jgomeze@meditex.es

J. C. Bergara
Intensive Care Unit (ICU), Hospital of Cruces, Baracaldo, Spain

A. Saiz
Service of Neurology, Hospital Clinic, Barcelona, Spain

I. Gabilondo · J. C. Gómez-Esteban · M. Agundez · M. Mendibe · R. Ciordia · J. J. Zarranz
Department of Neurosciences, University of Basque Country, Bilbao, Spain

We present a patient with anti-NMDA-R encephalitis with a previously unreported abnormal multifocal cerebral blood flow on Tc-99m HMPAO SPECT.

A 14-year-old girl was admitted to the ICU for an acute psychiatric episode that developed 48 h after an upper respiratory tract infection. She showed agitation, auditory and visual hallucinations and aberrant behaviour. A conventional neurological examination, CT of the brain and funduscopy were normal. A lumbar tap yield a colourless CSF with 140 lymphocytes/ml and a normal glucose and protein level. PCR for HSV DNA and cytology were normal or negative.

In the following days she worsened, developing a generalized dystonia, severe facial grimacing and oculogyric crisis with a decreased level of consciousness. Autonomic symptoms were present with hypertensive crisis, tachycardia and hypersalivation. The patient did not develop central hypoventilation. She showed generalized seizures and was treated with phenytoin.

Two gadolinium-enhanced brain MRI were normal (Fig. 1). Several EEGs showed continuous 2.5–3.5 Hz slow waves without spikes. Brain Tc-99m HMPAO SPECT images showed multiple focal areas of increased radiotracer uptake in both striatum and cerebral cortex more intense in the frontal lobes (Fig. 1). Antibodies to NR1/NR2 heteromers of the NMDA receptor were found in CSF (immunological studies performed by Drs F. Graus and A. Saiz Neurology Service, Hospital Clinic, Universitat de Barcelona). Ovarian teratoma or other tumors were not identified with repeated specifically oriented CT, MRI, or ultrasound. The patient did not improve after one high dose steroid course. A dramatic recovery was observed with the administration of IVIg at standard doses. Repeated brain-Tc-99m HMPAO-SPECT showed a near complete normalization. Brain MR Spectroscopy was performed after resolution of

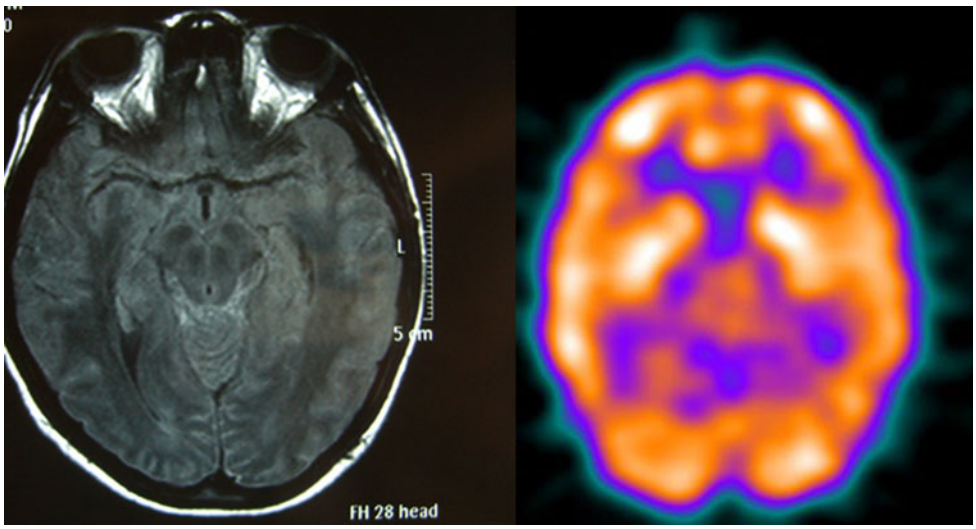

Fig. 1 *Left* MRI-Flair sequence in the area of frontal basal-limbic region was normal. *Right* Abnormal multifocal cerebral blood flow on Brain Tc-99m HMPAO SPECT

involuntary movements and was normal. Two months after discharge, the patient is asymptomatic and presents a complete amnesia of the episode.

The combination of dystonic movements, cerebrospinal fluid lymphocytic pleocytosis and psychiatric symptoms in a young woman should prompt the diagnosis of anti-NMDA-receptor encephalitis despite normal EEG and brain TC or MRI [1]. Muscle rigidity, hyperthermia, elevated serum levels of creatine kinase and rhabdomyolysis may occur in patients with anti-NMDA-R encephalitis and for this reason may be misdiagnosed as neuroleptic malignant syndrome if they have been exposed to neuroleptic drugs [6]. We have retrospectively reviewed a case report of our institution that could meet the diagnostic criteria for this syndrome. Another misdiagnosis is idiopathic or viral encephalitis. About 50% of patients with idiopathic encephalitis and psychiatric symptoms or dyskinesias may have this diagnosis [1, 3].

Anti-NMDA-receptor encephalitis is non-paraneoplastic in about 40% of patients [1, 3]. Younger patients are less likely to have tumors [3]. In our case we could rule out an ovarian teratoma or other neoplasm after a thorough imaging study. Neurological relapse occurs in 25% of these patients. A characteristic feature of patients is a persisting amnesia of the entire process [1], and also happened in our patient.

Reduced level of *N*-acetylaspartate in the basal ganglia has been reported in one patient with anti-NMDA-R encephalitis [5]. Functional image studies have been scarce and with contradictory findings. Recently Lizuka et al. [4] have described SPECT studies showing no significant focal changes during the acute stage of the disease in three quarters of patients, but in one patient SPECT showed frontotemporal hyperperfusion. In our patient the Tc-99m HMPAO SPECT showed an abnormal multifocal cortico-basal hyperperfusion pattern pointing to a possible involvement of fronto-basal circuits in the pathogenesis of this syndrome dominated by abnormal behaviour and movement disorders. In the appropriate clinical setting the finding of a similar SPECT pattern could help in the diagnosis of autoimmune NMDA-R encephalitis.

Conflict of interest statement There are no funding sources and potential conflicts of interest from each author that relate to the research covered in the article submitted.

References

1. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, Dessain SK, Rosenfeld MR, Balice-Gordon R, Lynch DR (2008) Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 7:1091–1098
2. Dalmau J, Tuzun E, Wu HY, Masjuan J, Rossi JE, Voloschin A, Baehring JM, Shimazaki H, Koide R, King D, Mason W, Sansing LH, Dichter MA, Rosenfeld MR, Lynch DR (2007) Paraneoplastic anti-*N*-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol 61:25–36
3. Florance NR, Davis RL, Lam C, Szperka C, Zhou L, Ahmad S, Campen CJ, Moss H, Peter N, Gleichman AJ, Glaser CA, Lynch DR, Rosenfeld MR, Dalmau J (2009) Anti-*N*-methyl-D-aspartate receptor (NMDA-R) encephalitis in children and adolescents. Ann Neurol 66:11–18
4. Iizuka T, Sakai F, Ide T, Monzen T, Yoshii S, Iigaya M, Suzuki K, Lynch DR, Suzuki N, Hata T, Dalmau J (2008) Anti-NMDA-receptor encephalitis in Japan: long-term outcome without tumor removal. Neurology 70:504–511
5. Kataoka H, Dalmau J, Taoka T, Ueno S (2009) Reduced *N*-acetylaspartate in the basal ganglia of a patient with anti-NMDA-receptor encephalitis. Mov Disord 24:784–786
6. Sansing LH, Tuzun E, Ko MW, Baccon J, Lynch DR, Dalmau J (2007) A patient with encephalitis associated with NMDA receptor antibodies. Nat Clin Pract Neurol 3:291–296
7. Tuzun E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J (2009) Evidence for antibody-mediated pathogenesis in anti-NMDA-R encephalitis associated with ovarian teratoma. Acta Neuropathol [In press]