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Case study

Sudden and isolated Broca's aphasia: A new clinical phenotype of anti NMDA receptor antibodies encephalitis in children

Kumaran Deiva [a,b,*], *Maria Carmela Pera* [a], *Hélène Maurey* [a], *Pascale Chrétien* [c], *Frédérique Archambaud* [d], *Viviane Bouilleret* [e], *Marc Tardieu* [a,b]

[a] *Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Hôpital Bicêtre, Pediatric Neurology Department, Le Kremlin Bicêtre, France*
[b] *National Referral Center for Neuro-Inflammatory Diseases in Children and University Paris-Sud, Le Kremlin-Bicêtre, France*
[c] *Assistance Publique Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Hôpital Bicêtre, Immunology Department, Le Kremlin-Bicêtre, France*
[d] *Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Biophysics and Nuclear Medecine Department, Le Kremlin-Bicêtre, France*
[e] *Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Neurophysiology and Epileptology Departement, Le Kremlin-Bicêtre, France*

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ABSTRACT

Background: Anti NMDA receptor (anti NMDAR) encephalitis is a well-characterized entity in children associating movement disorders, psychiatric features and speech difficulties. Novel phenotypes have been described in adults.
Methods and Results: A 4-year-old girl presented partial seizures which evolved towards sudden and isolated Broca's aphasia. Anti NMDAR antibodies were positive in CSF and serum confirming anti NMDAR encephalitis. Clinical recovery was observed after a specific treatment.
Conclusion: This case widens the clinical spectrum of anti-NMDAR encephalitis in children and awareness of this newly identified symptom is important as early treatment is a predictor of good outcome

* *Corresponding author*. Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Pediatric Neurology Department, National Referral Center for Neuro-Inflammatory Diseases in Children, 78, rue G Leclerc, 94275 Le Kremlin Bicêtre, France. Tel.: +33 0 145213158; fax: +33 0 145213231.
E-mail address: kumaran.deiva@bct.aphp.fr (K. Deiva).
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1. Case report

A previously healthy 4 year-old right handed female child born to healthy consanguineous parents, presented after 4 days of fever and repeated right partial motor seizures each lasting less than 2 min. She had no impairment of her consciousness and recovered completely after these episodes. Cerebro-spinal fluid (CSF) analysis identified 19 leukocytes, with 0.22 g/l of protein and no oligoclonal bands; PCR for herpes virus and enterovirus were negative and serology was negative for CMV, mycoplasma and chlamydia. EBV serology was suggestive of a past infection. ESR was normal, and antinuclear and anti TPO antibodies were negative. No abnormal finding was observed on conventional MRI; EEG revealed a generalized low voltage activity predominant in the left fronto-temporal areas. Valproic acid was then started. Eight days after disease onset, while seizures were completely under control, the patient suddenly presented isolated speech difficulties. Her consciousness was normal and speech evaluation showed that her receptive language was preserved but that expressive language was affected associated with anomia, and anarthria suggestive of Broca's aphasia. No other behavioural, clinical symptoms or seizures were observed. Waking EEG was characterized by unilateral left hemispheric slowing, and sleep EEG showed a repetitive pattern of focal theta rhythms over 10–15 s in the postero-temporal region which then spread to the whole left hemisphere for 45–60 s (Fig. 1). Cerebral FDG PETscan revealed a left hemispheric hypometabolism (Fig. 1). Treatment was switched to carbamazepine with no effect on either the aphasia or the EEG abnormalities. Further analysis of CSF and serum were positive to antibodies directed against the N-methyl-D-aspartate receptor (NMDAR) (1:100 in both serum and CSF; positive cut off value over 1:10), leading to the diagnosis of anti-NMDAR encephalitis. Intravenous Rituximab (375 mg/m^2) was started one and half month after disease onset, and the aphasia improved significantly within days; within 3 weeks the girl started talking again. Investigation for a tumour (thoraco-abdomino-pelvic CT) was negative. After 20 months of follow up, the child had completely recovered, was free of seizures

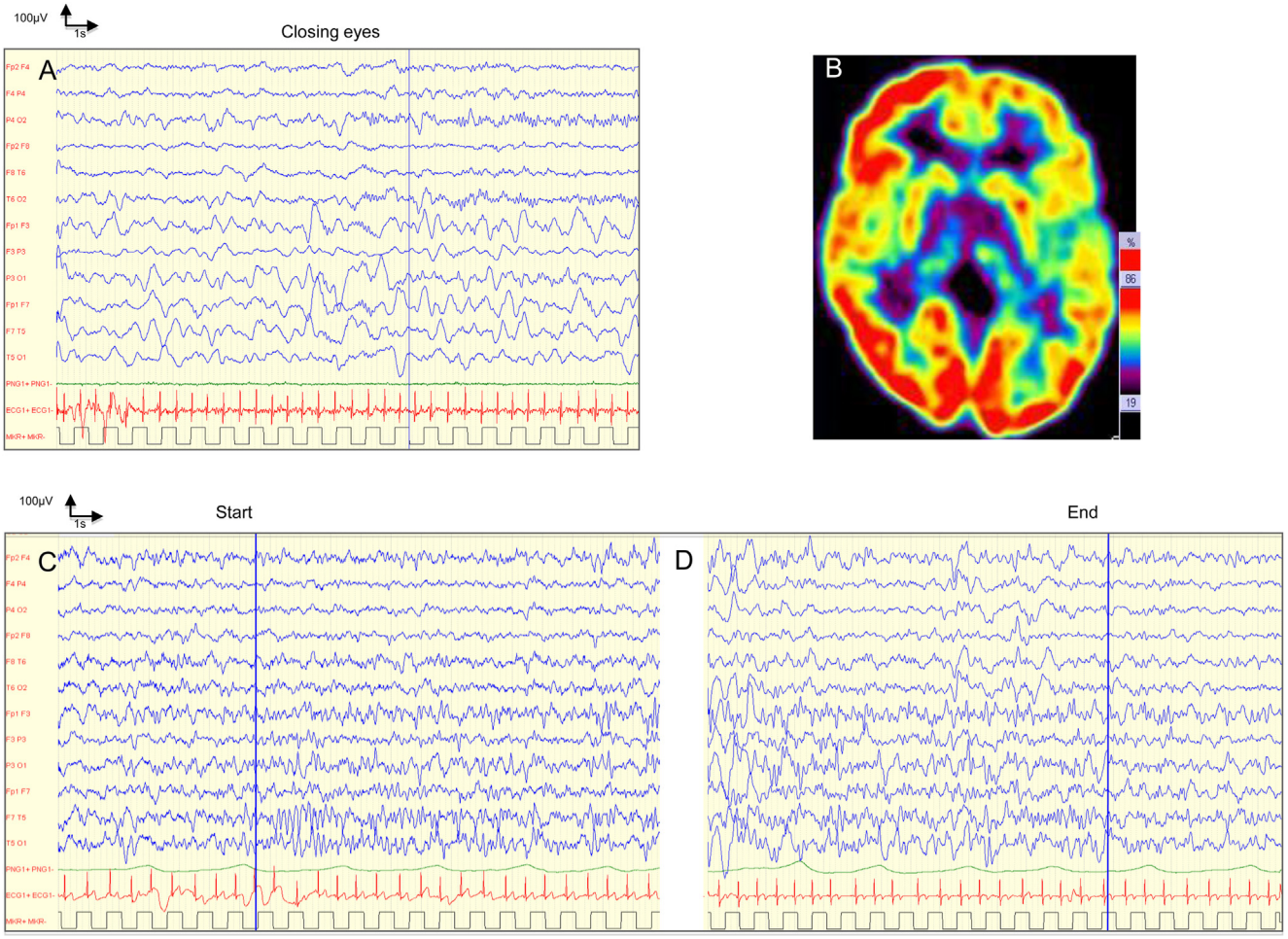

Fig. 1 – EEG pattern and PETscan: (A) Waking interictal EEG with unilateral left hemispheric slowing. (B) Axial PETscan slice in the AC-PC plane obtained 30 min after iv injection of 65 MBq of 18F-FDG showing the hypometabolism of the left hemisphere involving the frontal, parietal, and temporal cortex. (C and D) Sleep EEG showing a repetitive pattern starting by focal theta rhythms (10–15 s) in the postero temporal region (C) subsequently spreading to the whole left hemisphere for 45–60 s (D).

despite discontinuation of treatment, and anti-NMDAR antibody titre in serum has decreased (1:50).

2. Discussion

We report here a child with an incomplete form of anti-NMDAR encephalitis revealed by sudden and isolated Broca's aphasia following partial seizures.

Clinical symptoms at onset of anti-NMDAR encephalitis in children are usually seizures; there are also movement disorders in 60% of affected children and psychiatric and cognitive features in 40%.[1] Speech disorders have been described in cases of anti-NMDAR encephalitis and post infectious encephalitis at onset but with other symptoms.[2,3] Usually, 4 weeks after disease onset, most patients develop a set of common symptoms associating movement disorders, psychiatric features and speech difficulties.[4] In our case, the child presented partial seizures at onset, and subsequently, 8 days of disease onset, while she had completely recovered of seizures, she developed a sudden isolated Broca's aphasia with no abnormal movement or psychiatric features which persisted until the beginning of specific treatment. To our knowledge this is the first reported case of NMDAR encephalitis with an incomplete form associated with sudden and isolated Broca's aphasia.

Aphasia secondary to seizures, such as a Todd's palsy was initially considered in this case, because the repetitive pattern of focal theta rhythms during sleep spreading through the left hemisphere could have corresponded to epileptic discharges. Such abnormal EEG rhythms during sleep have been found in other epileptic syndromes, for example Landau Kleffner disease. However, similar electrical patterns have also been described in previous NMDAR encephalitis studies suggesting that these patterns do not necessarily correlate with seizures.[5] An alteration of neuronal network, probably a consequence of the presence of anti-NMDAR antibodies, has been suggested, and this was also supported by the corresponding hypometabolism in the left hemisphere.[6] Moreover, antiepileptic treatment was ineffective, probably consistent with an inflammatory and/or auto-antibody-associated dysfunction, further supported by the prodromal fever and pleocytosis in the CSF. Only a specific anti-CD20 treatment against B-cell allowed our patient to recover both clinically and electrically.[7] Moreover, this was associated with a decrease of anti-NMDA antibodies. However, although anti NMDAR encephalitis is the most relevant hypothesis (anti-NMDAR positivity, clinical response to the treatment associated with the decrease of antibodies), the possibility of another associated yet-to-be identified auto-antibody cannot be ruled out du to the atypical presentation.

Along other unusual cases of anti NMDAR encephalitis (transverse myelitis,[8] transient paroxysmal exercise-induced foot weakness[9]), this case widens the clinical spectrum of anti-NMDAR encephalitis in children who are less likely than adults, to have an underlying tumour and may have different clinical symptoms during disease evolution. Awareness of this newly identified symptom is important as early treatment is a predictor of good outcome.[4]

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Conflict of interest declarations

The authors have no conflicts of interest relevant to this article to disclose. There are no sponsors for this study.

KD, VB, MT: substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafting the article or revising it critically; MCP, HM, PC, FA : acquisition of data, revising the article critically and final approval of the version to be published.

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