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Case Report

CASE REPORT

Case Presentation of Anti-NMDA Receptor Encephalitis in a 4-Year-Old Boy

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ABSTRACT

We report a case of a 4-year-old boy from Oyo, Nigeria, presenting with prolonged seizures and coma with the subsequent development of oro-lingual-facial dyskinesia with frequent tongue thrusting, dysconjugate gaze and choreoathetoid movements of the limbs because of autoimmune encephalitis consistent with anti-N-methyl-D-aspartate (anti-NMDAR) encephalitis.

KEYWORDS: N-methyl D-aspartate, encephalitis, receptors, seizures

BACKGROUND

Anti-N-methyl-D-aspartate (Anti-NMDAR) encephalitis is an autoimmune disease that affects the NMDA receptors, which are neuronal extracellular membrane antigens that are found throughout the brain and play a role in synaptic transmission and plasticity that underlie memory, behaviour and learning [1]. The disease was first described by Dr Josep Dalmau in 2007 [2]. Clinical criteria for diagnosis were subsequently delineated by Graus *et al.* in 2016 [3]. Possible diagnosis as per Graus *et al.* includes three criteria: (i) subacute onset; (ii) at least one of the following (a) new focal central nervous system finding, (b) seizures without a seizure disorder, (c) cerebrospinal fluid (CSF) pleocytosis or (d) magnetic resonance imaging (MRI) features of encephalitis; and (iii) reasonable exclusion of other diseases [3]. Definitive diagnosis requires MRI and ideally electroencephalogram [3], unavailable in most facilities in low-resource settings. It occurs in men, women and children of all ages. Initially considered rare, the disease is now increasingly recognized as a significant diagnosis in the spectrum of brain illnesses related to malfunctions of the immune system. We present a case of probable anti-NMDAR encephalitis in a child with progressively deteriorating clinical course but with a near full recovery following treatment with high-dose steroidal therapy. To the best of our knowledge, this is the first reported case from West Africa.

CASE PRESENTATION

TO the patient referred to here was a 4-year-old boy living in Oyo, Nigeria. He was in good health, until a week before presentation. He presented with a prodrome of neck pain, generalized ill health and neck stiffness followed by a single non-febrile seizure without history of trauma, headache or vomiting. He was treated as an outpatient. The following day, he had another seizure and was admitted to the outlying hospital, where seizures continued and he lapsed into coma. On admission, he developed a high-grade fever, despite anti-malarial treatment, and was subsequently referred to our facility.

His coma and recurrent seizures persisted on admission to our hospital, where he was initially treated for cerebral malaria. Seizures were associated with bilateral medial upward rolling of eyes, and tonic–clonic contractions were associated with rhythmic jerking of the right upper and then right lower limb with the left side less affected. His response to standard treatment for cerebral malaria was poor. We then considered acute viral encephalitis; however, his normal CSF findings did not support this diagnosis. Initial CSF was clear and colourless; WBC count, <5 WBC/mm^3; glucose level, 88 mg/dl; protein level, 20 mg/dl; gram stain did not show any organisms; and CSF cultures were sterile. A second CSF analysis during Week 5 was also normal. It was not possible to test for herpes simplex virus (HSV) encephalitis, and this patient was never treated for HSV.

When he failed to improve, he was referred for a computed tomography, which only showed mild accentuation of contrast enhancement of the brain without focal findings consistent with cerebritis per report. Seizures continued with excessive salivation, despite a three-drug anticonvulsant regime consisting of optimal doses of phenobarbitone, carbamazepine and sodium valproate.

He remained comatose with Glasgow coma scores (GCSs) ranging from 3 to 8 and was later found to have spastic quadriparesis with poor head control and inability to speak or sit. His condition began to improve slightly during the fourth week of admission with lightening coma, cessation of seizures, GCS >11 and responding to his mother's call with head turning. He however was unable to talk and see.

Around this time, he developed difficulty in sleeping despite receiving high dose of phenobarbitone. He subsequently developed oro-lingual-facial dyskinesia with frequent tongue thrusting, dysconjugate gaze and choreoathetoid movements of the limbs. He was also mute. A consultation was arranged with a paediatric neurologist (J.B.L.) who suggest treating this case of presumed anti-NMDA encephalitis with high dose of intravenous methylprednisolone (30 mg/kg/day) for 5 days followed by oral taper of prednisolone, a steroid, for 8 weeks. He was discharged after a prolonged hospital stay of 7 weeks.

The patient made remarkable improvement following initiation of steroid therapy. He was able to be weaned off combination anticonvulsants and was discharged on phenobarbitone alone as a maintenance anticonvulsant. His subsequent progress has been slow but progressively gaining new skills with each clinic visit. At 10 months, he has now returned essentially back to his baseline.

DISCUSSION

To the best of our knowledge, this is the first case of possible anti-NMDAR (criteria as per Graus *et al.* [3] noted above) in the medical literature in Africa. The only other reported case was found on the Web in 'Patient stories' in one patient from South Africa [4]. Diagnosis was suspected only after development of characteristic insomnia associated with oro-lingual-facial dyskinesia, and choreoathetoid movements gave striking hints of this disease. This case suggests that autoimmune encephalitis does occur in Africa, and it should be borne in mind by physicians as a differential diagnosis in patients with recurrent non-febrile seizures associated with abnormal facial, tongue and limb movements. We did not observe the psychiatric manifestations mentioned by Dalmau *et al.* [2] In children, the first symptom to be recognized is often non-psychiatric, for example seizures, status epilepticus, verbal reduction or mutism as applicable in our patient [2]. We were hampered by the lack of the ability to assay for NMDAR antibodies and MRI in our setting. We have difficulty in obtaining treatments such as intravenous immunoglobulins and plasmapheresis; however, steroids, rituximab and cyclophosphamide are readily available. The first-line treatment with high-dose intravenous

steroids followed by oral steroids is relatively cheap and available in the region [2]. Prompt recognition and early use of high-dose steroid treatment can shorten the duration of the disease and possibly prevent complications.

While it cannot be proved by us, our child had anti-NMDAR encephalitis, as characteristic manifestations in our patient are highly suggestive of the disease or possibly another autoimmune encephalitis. Other diseases in our differential include Hashimoto's thyroiditis, Guillain–Barre syndrome and other postinfectious encephalitis like acute disseminated encephalomyelitis [5].

Anti-NMDAR encephalitis condition should be considered as a differential diagnosis in children presenting in the tropics with recurrent non-febrile seizures, variable loss of consciousness and dyskinesia.

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