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Unlocking the Puzzle: Anti-NMDA Receptor Encephalitis in a 4-year-Old Boy

Khandwala K, Hilal K*, Nadeem N and Mirza WA

Department of Radiology, Aga Khan University, Pakistan

***Corresponding author:** Kiran Hilal, Department of Radiology, Aga Khan University, Karachi, Pakistan, Email: kiran.hilal@aku.edu

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Abstract

Imaging of anti-N-methyl-D-aspartate receptor (NMDA) encephalitis is variable and non-specific, with lesions that can involve both white and grey matter depending on the underlying cause. We describe a case of anti-NMDA encephalitis in a 4-year-old male child who presented with history of unilateral focal fits, abnormal aggressive behaviour with episodes of psychosis including restlessness and self-harm (biting) for two months and abnormal movements of left hand. Imaging revealed multifocal abnormal signal areas involving right temporal lobe with other smaller enhancing foci in the right parietal subcortical white matter and right centrum semiovale. Anti-NMDA receptor antibodies were positive in CSF. The patient was treated with immunoglobulin and steroids and had a good recovery. This case highlights the imaging differentials and diagnostic challenges presenting in this age group.

Keywords: Encephalitis, Autoimmune; NDMA Receptor; MRI; Pediatric

Abbreviations: AE: Acute Encephalitis; MRI: Magnetic Resonance Imaging; HSV: Herpes Simplex Virus; ADEM: Acute Demyelinating Encephalomyelitis; NDMA: Anti-N-methyl-D-aspartate.

Introduction

Acute encephalitis (AE) in children has a broad clinical presentation and requires a high index of suspicion for early diagnosis and treatment. Anti-N-methyl-D-aspartate receptor (NMDA) encephalitis is well-characterized AE since it was first discovered in 2007 by Dalmau J, et al. [1]. The clinical presentation includes psychosis, memory loss, seizures, dyskinetic orofacial movement, ataxia, impaired level of consciousness, and autonomic instability. Reports on anti-NMDA encephalitis in children from South Asia are extremely rare. Although neuroimaging can be normal in up to 50% of cases, variable imaging patterns have been reported, including involvement of the medial temporal lobe, cerebral cortex, cerebellum, thalamus, hippocampus, basal ganglia, brainstem, and rarely the spinal cord [2,3]. Imaging of anti-NMDA receptor encephalitis, particularly in children, is non-specific, with abnormalities that can involve both white and grey matter. We describe an unusual case of anti-NMDA encephalitis in a 4-year-old male pediatric patient and the diagnostic challenges encountered within this age group; we also review the current related literature.

Case Presentation

A 4-year-old boy came to our hospital complaining of right sided jerky movements, associated with an episode of seizure with up rolling of eyes and frothing from mouth,

followed by loss of consciousness that lasted for 5 to 10 minutes. The parents also gave a history of aggressive behavior, restlessness, self-biting for the past 2 months. On initial examination the child was active, alert, oriented to time, place, and person. Neurological examination revealed generalized increased muscle tone, normal muscle bulk, normal power on right upper and lower limbs. Slightly reduced power (4/5) of left upper limb. Brisk reflexes were observed with upgoing plantars. The child weighed 12 kg.

He was initially managed with intravenous fluids, intravenous (IV) methylprednisolone, IV acyclovir and antiepileptics. A lumbar puncture was done, and CSF detailed report revealed no abnormality except for slightly increased glucose (94 mg/dl). CSF assay for bacterial and viral meningitis including polymerase chain reaction for Herpes Simplex virus was negative. Subsequently paired oligoclonal bands and CSF for autoimmune panel was sent to a different hospital because of clinical suspicion of autoimmune encephalitis.

Electroencephalogram findings showed bi-hemispheric as well as generalized seizure disorder. There were occasional generalized bursts comprising of paroxysmal fast activity intermixed with epileptic discharges. Additionally, moderate encephalopathy was seen. Few delta bursts suggested autoimmune encephalitis.

Magnetic resonance imaging (MRI) brain was done which revealed multifocal abnormal signal areas involving right temporal lobe with gyral expansion. Other smaller enhancing foci in the right parietal subcortical white matter and right centrum semiovale were also seen. The large lesion in the temporal lobe showed nodular perivenular/ependymal enhancement (Figure 1).

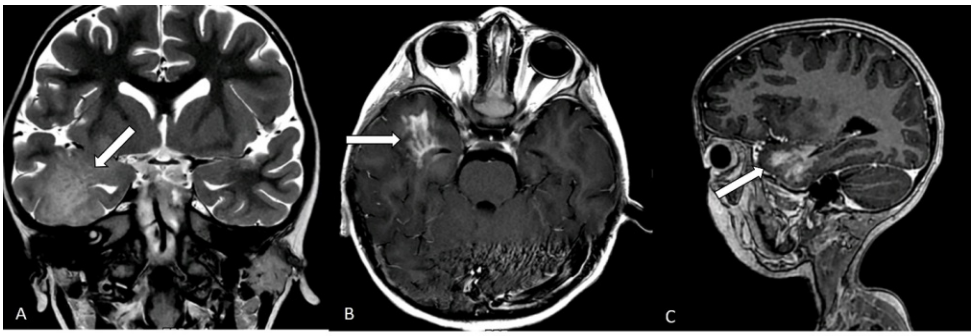

Figure1: MRI brain images showing right temporal lesion with gyral swelling (arrow in A) as well as white matter involvement with nodular perivenular and ependymal enhancement on post contrast sequences (arrows in B & C).

The differentials of encephalitis versus demyelination were given due to both grey and white matter involvement and multiplicity of lesions. Anti-NMDA antibodies were subsequently found to be positive in the autoimmune panel. The patient was treated with IV immunoglobulin and steroids and made an uneventful recovery without any clinically significant neurologic deficit. A follow-up MRI done after 45 days revealed improvement in the signal abnormality in the temporal lobe with development of atrophic changes (Figure 2).

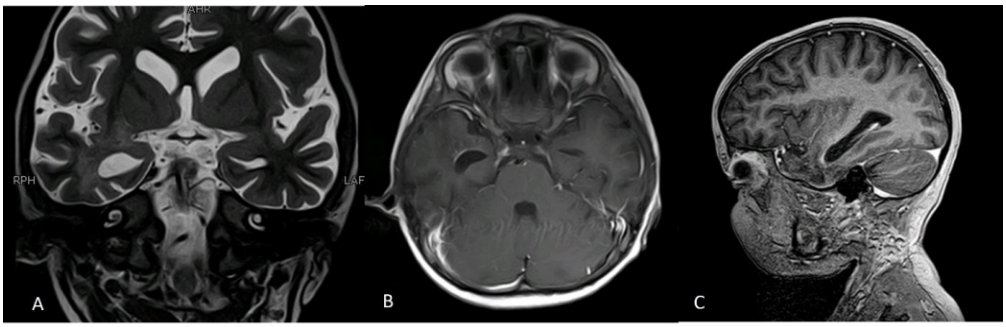

Figure 2: Follow-up MR brain after 45 days of treatment shows marked improvement in the disease process with development of gliosis and atrophy in the affected region and ex-vacuo prominence of the temporal horn of right lateral ventricle.

Discussion

Anti-NMDA receptor encephalitis affects adolescents and children with a male: female ratio of 1:4 and an incidence of roughly 1.5 per million per year [4]. Less than 10% of cases affect children below 12 years of age; however recently it has evolved to include a wide range of age groups and is now thought to be the leading cause of autoimmune encephalitis in children. The etiology can be paraneoplastic; more than half of women over 18 years and approximately 9% of girls under 14 years have an associated ovarian teratoma; however, it is not usual for men to have any underlying tumour [5]. Other post-viral aetiologies have also been proposed; approximately 20–30% of patients with herpes simplex virus (HSV) infection show positive seroconversion with anti-NMDA antibodies as part of a relapse not attributable to HSV relapse [6].

Imaging of anti-NMDA receptor encephalitis is highly variable. Imaging could be completely normal or there may be abnormalities involving white and grey matter. Extensive lesions in the temporal lobe with mass effect and this pattern of perivenular & ependymal enhancement have not been described previously in the pediatric population. Dalmau J, et al. [7] reported that only 55% of patients had increased FLAIR or T2 signal in the cortical or subcortical areas (hippocampus, basal ganglia, white matter) usually without any enhancement or hemorrhage. T. Zhang et al classified imaging of anti-NDMA receptor encephalitis into four types: normal, only hippocampal lesions, lesions not involving hippocampus and lesions in both hippocampus and other areas [2]. Our case did not have predominant involvement of the hippocampal region.

Around 3% of cases can have MRI or clinical features of demyelination syndrome including optic neuritis, neuromyelitis optica spectrum, acute demyelinating encephalomyelitis (ADEM), or brainstem dysfunction, and many may even test positive for either aquaporin-4 or myelin oligodendrocyte glycoprotein [8]. Our case also demonstrated some features of demyelinating encephalomyelitis on neuroimaging. Rarely even meningeal enhancement, cortical diffusion restriction and extensive demyelination may be present. Differential diagnosis on imaging includes herpes encephalitis, ADEM & other demyelinating disorders, gliomatosis, status epilepticus and acute stroke in cases of positive diffusion restriction.

Recently, hypo-metabolism in the medial occipital lobes has been described as a specific biomarker useful in differentiating anti-NMDA receptor encephalitis from other forms of autoimmune encephalitis on FDG-PET/CT [9]. Hippocampal atrophy appears to correlate with memory impairment and poorer prognosis [10].

Generally, the first line treatment is a combination of intravenous immunoglobulin and methylprednisolone. Other treatments include plasmapheresis, rituximab, and cyclophosphamide. Further workup of anti-NMDA receptor encephalitis is usually necessary with a whole-body MR or pelvic ultrasound for detection of an associated tumor/ovarian dermoid in suspected cases of paraneoplastic associations. However, recent reports suggest no need for extensive screening in the pediatric population with no risk factors, especially male children. Optimal outcomes are associated with prompt removal of the tumor in paraneoplastic cases, as well as early and aggressive immunosuppressive therapy have been shown to improve outcomes and markedly reduce the number of relapses [5,11].

Conclusion

In pediatric patients with anti-NMDA receptor encephalitis, imaging findings are highly variable and perhaps dependent upon the underlying cause of anti-NMDA receptor encephalitis. The imaging features might differ in pediatric versus adult patients and initial MRI can be normal in more than half of patients. We believe that anti-NMDA encephalitis is probably underreported in smaller children [12]. This case highlights the diagnostic challenges presenting in this age group.

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