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Communicating Hydrocephalus Associated with Relapsing Anti-N-Methyl-D-Aspartate Receptor (NMDAR) Encephalitis in an Adolescent Girl

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Abstract

Anti–N-methyl-D-aspartate receptor (NMDAR) encephalitis is uncommon cause of immune mediated encephalopathy in children. It usually manifests as psychosis, seizures and dyskinesia. We describe an unusual association with the phenotype of this disease. An 11 year-old girl presented with psycho-behavioral disturbances, headache, fever and episodic disorientation few weeks after fever and upper respiratory tract infection. Her MRI showed communicating hydrocephalus. She was found to have positive anti-NMDAR antibodies. She underwent VP shunt followed by immunomodulatory therapy resulting in resolution of headache and substantial improvement of alertness and psycho-behavior. Several months later she relapsed and remission was induced by a repeated course of immunomodulatory therapy. This report illustrates the remarkable phenotypic variability in this condition. The diagnosis of anti-NMDAR encephalitis should be considered in patients who present with subacute or relapsing encephalopathy associated with communicating hydrocephalus.

Keywords: Communicating hydrocephalus; Anti-N-methyl-D-aspartate receptor encephalitis; Psycho-behavioral disturbances; Immunomodulatory therapy

Introduction

Anti-NMDAR encephalitis is uncommon cause of subacute parainfectious or paraneoplastic immune mediated encephalopathy [1]. Typically, the disease manifests as acute psychosis, memory disturbances, seizures and dyskinesias [2-5]. Other features may include poor responsiveness, catatonia, central hypoventilation or hyperthermia [3-5]. The presence of anti- NMDAR antibodies in CSF in the appropriate clinical context are diagnostic. The neurologic outcome is usually favorable especially if treatment commenced promptly [4]. Although, phenotype was described as early as 1997, anti-NMDAR cellular and synaptic characteristics of the antibody were fully characterized by Dalmau et al., on 2007. Since then, lot of cases with idiopathic or presumed viral encephalitis were found to be NMDAR related and atypical presentations are being more frequently encountered.

Case Report

An 11 year-old girl was referred as a case of probable vasculitis. She had fever and upper respiratory tract infection that improved after oral antibiotics. Two weeks later, the fever got less frequent and of lower grade but she started to have psycho-behavioral disturbances as aggression, agitation bizarre behaviors, generalized headache, persistent vomiting and episodes of disorientation. She also had history of recurrent follicular tonsillitis and was hospitalized two years prior to her presentation with one month history of pyrexia of unknown origin. There was no history of recent travel, blood transfusion, raw milk ingestion or contact with animals or sick patients. We assessed the patient few weeks later when she had received antibiotics and she was on low dose oral steroids. On examination, she was febrile at 38.2 C, fidget and hyperactive but was alert and responsive with no skin rash, neck rigidity or meningsimus. She had bilateral grade III papilledema. The rest of her cranial nerves, motor, sensory and coordination examination were all unremarkable. Brain MRI revealed dilated lateral and third ventricles with multiple subcortical and periventricular patchy white matter changes in T2 and FLAIR without CSF flow obstruction (Figure 1).

CSF analysis revealed WBC 12 $\times 10^6$/l; neutrophils 56%; lemphocytes 34%; protein 381 mg/l ; glucose 3.2 mmol/ with negative cultures, cytology and serology. Anti NMDAR antibodies were positive both at CSF. No quantitative estimation of antibody titers was done. Her serum investigations revealed WBC 22 $\times$ 10^9/l; HB 82 g/l; PLT 686 10^9/l. ESR 6 mm/hr; CRP 177 mg/l. Blood workup for vasculitis, connective tissue diseases, malignancy, serology, cultures, endocrine and metabolic diseases were all negative. CT chest, abdomen and pelvis didn't show any evidence of associated primary systemic malignancy or infection. Her EEG showed bilateral frontal intermittent slow activity. She underwent urgent external ventricular drainage and VP shunt followed by a course of intravenous immunoglobulin and a course of pulse steroid

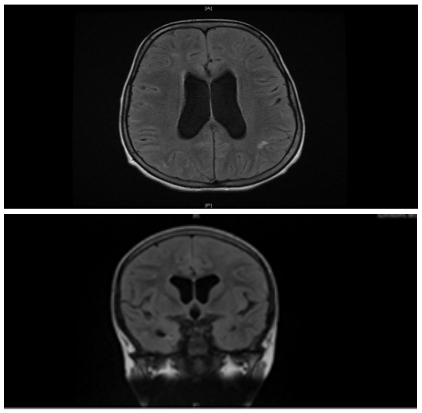

Figure 1: Axial and coronal MRI FLAIR, shows dilated lateral ventricles with multiple subcortical and periventricular patchy white matter changes.

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for 3 days then rituximab resulting in resolution of headache and better alertness and improvement of psycho-behavioral disturbances. Eight months later the patient came with relapse of similar clinical features but, without papilledema. Blood workup showed WBC 20 $\times 10^9$/l, ESR 97 mm/hr and CRP 164 mg/l with negative cultures and serology. CT brain didn't show any evidence of shunt dysfunction or increased ICP. Repeated EEG was similar to the earlier study of bilateral frontal intermittent slow activity. She received a course of IV pulse steroid followed by rituximab resulting in remission of fever and headache and dramatic improvement of alertness and psycho-behavior.

Discussion

The patient's clinical features are communicating hydrocephalous associated with episodic disorientation, psycho-behavioral disturbances, persistent pyrexia and headache. In view of these clinical features, CSF polymorphs, communicating hydrocephalus, our differential diagnoses were infectious encephalitis, CNS vasculitis, paraneoplastic, autoimmune or anti-NMDAR encephalitis. Prodromal symptoms as fever, headache and vomiting are common in anti-NMDAR encephalitis but, communicating hydrocephalus is not [1,3]. Typically, CSF reveals lymphocytic pleocytosis, normal or mildly elevated protein with oligoclonal bands and raised IGG index [4]. In our patient CSF showed leukocytosis of predominantly neutrophils and normal protein. The typical MRI shows non-specific high T2 or FLAIR signals [5]. Our patient's showed such features besides communicating hydrocephalus. The typical EEG shows slow activity which is the case in our patient. Although there are some differences between typical anti-NMDAR encephalitis and our patient's presentation, negative CSF cultures and other studies with positive anti-NMDAR antibodies, the lack of response to full course of antimicrobial therapy, with excellent response to immunomodulatory therapy makes us consider atypical anti-NMDAR encephalitis as the likely cause. This hypothesis would be further supported by finding of concurrent improvement of symptoms and a decline of CSF antibody titers post therapy which were not measured in our patient [2-5]. The proceeding URTI and associated tonsillitis may be implicated in generating auto antibodies against extracellular domain of the NR1 subunit of the NMDAR sharing similarities with antigens expressed by these infectious pathogens [1,2]. Such pathogens then have broken the patient's immune tolerance and triggered immune response [2]. In our patient the unusual association with hydrocephalus may be related to parainfectious etiology disturbing blood brain barrier and CSF homeostasis resulting in excess production and decreased absorption of CSF. The negative CSF microbiology may be result of partially treated encephalitis with a latent generation of auto antibodies against NMDAR. Although, anti-NMDAR antibodies cause reversible decrease receptor's cluster density and function without neuronal degeneration, the hydrocephalus may suggest other mechanisms involved in pathogenesis causing tissue injury mediated by complement or T cell mediated cytotoxicity that need to be further studied [2]. No previously similar case has been described in the literature though, other unusual presentations were reported. This report illustrates remarkable phenotypic variability in this condition. It also suggests that the diagnosis of anti-NMDAR encephalitis should be considered in patients who present with subacute or relapsing encephalopathy associated with communicating hydrocephalus.

References

1. Dalmau J, Lancaster E, Hernandez E, Rosenfeld M, Gordon R (2011) Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol 10: 63-74.
2. Hughes E, Peng X, Gleichman A, Lai M, Lei Z, et al. (2010) Cellular and synaptic mechanisms of anti-NMDA receptor encephalitis. J Neurosci 30: 5866-5875.
3. Florance N, Davis R, Lam C, Szperka C, Zhou L, et al. (2009) Anti-N-methyl-Daspartate receptor (NMDAR) encephalitis in children and adolescents. Ann Neurol 66: 11-18.
4. Titulaer M, McCracker L, Gabilondo I (2013) Treatment and prognostic factors for long-term outcome in patients with anti-*N*-Methyl-D-Aspartate (NMDA) receptor. Lancet Neurol 12: 157-165
5. Armangue T, Pedrol M, Josep Dalmau (2012) Autoimmune Encephalitis in Children. J Child Neurol 21: 1460-1469