CASE REPORT

Organic Disorder with Neuropsychiatric Symptoms - Case Report of Anti-NMDA Receptor Encephalitis with Neuropsychiatric Manifestations

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Abstract

Neuropsychiatric symptoms are symptoms that caused by organic brain disorders. Multiple neuropsychiatric symptoms can occur concurrently in the course of brain related organic disorders. Two main components of neuropsychiatric symptoms are cognitive impairment and disturbance of consciousness while other neuropsychiatric symptoms, such as hallucinations, delusions, mood disorders, anxiety, apathy, behavioural and personality changes also commonly occur. Some of the mild neuropsychiatric symptoms could possibly be the earliest manifestations of brain related organic disorders. Clinicians should carefully evaluate organic factors in the treatment of psychosis, especially in patients of very young age or older age. They should have enough knowledge and experience in the integrating neuroscience, that is, neuropsychiatry. The present report illustrates a case of organic disorder with neuropsychiatric manifestations. It is about a young male patient who was diagnosed with anti-NMDA receptor encephalitis and subsequently developed acute delirium secondary to the illness.

Keywords: Neuropsychiatric Symptoms, Delirium, Anti-NMDA Receptor Encephalitis

Case Report

Anti-NMDA receptor (NMDAR) encephalitis is an increasingly recognized entity. Here, we present a case of anti-NMDA receptor encephalitis in a 16 year old boy which was initially treated as viral encephalitis, but subsequently demonstrated to have anti-NMDA receptor encephalitis following cerebrospinal fluid analysis.

The patient, who is of Murut descent, was initially admitted to Queen Elizabeth Hospital, Kota Kinabalu, (HQE) in October 2016, having presented with recurrent seizure. He had first presented to Beaufort Hospital on 16/10/2016 following 2 episodes of generalized tonic clonic (GTC) seizures at home. Prior to the above, there was no reported fever, meningism, photophobia, blurring of vision, nor altered behaviour. There was also no history of previous seizure.

Whilst being assessed at the QEH Emergency Department, he had a further
episode of GTC seizure which was aborted with IV diazepam. At the time, the impression was meningoencephalitis presenting with seizures, with the primary differential being epilepsy. Bloodwork showed a raised white cell count of 17, neutrophil predominant. C-reactive protein was raised at 73. Liver and renal profiles were within normal limits. No organisms were grown from blood cultures and viral screening for HIV, Hepatitis B, and Hepatitis C was negative. Neither ECG nor CXR demonstrated any remarkable findings. His CT-brain (non-contrast) was also reported as normal. Initial CSF analysis following routine lumbar puncture was not suggestive of infection. EEG results were awaited at the time. Following neurology consult the diagnosis was revised to viral encephalitis. He was started on anticonvulsants, IV antibiotics, and IV acyclovir. The patient was then transferred to Keningau Hospital for continuation of therapy.

Whilst warded in Keningau Hospital, the patient began experiencing hallucinations which he reported to medical staff as follows:

1. ‘Something’ coming out from under the bed as well as from beneath his IV line.
2. A second IV line attached under his current IV line or close to it.
3. A pricking sensation all over his body that made him cry.

At this time he was referred to psychiatry for assessment.

Collateral history from his family revealed that they noted behavioural aberrancy over the past 3 days since his admission to Keningau Hospital, including, but not limited to, talking to himself as well as laughing and crying inappropriately. Furthermore, the patient repeatedly described the presence of 3 elderly human strangers in his room, 1 male and 2 female, whom he firmly believed meant him harm, which suggested visual hallucination, as well as persecutory delusion. In addition, he claimed somatic symptoms, describing an IV line inserted into his back, and the sensation that his left arm was boneless and that this was severely limiting its mobility. Following this the patient started demonstrating further signs of restlessness and aggression and had to be physically restrained for his own safety as he was kicking the walls and mirror in his room. He also appeared far more disoriented at night in addition to his insomnia.

Socially, the patient studied until standard 6 and subsequently refused to go to school. He has history of working in rubber estate and as a wireman. Patient was active in joining cycling marathon and has won prizes as well. He reportedly smokes a pack a day, and consumes alcohol, mainly beer and ‘tapai’ (a local, home-brewed rice-based liquor), 2 to 3 times a week, and frequently to intoxication, up until August 2016. This history suggested that the seizure was not due to delirium tremens, as the onset of the seizure was 2 months after the last intake of alcohol. He denied abuse of other illicit substances. There is no family history of mental health illness.

Throughout the consultation, he was agitated and restless with poor eye contact. The patient was intermittently shouting and crying, and kept insisting that there were two additional elderly women in the room. However, he remained oriented to time, place, and person at the time of the consultation.

The patient was diagnosed with acute delirium secondary to viral encephalitis by the psychiatry team. He was started on oral
risperidone 1mg ON, which was later increased to 1mg OM and 2mg ON following repeated episodes of aggressive behaviour on the ward.

During the admission, the patient developed repetitive, dyskinetic movements of his left arm, leg, and right hand. He complained persistently of the previously described hallucinations as well as restlessness and reduced nocturnal sleep. His EEG report described right hemispheric cortical dysfunction, likely secondary to a structural lesion. A contrast enhanced CT brain did not show any significant findings. The patient’s family was repeatedly counselled to consent for a repeat lumbar puncture but they declined. The diagnosis was revised to autoimmune encephalitis following a further neurology consult and we were keen on starting him on a course of IV methylprednisolone. However, at this time, his family elected to be discharged against medical advice as they felt that traditional or alternative medication/therapy would be more beneficial. Patient was discharged with oral risperidone and anticonvulsants.

A week later, this patient was readmitted to Keningau Hospital having had several seizures at home associated with fever. His behaviour was unmanageable at home as he remained uncooperative and had become more aggressive, progressing to hitting those around him. Appetite was poor and insomnia persisted. Traditional healing had been sought but was (thankfully) unsuccessful and brought no significant improvement to his demeanor.

Once again, during this admission, eye contact was poor, and he remained guarded and uncooperative during the consultation. He demonstrated jaw clenching, facial twitches, as well as choreoathetoid movements of his left arm and leg. A physical examination revealed bilateral upper limb hypertonia which was more pronounced on the left side. He had to be physically and chemically restrained (with IM haloperidol) due to worsening agitation and restlessness.

The patient’s immediate family consented for medical treatment at this time and the patient was pulsed with IV methylprednisolone 500mg OD for 3 days. Following that immunosuppression was maintained with oral prednisolone at 40mg/day. His risperidone was switched to oral olanzapine 5 mg ON, which was titrated up to 10mg ON, as well as oral lorazepam 1mg PRN/TDS. CSF samples from a repeat lumbar puncture showed anti NMDA receptor antibodies, which were not isolated from serum samples.

Following the above, his diagnosis was revised to anti NMDA receptor encephalitis with neuropsychiatric manifestations and he was started on IV immunoglobulin 0.4g/kg for 5 days and oral azathioprine which was gradually titrated from 25mg/day up to 100mg/day. A CT-TAP showed no obvious malignancies and ultrasound examination of the scrotum showed no abnormal masses. A routine MRI brain was requested but the patient and his family chose not to attend for the examination. He was subsequently discharged and his antipsychotics were gradually tapered off as his neuropsychiatric symptoms resolved. He remains under neurology follow-up at QEH but no further psychiatry input appears necessary at this time.

Discussion

Anti-NMDA receptor encephalitis is an autoimmune encephalitis disorder associated with IgG antibodies against the NR1 subunit of the NMDA [1]. It is associated with
ovarian teratomas in adult females, but there may be a higher incidence of non-paraneoplastic cases in children [2]. There is little data on the exact prevalence of this condition, both globally, and locally. However, it’s incidence is at least comparable to viral encephalitis, being identified more than four times as frequently, as the aetiological factor, in comparison to HSV-1, West Nile virus, or varicella-zoster virus [3]. It is recognized as a significant cause of encephalitis in Malaysia, accounting for 50% of encephalitis admissions over a year in a tertiary centre as described by Goh et al in 2011 [4].

Patients may present with non-specific viral-type symptoms, including headache, prior to the onset of psychiatric symptoms. The psychiatric manifestations of anti-NMDA receptor encephalitis are varied and include hallucinations, delusions, paranoia, anxiety, agitation, and poor coherence [5]. Associated neurological symptoms, such as seizures, insomnia, memory deficits, and dyskinesia, most of which were present in our patient, are not uncommon. There have also been reports of autonomic instability in some cases, described as hyperthermia, hypoventilation, tachycardia and bradycardia, cardiac pauses, and blood pressure volatility [6].

Relevant differentials to consider include schizophrenia, acute psychoses (not excluding the relevant organic causes such as viral encephalitis), neuroleptic malignant syndrome, and malignant catatonia [7]. Detection of the NR1 IgG antibodies from serum or CSF confirms the diagnosis, with CSF testing providing higher sensitivities compared to serum [8]. Other CSF findings include moderate lymphocytic pleocytosis, normal or mildly increased protein concentration, can oligoclonal bands [6]. The characteristic EEG finding in anti-NMDA receptor encephalitis is described as ‘extreme delta brush’ and its presence is associated with prolonged hospitalization [9]. Brain MRIs may be reported as normal, or could show transitory contrast enhancing lesions in the cortical or subcortical regions [10], but would be useful to exclude space occupying lesions and to screen for other organic causes.

Patients with recurrent symptoms and choreoathetosis following HSV encephalitis may have seroconversion to anti-NMDAR antibodies. This may occur 2 to 6 weeks from the initial infection, following or during recovery from HSV encephalitis [11].

General first-line treatment in confirmed cases include the administration of high dose IV methylprednisolone, and either IVIG or plasmapheresis, as well as tumour resection [12]. In the context of our patient, it may be prudent to consider significant nutritional deficiency, and to supplement this with the relevant micronutrients, i.e. B-vitamins and ascorbic acid, intravenously or via a nasogastric tube given his poor oral intake.

Clinical improvement with first-line therapy is normally evident within the first 4 weeks. Second-line therapy may involve rituximab and cyclophosphamide, and is usually effective when first-line treatments fail. Clinical recovery may take up to 18 months in some patients, with good outcomes reported in 80% of patients by 24 months [12]. Spontaneous recovery without tumour resection despite severe autonomic dysfunction requiring mechanical ventilation has also been reported [13]. Relapses may be more common in patients who were not administered immunotherapy at the first presentation [12].
Other factors to be considered in this part of Malaysia, and in the context of our patient, include the local cultural and religious beliefs. Local witch doctors or shamans, as well as quacks, are in abundance. Often, hallucinations and other neurological symptom, are not attributed to medical nor psychiatric disorders by the locals, who instead choose to consult spiritual healers for what they perceive as supernatural disturbances. Thus, early recognition, and subsequently, appropriate treatment may well be delayed. In the case of our patient, due to the lack of rapid clinical improvement, his parents elected to be discharged against medical advice. Furthermore, routine lumbar puncture is viewed with distrust, as the local belief is that it may cause paralysis and permanent physical weakness, and could worsen the underlying condition, despite clinical evidence indicating otherwise [14]. In addition, alcohol abuse and misuse is rampant in the region, a concern for consideration in the presentation of neuro-psychiatric disorders.

Geographically, cellular phone coverage remains poor in a large proportion of the Keningau and interior regions of Sabah. This leads to difficulty in contacting patients regarding rescheduled investigations, follow-up, as well as investigation results. Fixed follow-up appointments, planned weeks to months ahead, may negate some of these issues.

Consequently, it may be concluded that in the event of treatable conditions such as NMDAR, early psychiatric input may be helpful in alleviating both patient and parental concerns, in addition to symptomatic management, possibly improving patient compliance. Furthermore, it is vital that rapport between healthcare professionals and the patient’s carers be established as early as possible to better facilitate the appropriate care in such neuro-psychiatric disorders.

References


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