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Case Report

Acute Anti-N-Methyl D-Aspartate Receptor Encephalitis Following Covid-19 Vaccination

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Abstract

We present a rare case of acute anti NMDAR encephalitis after COVID -19 vaccination (Sinopharm). On literature review only 1 such case has been reported so far. Our patient initially presented with flu like symptoms and generalized weakness which started 1 day after COVID- 19 vaccine. 3 weeks later she received second dose of vaccine which led to worsening of her symptoms including progressive cognitive decline. She eventually deteriorated and required ICU management for 2 months due to depressed level of consciousness, respiratory and hemodynamic instability requiring intubation and ventilation support. During course of disease, she had clinical features consistent with NMDA encephalitis including constitutional symptoms, memory disturbance, confusion, fish mouthing movement and seizures requiring treatment with anti-epileptic medications. Diagnosis was confirmed after CSF NMDA testing as blood NMDA test was negative. The patient was treated with high dose steroids, IVIg, TPLEX and finally Rituximab. She responded very well to the complex treatment.

***Keywords:** N-methyl-D-aspartate receptor, Autoimmune, COVID-19, Cerebrospinal fluid, Intensive care unit*

Introduction

Anti-NMDAR encephalitis is an acute autoimmune neurological disorder [1]. The previous studies revealed that it might be caused by a virus, vaccine, or malignancy. Corona virus related pandemic had a huge impact on world [2]. There has been many reports and observations about corona virus related and vaccine related neurological conditions. Several cases were reported to be related to vaccination such as the H1N1 vaccine and tetanus / diphtheria / pertussis, polio vaccines and Japanese encephalitis vaccine [3]. However, only few COVID -19 vaccination and anti-NMDA receptor encephalitis related cases reported in the literature (11). We present a rare case of acute anti NMDAR encephalitis after COVID -19 vaccination by Sinopharm vaccine.

Case Report

The patient is a 33 years old Philippino woman who has been resident of United Arab Emirates on work permit, she presented to our hospital with progressive decrease in cognitive function and generalized weakness. She had no past medical history. Her illness started 1 day after taking COVID 19 vaccine (Sinopharm). She took the first dose on 6th January 2021 and the second dose on 27th January 2021. Patient did not feel well after 1st dose and had to take few days off work as she had flu like symptoms. She was PCR negative for COVID -19 at this point. As she continued to feel weak and lethargic, so she sought medical advice. She was told that she has functional illness. 3 weeks later she had second dose of vaccine, after this her symptoms became progressively worst. As per patient she could not get out of bed for 4 days after second dose due to generalised myalgia and she had an unexplained episode of urinary incontinence. Since then, she noticed progressive memory problem as she started to forget her name and some daily events which was noticed by her friends and colleagues. Seven weeks from her last vaccine dose she presented with upper respiratory tract infection like symptoms. She was treated by primary care physician with antibiotic, but she became worse and required hospitalisation on 4/4/2021. On admission it was noticed that the patient had cognitive dysfunction. She was conscious but inattentive, she was responding to simple commands variably with periods of mutism in between. No fever or focal neurological signs were recorded at that time. Brain CT and MRI were unremarkable. Lumbar puncture showed WBC 363 Cells/mm3, Lymph: 94 %, protein 1.57 g/L, CSF glucose 2.7 mmol/L, serum glucose was 5 mmol/L. Oligoclonal IgG bands was positive in CSF and polyclonal IgG bands in serum.

Gram stain and viral PCR panel were negative in CSF. She was started on Acyclovir IV, Ceftriaxone, and Dexamethasone IV. CSF TB screen was negative. During admission it was noted that the patient had episodes of abnormal crying, incoherent speech at times, and she looked encephalopathic. Within 3 days of hospital admission she developed urinary retention, generalised limb weakness and her consciousness level deteriorated abruptly. Off sedation her GCS became 4/15, she was noted to have extreme rigidity in all 4 limbs and axial muscles, she had hyperreflexia in all 4 limbs, plantar were mute, eyeballs were rolled up and she had flickering of bilateral eyelids which could be seen often, she also developed continues tongue and mouth movements disorder (dyskinesia) resembling fish mouthing movement. Repeated brain and spine MRI showed no abnormal lesions or Gd enhancement. She required intubation and ventilation for more than 3 months and remained in ICU for more than 8 weeks. She had episodes of tonic-clonic seizures during ICU stay and Keppra, Lacosamide and Phenytoin were started. Work up for vasculitis and malignancy were negative. Serum protein electrophoresis was unremarkable. HIV antigen/antibody complex, hepatitis B, Hepatitis C screen were also negative; Pan CT scan and pelvis MRI were negative. Possibility of autoimmune encephalitis was considered and soon after admission patient was started on IVIG course over 5 days. She was also given 5 sessions of plasma exchange in the ICU as she showed no improvement with anti-viral, antibacterial and IVIG treatments. Repeat viral PCR panel from CSF was again negative, despite that acyclovir and ceftriaxone were discontinued after 14 days. During admission she was noted to have severe hemodynamic instability and autonomic dysfunction requiring medical support in ICU. A repeated LP showed an improvement in WBC 11 Cells/mm3 which were predominantly lymphocytes 90%. Protein was 0.52 g/L, CSF Glucose was 2.6 mmol/L, serum glucose was 6.7 mmol/L. TB stain was again negative, TB PCR from CSF was also negative. Repeated CSF viral and bacterial molecular studies (PCR antigens) were also negative. EEG studies showed diffuse background slowing suggestive of encephalopathy along with low voltage EEG, bilateral spikes and slow wave discharges in fronto- central regions.

A follow up brain MRI after few days in hospital showed increased signal intensity within the sulci of the left temporal and bilateral occipitoparietal cerebral regions; they all showed enhancement on post contrast FLAIR sequence consistent with pathological lepto-meningitis or leptomeningeal changes after lumbar puncture (by this point patient has more than 4 Lumbar punctures). Requested paraneoplastic and non-paraneoplastic neuronal antibody panels for limbic encephalitis were normal; but CSF NMDAR antibody test came back positive 4 weeks after admission. In that time she still intubated and ventilated, GCS was 5/15 and she had severe rigidity in all 4 limbs, ongoing tongue and mouth dyskinesia and autonomic instability. At this stage she received Rituximab 1000 mg intravenously and 2nd dose was given after 2 weeks; she was also maintained on steroids throughout her admission. She made steady recovery in GCS over next 6-8 weeks, and we saw continues improvement in her clinical condition. She was finally discharged to in-patient rehabilitation facilities after 3 months of inpatient stay and at this stage her seizures were well controlled, her dystonic movements had completely resolved, generalized limbs and axial rigidity and GCS improved to the point that she was able to participate in rehabilitation program. She developed critical illness polyneuropathy from prolonged ICU stay (it was more than two months) which contributed significantly towards her physical disability. We met her 6 months after discharge and by this time she was off all anti-epileptics, steroids and anti-bacterial medications which she required for long time due to ongoing seizures, urine and chest sepsis. At 6 months review she had completely regained her function both physically and cognitively; she was out of rehabilitation centre and had gone back to her work.

Discussion and Conclusion

Anti-NMDA receptor encephalitis is an autoimmune condition which can be triggered by underlying tumour, infections or vaccinations [1]. Infection itself can precipitate an autoimmune encephalitis and may also cause neurological damage which can unmask other neuropsychiatric conditions This case reports suggest that some patients may present with neuropsychiatric symptoms or experience neuropsychiatric sequelae following COVID-19 infection. Previous studies revealed that vaccination might induce autoimmune encephalitis. A few cases were reported to be related to H1N1 vaccine, tetanus/diphtheria/pertussis and polio vaccine, and Japanese encephalitis vaccine. A case report of 15-year-old female patient who was diagnosed with anti-NMDA receptor encephalitis after a booster vaccination against tetanus, diphtheria, pertussis, and poliomyelitis suggest a link between [3]. Three patients developed the disorder after vaccination against H1N1 influenza, or after vaccination against tetanus, diphtheria, pertussis, and poliomyelitis [4]. In addition, herpes simplex encephalitis (HSE) was reported to be associated with anti-NMDA receptor encephalitis. A proportion of patients with HSE were shown to produce antibodies against NMDA receptors [5]. Two patients, an infant and an adult, had confirmed HSE and then developed confirmed anti-NMDA receptor encephalitis [6]. Also was reported a case that had confirmed anti-NMDA receptor encephalitis after receiving a Japanese encephalitis (JE) vaccination. Three patients showed some evidence of double infection of JE virus and herpes simplex virus, and an experiment of double infection of JE virus and herpes simplex virus in mouse brain has been reported [7].

In our case as patient has no past medical history or symptoms of pre- existing condition it's unlikely that she has any other trigger to CNS inflammation other the COVID vaccine. She had sever systemic side effects after 1st dose, but after 2nd dose she became worse and progressively worsened till she became hospitalized leading to 8 weeks ICU admission and prolong hospital stay. Her response to immuno suppressants was great which was expected given inflammatory nature of condition. We did numerous investigations to look for differential causes, but all investigations were normal.

Hsyuing Wang in her study investigated miRNA biomarkers to explore the relationship between anti-NMDA receptor encephalitis and COVID-19 infection or COVID-19 vaccination [8]. The results revealed that there were not many common miRNA biomarkers of COVID-19 and anti-NMDA receptor encephalitis-related tumors or vaccines. This may explain why the risk of anti-NMDA receptor encephalitis triggered by COVID-19 infection or COVID-19 vaccines is not high. Nevertheless, there remains a small risk that COVID-19 or COVID-19 vaccination could trigger anti-NMDA receptor encephalitis [9]. Therefore, for COVID-19 patients or people receiving COVID-19 vaccination who develop psychiatric or neurological symptoms, a diagnosis of anti-NMDA receptor encephalitis should be considered if other complications are excluded (10). There are only few case reports of NMDA encephalitis from COVID vaccine till this date. Although the cause of anti-NMDA receptor encephalitis is still not very clear in this stage, more disclosures of the vaccination-related cases can provide useful information for anti-NMDA receptor encephalitis management and prevention. This case highlights that research is needed to understand the intersection between COVID-19 infection and mechanisms implicated in other neuropsychiatric disorders, including the spectrum of autoimmune encephalitides.

Authors Contribution

HN Abbasi direct clinical care and contributed as main authors. A. Hassan, N. Soliman, A. Al Duhori, M. Szolics direct clinical care, review, and article correction.

Conflict of Interest

No competing interest for disclosure.

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References

1. Dalmau J, Bataller L. Limbic encephalitis: the new cell membrane antigens and a proposal of clinical-immunological classification with therapeutic implications. Neurologia 2007; 22: 526–37.

2. Nolen, L.T., Mukerji, S.S. & Mejia, N.I. Post-acute neurological consequences of COVID-19: an unequal burden. *Nat Med* 28, 20–23 (2022). https://doi.org/10.1038/s41591-021-01647-5

3. Wang H Anti-NMDA Receptor Encephalitis, Vaccination and Virus. Curr Pharm Des. 2020;25(43):4579-4588. doi: 10.2174/1381612825666191210155059. PMID: 31820697.

4. Autoimmune Encephalitis After SARS-CoV-2 Infection Case Frequency, Findings, and Outcomes Cristina Valencia Sanchez, Elitza Theel, Matthew Binnicker, Michel Toledano, Andrew McKeon Neurology Dec 2021, 97 (23) e2262-e2268; DOI: 10.1212/WNL.0000000000012931

5. Wang H COVID−19, Anti-NMDA Receptor Encephalitis and MicroRNA, Front. Immunol. 22 March 2022 | https://doi.org/10.3389/fimmu.2022.825103

6. Acute Psychosis Due to Anti-N-Methyl D-Aspartate Receptor Encephalitis Following COVID-19 Front. Neurol., 04 November 2021 https://doi.org/10.3389/fneur.2021.764197

7. Hayashi, K.; Arita, T. Experimental double infection of -viJapanese encephalitisrus and herpes-simplex virus in mouse-brain. *Jpn. J. Exp. Med.* 1977, *47*, 9–13.

8. Wang H Anti-NMDA Receptor Encephalitis, Vaccination and Virus. Curr Pharm Des. 2020;25(43):4579-4588. doi: 10.2174/1381612825666191210155059. PMID: 31820697.

9. Wang H COVID−19, Anti-NMDA Receptor Encephalitis and MicroRNA, Front. Immunol. 22 March 2022 | https://doi.org/10.3389/fimmu.2022.825103

10. Autoimmune Encephalitis After SARS-CoV-2 Infection Case Frequency, Findings, and Outcomes Cristina Valencia Sanchez, Elitza Theel, Matthew Binnicker, Michel Toledano, Andrew McKeon Neurology Dec 2021, 97 (23) e2262-e2268; DOI: 10.1212/WNL.0000000000012931

11. Acute Psychosis Due to Anti-N-Methyl D-Aspartate Receptor Encephalitis Following COVID-19 Front. Neurol., 04 November 2021 https://doi.org/10.3389/fneur.2021.764197

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