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Case Report

Paraneoplastic Limbic Encephalitis – A Case Report

Rawan Alshammari*, Talal Alenezi, Ponnusamy Santhamoorthy, Beena Yousef Omar Balmasoud, Mohammad Shamshah, Huda Alfodari, Mishal Abu Almelh

Department of Neurology, Department of Intensive Care Unit, AL-Adan Hospital – Kuwait

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***Corresponding author:** Rawan Alshammari. Department of Neurology, Department of Intensive Care Unit, AL-Adan Hospital – Kuwait.

ABSTRACT

Objective

We present a case of Anti NMDAR encephalitis with ovarian teratoma, describing the presenting features, diagnosis and management plan.

Early Electroencephalography showed typical features of Anti NMDAR encephalitis which promoted the early diagnosis of ovarian teratoma and immediate surgical removal.

All approved treatment failed but finally improved with ocrelizumab.

Introduction

Anti-N-methyl-D-aspartate receptor encephalitis is a paraneoplastic syndrome which is invariably related to cancer, as ovarian teratoma; patient typically will have a range of symptoms as, memory deficits, seizures, decrease level of consciousness , dyskinesia , autonomic instability as hyperthermia, fluctuations of BP, cardiac problems, rigidity, sometimes hypoventilation that require mechanical ventilation and need ICU admission. Anti – NMDAR encephalitis that associated with teratoma is life threating conditions that need multidisciplinary care and immediate surgical removal.

Case Report

We presented a case of a young girl who had a symptoms of viral illness , then developed psychological symptoms and then went into status epilepticus.

She was admitted to the ICU and was diagnosed with paraneoplastic encephalitis related to ovarian teratoma.

The patient received all the treatment options and surgical removal of the tumor was done.

Conclusion

Ocrelizumab showed a great improvement when all other treatment options failed.

EEG can help for early diagnosis and management of the case.

Keywords: Limb; Ovarian; Cardiac; surgery

CASE REPORT

21 years old American girl, who is a Dental college student in USA, She came to Kuwait for winter vacation on 16/12/2018. She had fever and headache for 2 days on 2 and 3 of JAN. 2019, on 3/1/2019 night, when she was having dinner with her family, she was inappropriately laughing, joking and, behaving abnormally with the waiter. She was passing comments in a disinhibited manner.

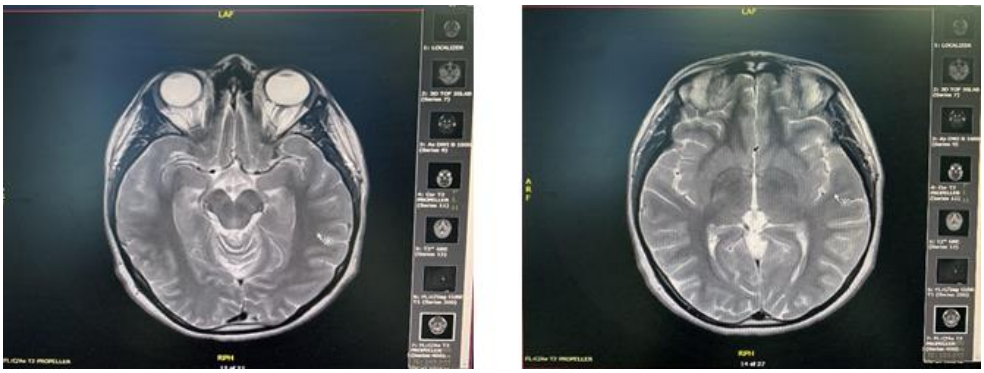
After an hour she developed one attack of generalized tonic-clonic seizure associated with loss of consciousness. On 03/01/2019 she was admitted to the medical ward, where she was getting attacks of crying, laughing and, was doing pedaling movements like cycling, also she had attacks of generalized tonic-clonic seizure with loss of consciousness in between. She was inappropriately joking and passing comments about the attending doctors and nurses. She was given injection diazepam 10mg IV bolus and was started on injection levetiracetam 1gramIV and continued 1.5gram BD. The seizures continued and she went into status epilepticus and was shifted to ICU immediately for the management of status epilepticus.

Status epilepticus was managed in ICU with IV levetiracetam 1500mg BD, injection Vimpat started with 50mg BD and, increased to 150mg BD, Tab clonazepam started 0.5 mg BD then increased to 2mg TDS and Tab Triliptal 300mg BD. Midazolam infusion was started 5mg per hour and was increased to 10 mg per hour, propofol also been used for sedation with acyclovir 750 TDS IV .She was kept on continuous sedation, in between when we reduced the sedation to assess her neurological status , she was having the seizures and abnormal movements in the form of dyskinesias which warranted to put her back on sedation. On 05/01/2019 EEG was done which showed a slow wave with delta brush, characteristic of NMDA receptor antibody encephalitis. She was already on acyclovir 750mg TDS from 03/01/19 , as the EEG showed characteristic delta brush appearance consistent with ANTI-NMDAR Antibody encephalitis , we decided to start IVIG 0.4gram/kg and continued for 5 days , without waiting for NMDAR Abs. CT chest and abdomen were done on 08/01/2019 which showed ovarian teratoma. She was seen by the gynecologist who wanted to remove the ovarian teratoma with bilateral ovariectomy. The mother of the patient refused for bilateral removal of the ovaries and requested to retain the right ovary. On 10/01/2019, the gynecologist surgically removed the left ovarian teratoma along with left salpingectomy. There was no improvement after IVIG, hence injection methylprednisolone 1gram IV OD was given for 5 days. She continued to have status epilepticus and we started injection Rituximab 500mg IV infusion weekly once for 4 weeks and had plasmopharesis x 5 sessions without any improvement. She had oromandibular dyskinetic movements that were controlled with Tab. Tetrabenazine 12.5mg BD, she also had blepharospasm and hypersalivation which was managed with scopolamine patch. She continued to have recurrent generalized seizures and abnormal movements, It was planned to start injection cyclophosphamide but not started.

Here in our case , the typical Delta brush appearance in early Electroencephalography prompted investigation and established the diagnosis of ovarian teratoma.

INVESTIGATIONS

MRI brain showed bilateral temporal meningeal enhancement in both lobes



L.P CSF – cells 95/ mononuclear 95%, 5% PMNs, protein 542, glucose 3.61, no bacteria was seen.

Molecular detection of CSF Viral panels is –ve

IgG Ab CSF (Anti-**NMDAR +ve**, Anti-CASPR2 -ve, Anti-AMPAR1 -ve,Anti-LGI1 –ve, Anti-AMPAR2 –ve, Anti-GABARB1/B2 –ve)

Autoimmune screening (ANA, Anti-dsDNA, Anti-B2GP1 IgG + IgM,ACL, MPO , PR3 ab , RF ,U1RNP all are negative)

CBC, biochemical admission profile: normal

CT chest minimal bilateral pleural thickening

CT abdomen: ovarian teratma measured about 17x16x15cm diameters mainly cystic with small soft tissue components , internal septations and multiple calcified nodules compressing nearby structures (uterus, adnexa and bowel loops).

Blood &CSF: NMDA receptor antibody positive.

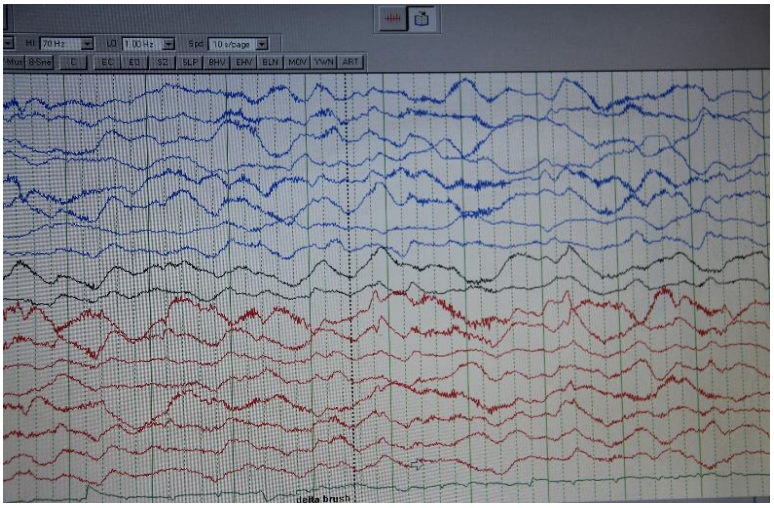
Toxoplasmosis IgG +ve, IgM –ve , BHcG –ve

PET SCANNING

Chest: Mild FDG-avid 2 intra pulmonary nodule is posterior segment of right upper lobe of lung and SVV max 2.2 (The significant uptake in 2.5 and above), there is bilateral mild FGD avid minimal pleural effusion with SUV-max of 2.5.

Brain: FDG- avid bilateral fronto-temporal region pronounced in the right side due to limbic encephalitis.

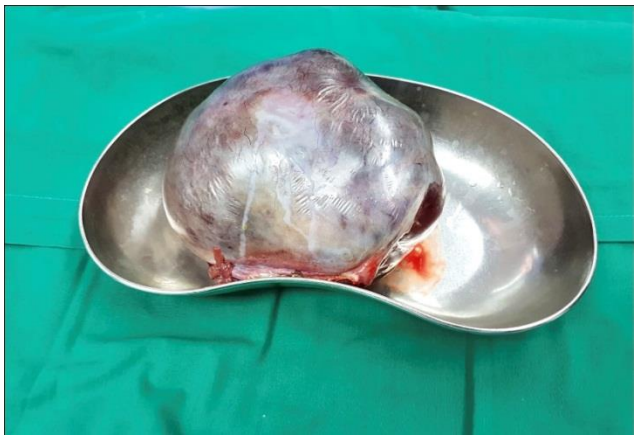
EEG: Showed slow wave with delta brush, characteristic of NMDA receptor antibody encephalitis.



Histopathology of the left ovarian teratoma

Sections showed cystic lesion composed mature and immature components, mature component consists of skin, central nervous elements , bone structures , chondroid tissue , and GIT tissue .Immature component of neurogenic elements seen in 2 foci.

Opinion of histopathology: immature teratoma grade 2



In summary the treatment in ICU was

1. IVIG 0.4 g IV OD x 5 days.
2. Plasmopharesis x 5 sessions given.
3. IV methylprednisolone 1 gram IV OD x 5 days.
4. Rituximab 500mg IV once weekly and completed 4 doses.

Anticonvulsants

1. T.levetiracetam 1.5 g BD
2. T.lacosamide 150mg BD

3. T.trileptal 300 mg BD

Outcome and follow-up

The plan in Al-Adan hospital in Kuwait was if oromandibular dyskinesia increases plan to give botox injections by movement disorder specialist . Medical oncology opinion regarding further management for immature teratoma. But the patient went to Australia by private flight to continue her treatment and she was vitally stable, under sedation and on Mechanical ventilation with tracheostomy. In Australia, she received again rituximab without any respond or improvement, so they decided to start her on ocrelizumab 300mg as initial dose and after 2 weeks with the same dose; then a maintenance dose of 600 mg once every 4 months was given after the initial dose, in which she responded to it and begins to improve after 1 month.

DISCUSSION

Anti-NDMAR encephalitis is a life-threatening condition with a wide spectrum of symptoms. The initial prodromal phase is a nonspecific viral-like symptom disease with headache, nausea, vomiting, fever, which later on progresses rapidly into neuropsychiatric abnormalities.[1] Anti-NMDAR encephalitis was described first in 1997 by Dalmau, et al. in two isolated case reports.[2] The early stage symptoms include confusion, memory loss, hallucinations, delusion, mood disturbances, anxiety, self-harming behaviors, seizures and dyskinesia, the majority of these patients consult psychiatrists initially.[3] Many of them are misdiagnosed with psychiatric disorders and are started on anti-psychotics. However, these patients do not respond to these drugs and rapidly progress to late-stage symptoms of decreased level of conscious, hypoventilation, and autonomic instability manifesting as fluctuations of blood pressure and heart rate, hyperthermia, and urinary incontinence. The disease affects young adults with a median age of 21 years, mostly females rather than males with a percentage of 80% ,[2,4] most commonly, the tumors located in the ovary; however, rarely mediastinal teratomas have also been implicated.[5] Reports have suggested that anti-NMDAR encephalitis can be related to other germ-cell and rarely non-germ cell tumors.[2,4,5] Studies showed that the syndrome is a paraneoplastic process due to an antibody to an unidentified antigen expressed in the hippocampus.[6] The antibody was discovered to be the anti-NMDA-receptor. [5] In this disease process, antibodies are generated in response to the neural elements within the teratoma. The autoantibodies react with the NMDA Receptor 1 (NR1) subunit of the ligand-gated cation channels NMDA receptor that is primarily expressed in the hippocampus and forebrain, that are implicated in memory and learning. Diagnosis of encephalitis should be considered in patients with acute onset of neuropsychiatric symptoms unresponsive to antipsychotic medications. Serum and CSF studies for viral and autoimmune causes of encephalitis, MRI, and EEG should be performed to obtain a specific diagnosis. It is important to note that although brain MRI may be within normal limits in most of the patients, but 90% of these patients commonly show EEG abnormalities, so early EEG can help in early diagnosis and treatment for the disease. As in our patient that showed a Delta Brush waves that is specific to Anti-NMDAR encephalitis.[4]

It is also important to do other imaging studies such as pelvic ultrasound, MRI, CT, and positron emission tomography to evaluate for an underlying tumor, as here we did the full PET scan for our patient. In rapidly decompensating patients with a clinical suspicion of anti-NMDAR encephalitis, imaging and removal of any detected neoplasms should be considered without delay, as in this case. Any delay in treatment may result in deterioration of the autoimmune process with progression to autonomic instability, catatonia, status epilepticus, or coma and even death.[4]

The majority of the patients who undergo surgical excision of the tumor and immunosuppressive treatment are found to have a significant improvement in the neurologic status.[2] Tumor resection has been recommended as a first line treatment for anti-NMDAR encephalitis. Then after that the use of immunomodulatory regimens, including steroids, intravenous immunoglobulin, and plasmapheresis.[7,8] Ocrelizumab have been showed an improvement for the condition when other treatment methods failed, it should be given as initial dose of 300mg then after 2 weeks with the same dose, then after that a maintenance dose of 600mg (once every 6 months) for 2 years with a 4 doses . Here in our case, they used the same dose with period of 4 months to fasten the recovery , instead of 6 months for the maintenance.[9] The main immunosuppressive therapies commonly used include intravenous steroids and IVIG or plasmapheresis as the first line with rituximab, cyclophosphamide as the second line and ocrelizumab when all options failed.[9]

CONCLUSION

Early diagnosis of Anti-NMDAR encephalitis is very important; as the associate teratoma can be diagnosed promptly and the surgical removal of the tumor can be a great in the prognosis and recovery of the patient. For our case, we ordered EEG that showed a specific characteristic of limbic encephalitis and surgical removal of the tumor was done. Ocrelizumab showed a great improvement for the patient condition from the first month.[9] It is worth treating with ocrelizumab when other approved therapy failed and it can be lifesaving.

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