NMDA-receptor associated encephalitis in a woman with mature cystic ovarian teratoma - a case report

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I. INTRODUCTION

N-methyl-D-aspartate receptor (NMDA-R) antibody-associated encephalitis has been reported in the international neurological literature to be associated with mature or immature ovarian teratomas (OTs). However, few cases of encephalitis were diagnosed in Hungary. In 2011 Hollody et al. described the first case of anti-NMDA receptor associated encephalitis in Hungary [1].

II.OBJECTIVE

Our aim was to present a case of NMDA-R antibody- mediated encephalitis in a woman with OT thereby providing information facilitating diagnosis of OT in women, who present with symptoms of encephalitis.

III. CASE PRESENTATION

The patient was admitted initially on 18/11/2012 to Whipps Cross University Hospital with a 3 week history of encephalopathy, including confusion, disorientation, behavioural disturbance with agitation and features of paranoia and at least one reported generalised tonic clonic seizure

a) ***Neurological examination*** at presentation revealed confusion and disorientation. The general medical examination was unremarkable.

b) ***Diagnostic algorithm and treatment***

The lumbar puncture on **18/11/2012** revealed an increased number of white blood cells (49; 100% lymphocytes) in the CSF, a glucose level (3.7 mmol/L and a protein level of (0.18 g/L), with no pathogenic organism. The blood test showed a white cell count of 10.2 x10 ₉/L and the urea and electrolyte levels, liver function tests and full blood count were otherwise normal, including a C-reactive protein (CRP<0.2 mg/L) (Table 1). She was treated empirically with acyclovir to cater for the possibility of atypical viral encephalitis. Phenytoin and lamotrigine were also given to prevent the generalised tonic-clonic seizures.

The brain MRI scan indicated bilateral hyper intense hippocampal lesions (Table 1). The radiologist suggested a tentative diagnosis of autoimmune encephalitis, probably mediated by NMDA-R antibodies. NMDA-R and voltage-gated potassium channel antibodies were measured. Prednisolone (60 mg) was started. The cognitive status of the patient gradually deteriorated further, her level of consciousness fluctuated (Glasgow Coma Scale (GCS): 8 to 14) and she was markedly agitated, requiring risperidone and haloperidol.

She developed ***acute kidney injury*** *(*creatinine: 169 umol/L), which improved in response to adequate intravenous hydration and eventually normalised (creatinine: 74 umol/L) The lumbal puncture was repeated on 23/11/2012, the CSF was found to be acellular (glucose: 4.1 mmol/L, protein 0.23 g/L) and no organism was detailed. The neurological review raised the possibility of a complex partial status epilepticus, and the dosage of lamotrigine was increased to 50 mg.

The patient was transferred to the Royal London Hospital for further treatment On examination, eyes were open spontaneously, tracking and blinking to menace. Pupils were equal and reactive to the light, corneal and vestibule-ocular reflexes were intact. There was incomprehensible vocalisation. The patient did not follow the simple 1-step commands. Reflexes were symmetrical and plantars were bilaterally flexor. Examinations of the chest and abdomen were unremarkable and the result of electroencephalography (EEG) was normal. Further blood test results demonstrated that the included Thyroid Stimulating Hormone (TSH) was moderately elevated at 5.8 (fT4: 18.7) because of the hypothyroidism. The ammonia (9 mmol/L) and complement levels were in the normal ranges. A normal pattern was seen on serum protein electrophoresis. A 5-day course of intravenous immunoglobulin was administered because of the suspected autoantibody-mediated encephalitis. NMDA-R antibodies were found positive in several serum and CSF samples and the diagnosis of NMDA-R antibody- mediated autoimmune PLE was confirmed. The pelvis MRI suggested ***an OT in the left ovary***. The patient underwent left *oophorectomy* and the left ovary containing a cystic tumour was removed. Histological examinations revealed a mature cystic OT (Table 1). In the meantime, the patient suffered several generalized tonic clonic seizures, and also several episodes of dysautonomia, with cardiovascular lability. Admission to a high dependency unit became necessary. During this time she contracted aspiration pneumonia, which was treated and resolved on treatment. She also manifested the typical orofacial dyskinesia characteristic of this disorder. She completed a 5-day course of plasma exchange. Following removal of the OT and plasma exchange, she displayed a significant clinical improvement. She remained stable from a cardiovascular aspect. She is now seizure-free, her level consciousness is stable, her cognition is improving and the orofacial dyskinesia has subsided, but she still requires cognitive rehabilitation and neurology follow-up in the Department of Psychiatry. Her corticosteroid treatment gradually has been tapered off as indicated by the immunology follow-up at the Department of Rheumatology, whereas the azathioprine treatment is still continuing in order to prevent a relapse of the neurological symptoms. The azathioprine therapy is planned to last for one year.

Table 1. Diagnostic algorithm of patients with NMDA-receptor antibody mediated encephalitis

Diagnostic procedures	Results
Lumbar punction and analysis of cerebrospinal fluid (CSF)	CSF glucose level: 3.7 mmol/L CSF protein level: 0.18 g/L No pathogenic organism
Blood test (hematology and biochemistry)	White blood cell (WBC): 10.2x10 ^{9} L C-reactive protein (CRP): < 0.2 mg/L
Brain Magnetic Resonance Imaging (MRI)	Bilateral hyperintense hippocampal lesions
Electroencephalography (EEG) assessment	Normal record. Posterior l0-l2 c/s alpha rhythm.
Staging computed tomography (CT) of chest and abdomen	There were no evidence of metastatic lesion
Vaginal ultrasound examination	There were no evidence of metastatic lesion
NMDA-R and voltage-gated potassium channel antibodies examination from CSF and serum samples	NMDA-R antibodies were found positive in two samples CSF and serum
Pelvis MRI	A 3.3 cm functional follicle and dermoid cyst were seen within the left ovary.
Histological examination of the teratoma (citology and immunology)	Macroscopy: A previously opened cystic ovary measuring 660x30x20 mm. Sectioning revealed sebaceous type material and fatty tissue along with cystic ovarian tissue. Microscopy: The cyst wall contains various type of tissue including skin, fat, cartilage and sweat glands. There was no somatic dysplasia or malignancy.

V. REFERENCES

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IV. CONCLUSION:

Cystic teratomas are common benign ovarian lesions in women of reproductive age. Although the association of OTs and NMDA-R antibody-associated encephalitis has been described in the international neurological literature [2-7], this relationship needs to be considered from on the interdisciplinary aspect by the health care providers.

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