CASE REPORT

Sore eyes and psychosis

Samantha Colley,[1] John Smith[2]

[1]Hull Royal Infirmary, Hull, UK
[2]Department of Acute Medicine, Harrogate & District Hospital, Harrogate, UK

Correspondence to
Dr Samantha Colley,
sambeze23@doctors.org.uk

Accepted 31 July 2014

SUMMARY

We present the case of a 30-year-old woman who presented with sexual disinhibition and altered behaviour following an episode of optic neuritis. Her only history was of anxiety disorder. Her differential diagnosis was neurological versus psychiatric. Routine blood tests were unremarkable at this stage. MRI revealed non-specific change and lumbar puncture revealed a slight lymphocytosis and elevated protein and glucose in the cerebrospinal fluid (CSF). PCR on the CSF was negative for viruses: Adenovirus, varicella zoster virus, herpes simplex virus, enterovirus and parechovirus. She was initially treated with intravenous acyclovir to little effect. Antipsychotics olanzapine and haloperidol were also trialled and continued for 3 weeks in total. Once again these medications failed to affect the patient's behaviour but she did begin to show the side effects associated with these medications. Further test results became available at this point—she was anti-*N*-methyl D-aspartate (NMDA) receptor antibody positive. A diagnosis of anti-NMDA receptor antibody encephalitis was made. The patient was started on cyclophosphamide and methylprednisolone to good effect.

BACKGROUND

N-methyl D-aspartate receptor (NMDAR) encephalitis commonly presents with neuropsychiatric features.[1]

Anti-NMDAR encephalitis was first described in as a syndrome in 2007[2] and is often not considered acutely as part of the differential diagnosis in patients presenting with psychiatric symptoms. This case is presented to increase awareness and aid rapid diagnosis that may prevent progression to seizures, autonomic dysfunction and intensive care treatment.

Anti-NMDAR encephalitis can be paraneoplastic in presentation.[3] Most of these cases are associated with ovarian teratoma or small cell lung cancer. The encephalitis can precede the discovery of the teratoma by many years and they have been found up to 4 years after initial presentation.[3] This often leads to long-term follow-up and repeated scanning long after the primary encephalitis.

CASE PRESENTATION

We present a 30-year-old woman who presented acutely to the acute medical department with clinical features suggestive of optic neuritis of the left eye.

Previous relevant history included anxiety-affective disorder without pharmacotherapy.

The patient was married with a 12-month-old child, smoked 15 cigarettes a day and consumed 20 units of alcohol a week. She took no prescription, over the counter or illicit medication.

Clinical examination revealed relative afferent pupillary nerve defect in the left eye and subsequent MRI of her brain revealed high signal on T2 in relation to the posterior aspect of the head of the left thalamus and adjacent internal capsule. There was a second area of high signal in periventricular white matter lateral to the left lateral ventricle. A third focal lesion was seen inferiorly in the left frontal lobe. With respect to the orbits the left optic nerve appeared somewhat ill-defined and swollen at the apex of the orbit on coronal fat saturation series. These MRI findings were discussed as abnormal but not typical or specific of multiple sclerosis (figures 1 to 3).

At this stage other than routine blood tests no further tests were sought. Lumbar puncture was not performed. The patient was treated successfully with intravenous methylprednisolone (1 g once daily for 3 days) with good clinical resolution of her symptoms. A working diagnosis at this point was still of multiple sclerosis although the imaging was not typical. As a result a routine outpatient referral to neurology made where the patient and imaging could be reviewed.

Three weeks later she represented with disinhibition and sexually inappropriate behaviour that was out of character. There were also features of low mood. She presented to the local emergency department and was subsequently discharged for community mental health input. Community mental health input identified social and sexual disinhibition, profuse swearing and noted pressure of speech. She was admitted to a local mental health unit under Section 2 of the Mental Health Act.

Examination at this time revealed normal neurological and systemic examination. The relative afferent pupillary defect had resolved at this stage.

INVESTIGATIONS

Pathological investigations including full blood count, liver function and renal function were normal. There was a slight acute phase response with a C reactive protein of 16 m/L. Neurological opinion was sought and neurological condition was suspected. The patient was transferred to the local acute medical service.

Repeat MRI of the brain revealed no new changes and CSF analysis revealed 41×10^6 white cell count with 90% lymphocytosis. Protein was slightly elevated at 0.47 g/L. Resulting viral PCR was negative for adenovirus, varicella zoster virus, herpes simplex virus, enterovirus and parechovirus. CSF electrophoresis was negative.

To cite: Colley S, Smith J. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2013-201956

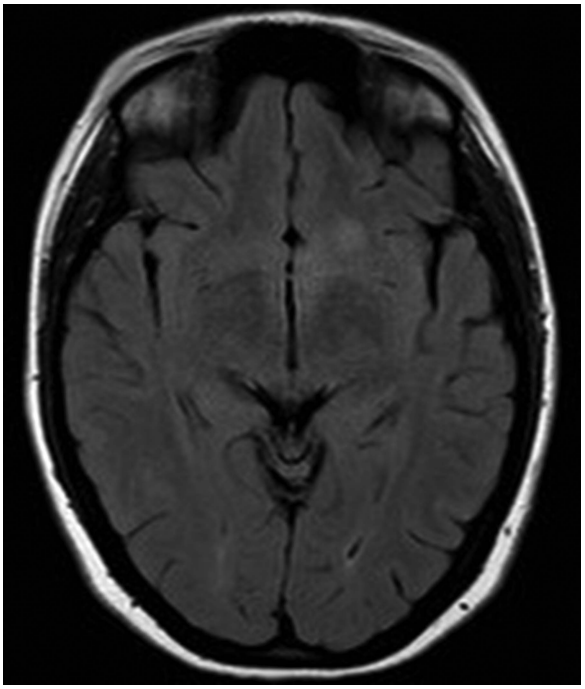

Figure 1 Lesion inferiorly in the left frontal lobe.

Serologies for syphilis, lyme disease, HIV and hepatitis B surface antigen were all negative. Serum ACE was also negative. Paraneoplastic screening: Anti-Hu, Yo, Ri, Ma1, Ma2, anti-CV2/CRMP5 and amphiphysin were negative. An autoantibody screen including: antinuclear; perinuclear antineutrophil cytoplasmic antibodies (p-ANCA); cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA); antivoltage-gated potassium channel antibodies (anti-VGKC) and antivoltage-gated calcium channel antibodies (anti-VGCC) was also negative. Antiaquaprotein four antibodies were not tested for. Antimyelin basic protein antibodies were not tested for.

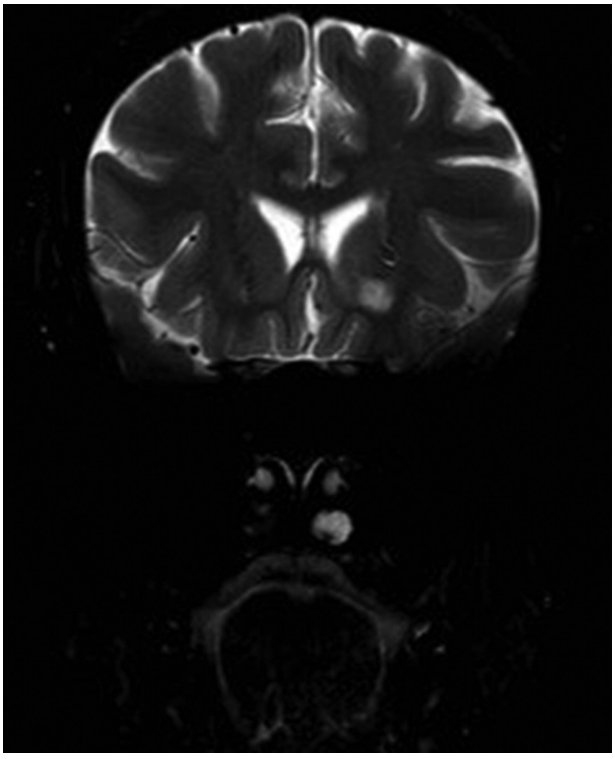

Figure 2 High signal lesion in relation to posterior aspect of the head of the left thalamus.

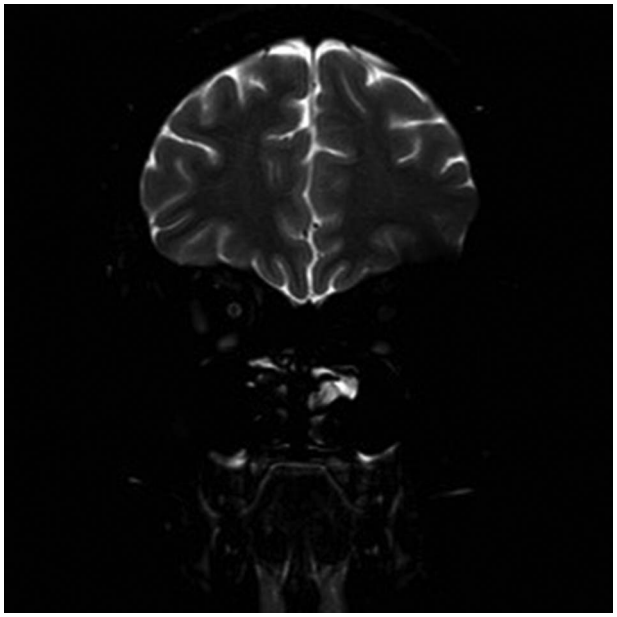

Figure 3 Coronal fat saturation series: Ill defined left optic nerve.

EEG with visually evoked potentials (VER) revealed consistent response with left VER mildly delayed in fitting with the previous diagnosis of optic neuritis, with EEG artefact, low amplitude and contained diffuse β activity (possibly sedative related). It did not show any clear suggestion of an encephalitic state.

Further serology returned and was positive to anti-NMDAR antibody.

DIFFERENTIAL DIAGNOSIS

NMDAR encephalitis classically presents with symptoms including: psychosis, hallucinations, personality changes and memory problems. Following this a psychiatric assessment is often sought prior to medical work up. This is not unusual and is what happened with this case. Thus differential in this case is neurological illness versus psychiatric illness.

However, in this case one also needs to consider how the preceding optic neuritis figures in this condition because an initial presentation as neuritis is atypical at the least. Is this just an atypical presentation of NMDAR encephalitis or is there another pathology that links the two such as multiple sclerosis? Or even more unlikely is it just a coincidence these symptoms occurred together?

TREATMENT

Initially the patient received 8 days of 750 mg acyclovir three times daily before it was discontinued. At the time of NMDA confirmation she had also receiving olanzapine 10 mg twice daily for 10 days and haloperidol 2.5 mg twice daily. When NMDA tests came back positive she was started on methylprednisolone 500 mg with cyclophosphamide 500 mg. Three pulses weekly for 3 weeks and then another three pulses every other week for a total of six pulses. Thereafter azathioprine was initiated and continued at a dose of 150 mg daily.

OUTCOME AND FOLLOW-UP

The patient remained under Section 2 of the Mental Health Act for 14 weeks and remained on azathioprine for 12 months. Subsequent imaging (ultrasound-abdomen and pelvis and CT chest, abdomen and pelvis) failed to identify a primary tumour and 30 months after presentation the patient is well. She was treated on 150 mg azathioprine daily for 12 months and then this was reduced by 50 mg every 2 months. She is now off all medication and remains well. She has no memory of her acute presentation and hospital stay.

Her original presentation of optic neuritis was approximately 3 years ago, after discharge from hospital with the diagnosis of encephalitis she was reviewed bi-annually by the neurologists. She has had no recurrence of any symptoms and has now been officially discharged from regular follow-up. Neurologists have discussed the atypical MRI scan with the patient. They have said while neither clinically nor radiologically classical for multiple sclerosis should she become unwell again this would be an avenue to investigate.

DISCUSSION

The presence of florid psychiatric features at presentation can distract clinicians from a full clinical history and examination. In this case the presentation with optic neuritis and the subtle white matter changes on MRI performed a primary diagnosis of psychiatric disorder less suitable for this patient. However, a high index of suspicion is the only way of avoiding missing the opportunity of treating these typically young women presenting with aggressively deteriorating mental health symptoms. The delay in obtaining results even when anti-NMDAR antibody encephalitis is suspected can led to major delay in the initiation of treatment. In this case it took 12 days for the results to become available. Suspicion is vital acutely. Dalmau *et al*[4] describe a multistage disease process presenting primarily with altered behaviour, faltering memory and progressing to autonomic dysfunction and death.

Anti-NMDAR antibody encephalitis has been described as a paraneoplastic phenomenon typically due to ovarian malignancy.[3] Initial pelvic imaging in this patient has been normal and resulting extensive CT imaging at 1 year failed to isolate a delayed presentation of malignancy.

This case presents optic neuritis leading to an eventual diagnosis of NMDAR encephalitis. It is possible that optic neuritis and anti-NMDA encephalitis occurring in the same patient is coincidental but this is thought unlikely. It could be that these two separate conditions are potentially part of the same autoimmune triggered syndrome as previously suggested by Kruer *et al*[5]; although a unifying diagnosis could be Neuromyelitis Optica or spectrum syndrome this woman did not have transverse myelitis clinically and aquaporin four antibodies were hence not tested for. Similarly this woman could have multiple sclerosis; however, she has had two MRI's which were in no way progressive and were not typical for multiple sclerosis, furthermore she had a high initial white cell count in her CSF again not in keeping with this diagnosis.

Lastly as first suggested by Motoyama *et al*[6]; optic neuritis may be an atypical symptom of NMDAR encephalitis. In the case noted the previous optic neuritis was recurrent, however, it is again a case where the two diagnoses were linked. Thus if it is a symptom testing for anti-NMDAR antibody at the initial presentation of optic neuritis may yield a positive result. Following this a patient then be started on disease modifying agents and potentially stop the progression to encephalitis. It is possible that optic neuritis is a presenting feature of NMDA encephalitis but in some it is subclinical.

Only through increased awareness of NMDAR encephalitis will doctors consider it as a diagnosis and maybe look more closely for optic neuritis as a symptom, only then will we find enough cases to prove or disprove a link.

Learning points

- *N*-methyl D-aspartate receptor (NMDAR) encephalitis is still a relatively new and rare diagnosis.
- Please consider NMDA encephalitis or other inflammatory encephalitis in patient presenting with neuropsychiatric feature.
- Early diagnosis may avoid intensive treatment unit admission–mortality is still high.[7]

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Dalmau J, Gleichman AJ, Hughes EG, *et al*. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7:1091–8.
2 Dalmau J, Tuzun E, Wu H, *et al*. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007;61:25–36.
3 Haththotuwa HR, Malhas L, Jagadeeswaran A. Anti-NMDA receptor encephalitis: an intensive care perspective. *Intensive Care Soc* 2012;13:147–50.
4 Dalmau J, Lancaster E, Martinez-Hernandez E. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol* 2011;10:63–74.
5 Kruer MC, Koch TK, Bourdette DN. NMDA receptor encephalitis mimicking seronegative neuromyelitis optica. *Neurology* 2010;74:1473–5.
6 Motoyama R, Shiraishi K, Tanaka K. Anti-NMDA receptor antibody encephalitis with recurrent optic neuritis and epilepsy. *Rinsho Shinkeigaku* 2010;50:585–8.
7 Day GS, High SM, Cot B. Anti-NMDA receptor encephalitis: case report and literature review of an under-recognised condition. *JGIM* 2011;26:811–16.