Life and limbic threatening condition: A rare case of refractory seizures due to anti-NMDA-receptor encephalitis - Abstract No: 27

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Introduction

Limbic encephalitis is a rare, acute, life-threatening disease caused by antibodies to the NR1 subunit of the N-methyl-D-aspartate receptor (NMDA-R)1. Initial symptoms are typically vague and non-specific, and as a result of a prolonged prodromal phase a psychiatric diagnosis is commonly considered; definitive diagnosis and management is therefore often delayed2, commonly involving critical care services while the patient is stabilised.

Description

A 22 year-old woman with fluctuating consciousness and autonomic instability was referred to our neurosciences critical care unit. Previously fit and well, she had presented to an outlying hospital with confusion and behavioural disturbance, following three weeks of progressive non-specific neurological symptoms and personality change. Initially admitted to a psychiatric unit, she was subsequently treated for presumed infectious encephalitis given an extensive travel history, recent treatment for a UTI on holiday two months prior, and high risk of exposure to agricultural diseases, however all microbiological and initial autoimmune screens were negative. Nine days after admission to hospital she required intubation for refractory status epilepticus, which was resistant to multiple antiepileptic agents. She was subsequently managed with a thiopentone infusion, guided by continuous CSA monitoring to assess for suppression of nonconvulsive seizures3.

High dose steroids and five cycles of plasma exchange were started by the neurology team for presumed non-infective encephalitis, and at two weeks NMDA-R autoantibodies were confirmed. A course of IV immunoglobulin had no clinical effect so one month into her admission a course of rituximab was given, achieving seizure control and allowing thiopentone to be discontinued. Management was complicated throughout by autonomic instability, with episodes of tachyarrhythmia, pyrexia and hypertension accompanying seizure activity, and she experienced a PEA arrest thought to be secondary to bradycardia, although this did follow her second dose of rituximab therapy. She had several episodes of sepsis on immunosuppression, but made a good neurological recovery soon after starting rituximab, with a progression through dystonic movements through to speaking seemingly following the course of her initial illness in reverse. She was discharged after 118 days in critical care – 108 days ventilated – into a neuro-rehabilitation programme.

Although serial EEG suggested a focal abnormality in the right temporal region, MRI head demonstrated nil other than mild atrophic changes (figure 1), and extensive investigation with US, MRI, PET-CT (figures 2 and 3), and biomarkers have revealed no causative tumour.

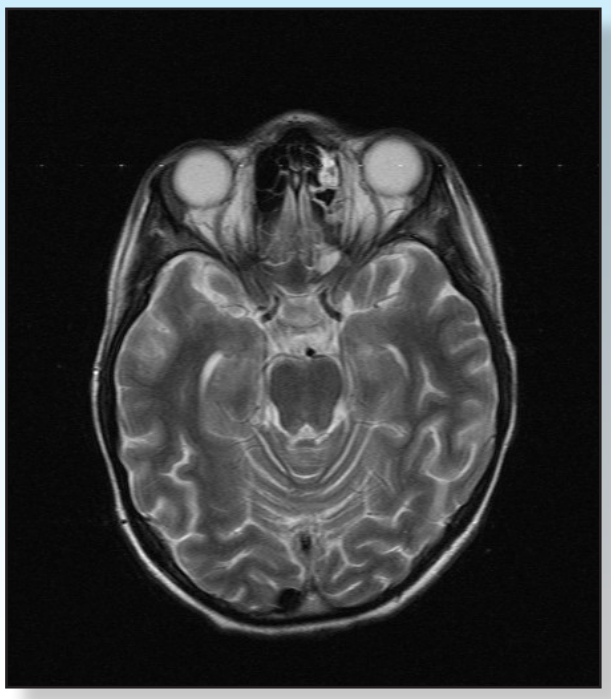

Figure 1: T2-weighted MRI brain showing mild atrophic changes and sinusitis.

Discussion

Limbic or anti-NMDA-R encephalitis typically presents, as in this case, in young women with a prolonged non-specific neuro-psychiatric course followed by the development of intractable seizure activity and profound autonomic instability4. A detailed history and high index of suspicion are required to make the presumed diagnosis and start definitive treatment, as confirmatory serological testing often takes several weeks.

There is a recognised association with ovarian teratomas and bronchial malignancies; however, causative tumours cannot be found in up to 50% of patients. Although surgical excision has been suggested as definitive therapy, with prophylactic oophorectomy suggested even if a tumour has not been identified in refractory cases, exhaustive investigations for these should not delay immunosuppressive therapy5. Prognosis is good, especially with identification and removal of a causative malignancy and early immunotherapy6, although a prolonged hospitalisation and period of rehabilitation should be anticipated7.

Limbic encephalitis is likely an under-recognised disease in the critical care unit, mimicking more common disease. It should be considered early in patients with refractory seizures and a neuropsychiatric illness, to allow timely consultation and referral to tertiary neurosciences services, ensure optimal management of this condition.

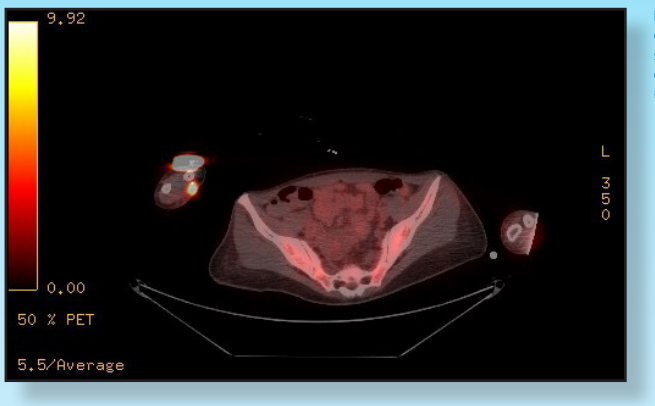

Figure 2: Pelvic PET-CT showing diffuse FDG uptake in the axial skeleton and pelvis, which was considered reactive in nature, but normal pelvic viscera.

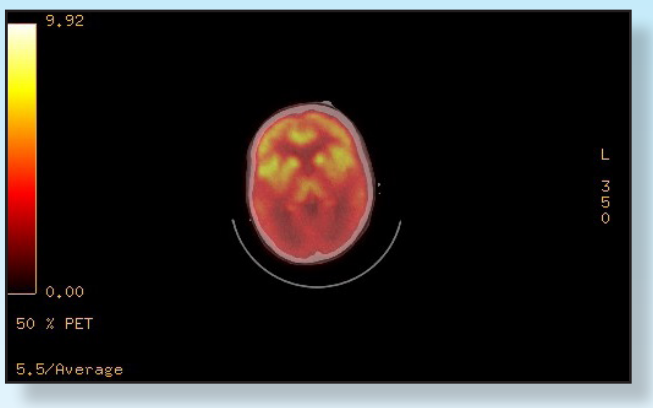

Figure 3: PET-CT of the head demonstrating diffuse photopenia in the parietal and occipital lobes, related to metabolic activity due to ongoing encephalitis.

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