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Anti-NMDA receptor encephalitis presenting as aseptic meningitis

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Abstract

Presentation

A man in his forties presented with a 3 week history of headache and recurrent pyrexia. He was treated empirically with anti-microbials for meningitis and improved clinically. The patient re-presented 6 weeks later with a profound frontal lobe syndrome and apraxia.

Diagnosis

An autoimmune encephalitis panel was sent and identified the presence of anti- NMDA receptor antibodies in the CSF.

Treatment

The patient was empirically treated with intravenous methylprednisolone and intravenous immunoglobulins with good effect pending the antibody results. There was a marked improvement in cognition, behaviour and ability to interact.

Discussion

This is an unusual presentation of anti-NMDA receptor encephalitis initially presenting as an aseptic meningitis.

Introduction

We report a case of anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis which initially presented as an aseptic meningitis. Anti-NMDAR encephalitis is most typically seen in young women and may be associated with an ovarian teratoma[1]. It is particularly unusual that it presents following clinical resolution of an aseptic meningitis. However, a biphasic pattern of illness has been described with an initial meningitis and subsequent encephalitis weeks to months later[2]. This case highlights the importance of consideration of an autoimmune encephalitis when no pathogen is identified and a biphasic illness is evident[2].

Case Report

A 44 year old gentleman presented with a 3 week history of headache, a discrete episode of expressive dysphasia and a separate episode of right hand paraesthesia. The patient was

noted to be diaphoretic at night. He had been treated for sinusitis in the community without resolution of his symptoms. A CT-Brain was unremarkable and the patient underwent a lumbar puncture which showed a pleocytosis (98% mononuclear cells) (see table 1). At this point the patient was treated with aciclovir, ceftriaxone and vancomycin. The patient responded well to anti-microbial therapy and was discharged after 3 weeks.

Six weeks later the patient re-presented with a 1 week history of cognitive deterioration. The patient's family reported his difficulty carrying out learned motor tasks, emotional lability, intermittent headaches and personality change. On examination the patient was noted to be bradyphrenic, with marked difficulty in following commands. The patient was abulic. Of note there were no features of meningism. The cranial nerve and limb examination were within normal limits.

A repeat lumbar puncture carried out showed a small number of mononuclear cells (see table 1). The initial working diagnosis was that of encephalopathy of unknown aetiology. MRI brain imaging was normal. The patient was recommenced on antimicrobials pending CSF results. CSF cultures were unrevealing and antimicrobials were stopped.

The patient developed seizure activity during this admission and was commenced on Levetiracetam. Electroencephalogram (EEG) was carried out, see figure 1.

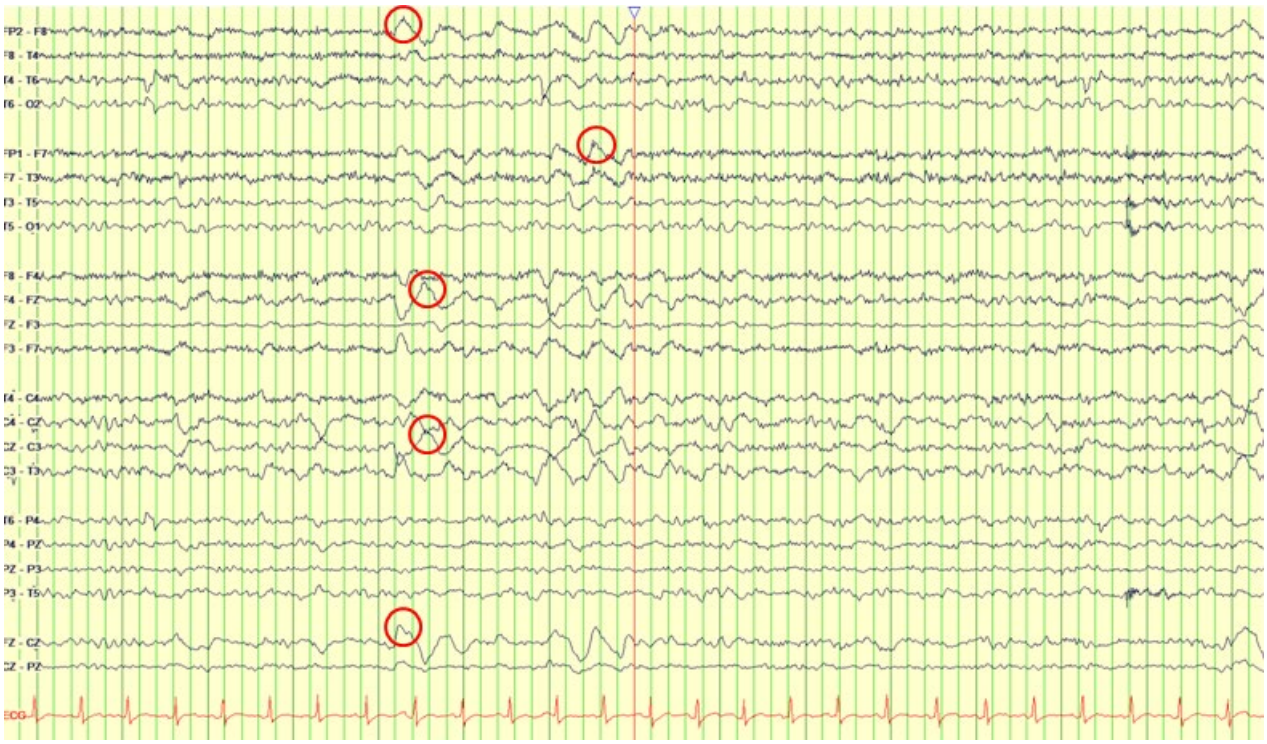

Figure 1. Electroencephalogram recording. Double banana montage, right over left orientation. Frequent runs of irregular and sharp and delta over the anterior quadrant indicative of severe localised dysfunction.

A repeat lumbar puncture was arranged for an autoimmune encephalitis screen, along with serum testing (Table 1).

	Leucocytes (cells/mm^3)			Cell Differential	CSF Glucose (mmol/L) (2.2-3.9)	Serum Glucose (mmol/L) (3.9-7.8)	CSF Protein (g/L) (0.15-0.45)	CSF Culture:	CSF Autoimmune Encephalitis Screen
	Tube 1	Tube 2	Tube 3						
Initial CSF	89	104	102	95% Mononuclear cells	2.5	NA	0.47	No growth	-
Repeat CSF	6	15	11	95% Mononuclear cells	3.0	NA	0.43		Anti-NMDAR Antibody Positive

Table 1: CSF results from initial lumbar puncture and repeat lumbar puncture after second presentation. FilmArray PCR was negative. NA: not available

A working diagnosis of autoimmune encephalitis was made and empiric treatment was commenced pending autoimmune encephalitis antibody results. The patient was commenced on 5 days of intravenous immunoglobulins and 10 days of intravenous methylprednisolone. There was a clinical response to the treatment with improvement in cognition and orientation, resolution of headaches and ability to engage and follow commands. Anti-NMDAR antibody was identified in the CSF only, approximately 4 weeks after CSF and serum samples were sent.

On follow up the patient's personality changes were largely resolved and he had returned to carrying out his normal routine tasks and activities. The patient has now returned to his former baseline.

Discussion

Anti-NMDAR encephalitis is a well established immunotherapy-responsive condition typically presents with a change in behaviour with marked psychiatric and cognitive manifestations[1]. This gentleman met the clinical criteria for 'probable' Anti-NMDAR encephalitis while autoimmune results were pending and was treated empirically. Anti-

NMDAR antibodies should be checked in both CSF and serum rather than serum alone, as a review of 250 anti-NMDAR encephalitis demonstrated that anti-NMDAR antibodies are always present in CSF while anti-NMDAR antibodies are detected in serum in 87% of cases[3].

A prodrome of pyrexia and aseptic meningitis or viral encephalitis has been rarely reported in the literature as the heralding features of anti-NMDAR encephalitis[2,4]. Our clinical impression is that this gentleman initially had an aseptic meningitis and later developed anti-NMDAR encephalitis. The mechanisms underlying the development of anti-NMDAR encephalitis post aseptic meningitis are poorly understood. One hypothesis is that meningitis may result in disruption of the blood brain barrier allowing infiltration of anti-NMDAR specific B cells[5]. This would require patients to have pre-formed circulating anti-NMDAR specific B cells. Interestingly, there is a high seroprevalence of anti-NMDAR subunit-NR1 autoantibodies in both affected patients and healthy controls lending support for this potential pathogenic mechanism[6].

This case highlights the rarity of anti-NMDA receptor encephalitis presenting as an aseptic meningitis. We believe it is of value to practising clinicians particularly when a patient presents with encephalopathy following recovery from aseptic meningitis.

Declarations of Conflicts of Interest:

None declared.

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