CHARACTERIZING THE FEATURES, COURSE AND TREATMENT OF NEUROPSYCHIATRIC SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH AUTOIMMUNE ENCEPHALITIS

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INTRODUCTION

Autoimmune encephalitis (AE) is a rare condition but increasingly recognised in children and adolescents [1]. Although considered to be underestimated, the incidence for antibody-mediated AE in paediatric patients is around 1.5 in a million [2] and it is a common cause of encephalopathy in this age population [3].

Early recognition of AE is key, with the prognosis dependent on prompt immunomodulatory treatment. Psychiatric presentations are common in AE and difficult to differentiate from a primary mental health disorder, so the diagnosis is often not considered early. We aimed to describe the psychiatric symptomatology, disease course and management of children with an AE.

METHOD

Retrospective review of neuropsychiatric manifestations, course and treatment of children diagnosed with AE between 2016-2019 at the liaison psychiatry services in two UK paediatric neuroscience centres. Psychiatric symptoms were categorised in four main clusters (behavioural, speech, mood and psychotic features).

CONCLUSIONS

Within the limitation of this small cohort, the presence of multiple concurrent psychiatric symptoms, (particularly sleep disturbances), in a child presenting with an acute/sub-acute psychosis, in addition to the absence of other neurodevelopmental co-morbidities, poor cognitive function, and poor or adverse reaction to anti-psychotics should alert the psychiatrist to an autoimmune aetiology, prior to onset of more recognisable neurological features.

This information may inform clinicians of the clinical features that should raise suspicion of AE, prompting further investigations and pragmatic treatment decisions to target the underlying cause of the psychiatric symptoms.

RESULTS

16 patients (mean age 11.31, SD 2.98; 13 females) were identified of which 7 had NMDAR-antibodies (CSF and/or serum). Two had neurodevelopmental disorders and none of them had previous mental health problems.
At presentation, symptoms were only psychiatric in 37.5% (6/16), only neurological in 18.8% (3/16); and mixed in 43.7% (7/16). The most frequent neuropsychiatric symptoms were psychosis (81.2%), disrupted sleep patterns (75%), mood dysregulation (75%), abnormal speech (56.2%), and disordered eating (37.5%) (Table 1).
During the course of the illness, all patients had 2 or more psychiatric symptoms, with 43.7% (7/16) presenting concurrent symptoms in four clusters (behavioural, speech, mood and psychotic features), 18.7% (3/16) in three and 37.5% (6/16) in two (Table 2).

All cases eventually developed neurological symptoms, with delirium (81.2%) and seizures (68.7%) being the most common (Table 3).

Antipsychotics were poorly tolerated and produced worsening of symptoms in 25% of the cases (both NMDAR positive and non-NMDAR patients). Pharmacological treatment with benzodiazepines associated a better response and tolerability.

Table 1. Psychiatric Features of Paediatric AE

Symptom cluster	NMDAR +ve N=7 (%)	NMDAR -ve N=9 (%)	Total N=16 (%)
Behavioural changes	**7 (100)**	**8 (88.9)**	**15 (93.7)**
Agitation	6 (85.7)	8(88.9)	14 (87.5)
Anger outbursts/ aggressiveness	5 (71.4)	6 (66.7)	11(68.7)
Disinhibition	3 (42.8)	2 (22.2)	5 (31.2)
Personality changes/regression	4 (57.1)	3 (33.3)	7(43.7)
Repetitive or stereotypical behaviours	3 (42.8)	1 (11.1)	4 (25)
Eating	**2 (28.6)**	**4 (44.4)**	**6 (37.5)**
Hyperphagia	1 (14.3)	0 (0)	1 (6.2)
Reduced appetite	1 (14.3)	4 (44.4)	5 (31.2)
Sleep patterns *	**7(100)**	**5 (55.5)**	**12 (75)**
Insomnia	7(100)	2 (22.2)	9 (56.2)
Hypersomnia	0 (0)	2 (22.2)	2 (12.5)
Sleep walking	1 (14.3)	1 (11.1)	2 (12.5)
Vivid dreams	0 (0)	2 (22.2)	2 (12.5)
Speech	**5 (71.4)**	**4 (44.4)**	**9 (56.2)**
Disorganized speech	2 (28.6)	1 (11.1)	3 (18.7)
Echolalia	2 (28.6)	0 (0)	2 (12.5)
Mutism	1 (14.3)	1 (11.1)	2 (12.5)
Pressure of speech	1 (14.3)	1 (11.1)	2 (12.5)
Mood symptoms	**6 (85.7)**	**6 (66.7)**	**12 (75)**
Irritability	1 (14.3)	2 (22.2)	3 (18.7)
Mood liability	4 (57.1)	4 (44.4)	8 (50)
Anxiety	1 (14.3)	2 (22.2)	3 (18.7)
Psychotic symptoms	**5 (71.4)**	**8 (88.9)**	**13 (81.2)**
Delusions	4 (57.1)	5 (55.5)	9 (56.2)
Paranoid ideas	3 (42.8)	4 (44.4)	7 (43.7)
Capgras	0 (0)	2 (22.2)	2 (12.5)
Grandiose ideas	1 (14.3)	0 (0)	1 (6.2)
Hallucinations	**5 (71.4)**	**7 (77.8)**	**12 (75)**
Visual hallucinations	4 (57.1)	6 (66.7)	10 (62.5)
Auditory hallucinations	4 (57.1)	3 (33.3)	7 (43.7)
Tactile hallucinations	0 (0)	1 (11.1)	1 (6.2)

*Sleep disturbance was statistically significant for NMDAR positive AE

Table 2. Quantification of psychiatric clusters in AE

Number of symptom clusters	N Total	N NMDAR+	N NMDAR-
Presence of the four main clusters (behavioural, speech, mood and psychotic features)	7/16	4/7	3/9
Presence of three main clusters	3/16	1/7	2/9
Presence of two main clusters	6/16	2/7	4/9
Presence of one main cluster	0/16	0/7	0/9

No significant differences in psychiatric symptoms between NMDAR positive and NMDAR negative AE

Table 3. Neurological Features of AE

Symptom cluster	N	% of total cases
Headache	2	12.5
Catatonia	4	25
Delirium	13	81.2
Choreoathetoid movements	1	6.2
Dystonia	3	18.7
Dyspraxia	2	12.5
Orofacial dyskinesia	1	6.2
Ocular myoclonus	1	6.2
Rigidity	4	25
Seizures	11	68.7
Short term memory impairment	10	62.5
Tremor	3	18.7
Weakness	1	6.2

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