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Mini Review

Autoimmune Encephalitis in Children: A Short Review

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Abstract

Autoimmune encephalitis (AE) comprises an expanding group of clinical syndromes that can occur at all ages, but preferentially affect younger adults and children. These disorders associate with antibodies against neuronal cell surface proteins and synaptic receptors involved in synaptic transmission, plasticity, or neuronal excitability. The spectrums of symptoms include psychosis, catatonia, alterations of behaviour and memory, seizures, abnormal movements, and autonomic dysregulations. Inflammatory findings in the cerebrospinal fluid may be present. Magnetic resonance imaging (MRI) may also demonstrate abnormalities for better diagnosis, particularly on fluid-attenuated inversion recovery or T2-weighted images. Patients may initially be diagnosed with idiopathic encephalitis, likely viral but with negative viral studies. Autoimmune encephalitis should be included in the differential diagnosis of any patient, especially if young, with a rapidly progressive encephalopathy of unclear origin. AE is well responsive to immune therapy, with prompt diagnosis and treatment strongly beneficial.

Keywords: Autoimmune encephalitis; NMDA; Steroids

Abbreviations: AE: Autoimmune encephalitis; MRI: Magnetic Resonance Imaging

Introduction

Encephalitis refers to an inflammatory disorder of the brain causing disastrous symptomatologies. The causes of encephalitis are numerous but finding a causative agent is always a difficult task. A study by the California Encephalitis Project, a centre focused in the epidemiology and aetiology of encephalitis, found that 63% of the patients remained without an aetiology after a battery of tests for 16 potential infectious agents [1]. Recently many auto antibodies are discovered who target specific antigens in the CNS and cause features of clinical encephalitis [2]. The immunological trigger of autoimmune encephalitis is varied and in many cases yet to be established. In some patients the presence of a systemic tumour that expresses the target neuronal/synaptic proteins appears to be important, but it's more common in adult age groups. Any immunological type of autoimmune encephalitis can have a relapsing course and therefore the diagnosis of these disorders should be considered in patients with a past history of encephalitis or relapsing encephalopathy [3-8] (Table 1).

Table 1: classification, mechanism and salient features of autoimmune encephalopathy.

	Mechanism	Features	Diagnosis	Treatment
Demonstrated immune mechanism				
Anti NMDAR Immune mechanism[3]	Ab againstNR1 subunit of NMDAR. Disrupt function by cross linking and internalization of receptors	Psychosis, seizures, dyskinesia, autonomic dysfunction[4]	EEG: abnormal; "extreme delta brush" pattern[6] MRI: nonspecific findings CSF: pleocytosis and/or increased protein in >80%	Immunotherapy Second line drug: rituximab, cyclophosphamide

Limbic encephalitis[7,8]	Antibodies against intraneuronal antigens: Hu, Ma2, amphiphysin, GAD Antibodies against synaptic antigens: GABABR, mGluR5	Severe short-term memory loss, seizures	EEG: temporal lobe epileptic activity; slowing MRI: increased T2 and FLAIR signal in limbic region CSF: pleocytosis and increased proteins	Immunotherapy Good response to cell surface autoantigens
Strongly suspected immune mechanism				
Opsoclonusmyoclonus and other cerebellarbrainstem encephalitis[9]	Anti Hu ab found sometimes Found in neuroblastoma and teratoma	Opsoclonus, irritability, ataxia, Fall, myoclonus, Tremor	CSF - B-cell activation MRI: cerebellar atrophy	Immunotherapy Mild response to neuroblastoma associated Good response to teratoma associated
Bickerstaff encephalitis[10]	GQ1b antibodies	Ophthalmoplegia, ataxia, hyperreflexia.	MRI: T2-signal abnormalities in the brainstem, thalamus, and cerebellum) NCS: predominant axonal degeneration, less frequent demyelination	good outcome with steroids, IVIG and/or plasma exchange
Hashimoto encephalitis[11]	TPO antibodies	Stroke-like symptoms, tremor, myoclonus, aphasia, seizures, ataxia	EEG: slow activity CSF: elevated protein	Steroid-responsive
Rasmussen encephalitis[12]	Most likely immune mediated (unclear mechanism)	partial seizures, cognitive decline, focal deficits, brain hemiatrophy	MRI: progressive unilateral hemispheric atrophy	Limited response to Immunotherapy
Basal ganglia encephalitis	D2R ab in some cases	seizure and behavior disorder	Variable basal ganglia T2/FLAIR abnormalities	Mostly monophasic, can relapse
Possible immune mechanism				
[C]LIPPERS: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids[13]	Unknown	Episodic diplopia, symptoms of brainstem and spinal cord dysfunction	MRI: enhancement Of pons and medulla, brachium pontis, cerebellum, midbrain, and, occasionally, spinal cord	Steroid responsive
ROHHAD: rapid onset obesity with hypothalamic dysfunction,hypoventilation and autonomic dysregulation[14]	Unknown Associated with neural crest tumors	Rapid onset obesity, hyperphagia, abnormal behavior,	MRI, usually normal	Limited response to immunotherapy
autonomic dysregulation[14]		autonomic dysfunction, and central hypoventilation		

Management

Despite the severity of many patients' symptoms, the majority of patients respond to treatment. Recovery can be slow and some disorders have a tendency to relapse. Corticosteroids and/or intravenous immunoglobulins (IVIg) or plasma exchange are considered first-line therapies and should be considered in all patients. If the AE is associated with paraneoplastic picture then the primary tumor should be treated first. Patients who do not respond to the first-line therapies second-line immunotherapy with rituximab and/or cyclophosphamide should be started very soon [9-15].

Conclusion

AE is not so uncommon in children. They mostly mimic different psychiatric diseases. Most of the diseases are treatable. Steroid and other immunotherapy form primary treatment modality. Any child with features of unexplained psychosis, dementia, seizure, autonomic dysfunctions etc should be suspected for possibility of AE after ruling out other common causes. All neurophysicians as well as pediatricians must possess adequate knowledge about AE for early diagnosis and better management

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