Speech and language abnormalities and their outcomes in autoimmune encephalitis in children: A case series

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Sri Lanka Journal of Child Health, 2023; **52**(1)**:** 114-117
DOI: http://dx.doi.org/10.4038/sljch.v52i1.10487
(Key words: Autoimmune encephalitis, Speech disorders, Rehabilitation, Cognition)

Introduction

Autoimmune encephalitis (AIE) is responsible for up to 40% of admissions with clinical features of encephalitis[1]. It manifests as a myriad of clinical symptoms[2]. Speech disorders / deficits are increasingly recognized, in children presenting with N-methyl-D-aspartate receptor (NMDAR) encephalitis[3]. Frequent evaluation and intervention for speech and language and cognitive rehabilitation help improve their overall long-term outcome[3-5]. We describe a case series of six children with AIE with deficits in speech and language as the dominant manifestation and their long-term outcome with rehabilitation.

Case reports

Six children fulfilling the diagnostic criteria for 'Probable AIE' based on classification by Graus F, *et al*[6] (Table 1), were selected following clinical, laboratory, electroencephalography and neuro-imaging evaluation. All six children presented to University Paediatric Unit, Lady Ridgeway Hospital, Colombo between 2017 and 2020 and were prospectively followed up.

Table 1: ***Diagnostic criteria for possible autoimmune encephalitis***[6]

Diagnosis can be made if all three following criteria are met:
1. Subacute onset (Rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status*, or psychiatric symptoms
2. At least one of the following: • New focal central nervous system findings • Seizures not explained by previously known seizure disorder • Cerebrospinal fluid pleocytosis (white blood cell count of more than five cells per mm^2) • Magnetic resonance imaging (MRI) features suggestive of encephalitis#
3. Reasonable exclusion of alternative causes

**Altered mental status is defined as decreased or altered level of consciousness, lethargy, personality change.*
 # Brain MRI hyperintense signal on T2-weighted fluid attenuation recovery sequences highly restricted to one or both medial temporal lobes (limbic encephalitis), or in multifocal areas involving grey matter, white matter or both compatible with demyelination or inflammation

Case 1

A previously healthy 13-year-old girl presented with inappropriate use of language, crying spells, auditory and visual hallucinations, followed by progressive drowsiness and altered behaviour. She developed orofacial dyskinesia, spitting and subsequent loss of speech. On recovery from her comatose stage with treatment, receptive language showed speedy improvement but there was marked delay in retrieval of speech. Initially, high frequent single words emerged in her speech. This was however, restricted by echolalia and verbal dyspraxia. She started using hand gestures to communicate her needs. The AIE resulted in a significant decline in her working memory and verbal fluency, directly affecting her communication abilities. After three years of rehabilitation, she still had significant issues in social communication, emotional regulation, learning skills in mathematics and adjustment skills which were affecting her schooling.

Case 2

A 12-year-old girl was admitted with complaints of abnormal behaviour and communication difficulties. This rapidly developed into disoriented speech, receptive aphasia, orofacial dyskinesia and expressive speech regression except for infrequent sudden verbal outbursts. As her conscious status improved with intravenous (IV) immune therapy, speech and language rehabilitation was commenced. Regression in cognitive skills extensively affected her communication and learning abilities.

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(Received on 05 July 2022: Accepted after revision on 19 August 2022)
The authors declare that there are no conflicts of interest
Personal funding was used for the project.

Improvement in memory was seen after discharge, contributed to by the stimulating exposure of the home environment. In expressive language, single words emerged in the form of echolalia but was largely affected by semantic and phonemic paraphasia. After three years of symptom onset, she is continuing speech therapy for persisting auditory processing disorder, paraphasia, working memory and restricted narrative language skills. She also receives individualized educational support for impaired abilities in reading and writing.

Case 3

A 3-year-old boy presented with progressive loss of language skills over 2-3 weeks. He exhibited speech regression manifesting as restricted use of verbal communication with marked changes in his intonation patterns, agitation and behavioural alterations. He was disoriented and irritable throughout hospital stay and was not compliant to speech and language assessments attempted after two weeks of clinical course. Oral movements such as tongue thrust, lip smacking and teeth grinding could be observed. At one-month post-discharge, he had regained expressive language skills although parents were concerned about persisting attention deficits and temper tantrums. After two years of follow up, at 5 years of age, he shows reduced attention span, pragmatic language delay, atypical speech pattern. including echolalia and prosodic deficits.

Case 4

A 7-year-old healthy girl, presented with fever and emotional lability for one week. In second week, she developed aphasia, oral dyskinesia and convulsions. Assessment revealed effect on cognition, expressive language, behaviour and social skills. With intervention for speech and language skills, speech patterns gradually emerged with delayed echolalia and anomia in high frequency vocabulary. Her social skills and behaviour improved after returning to the home environment after two weeks of intervention. Review after 8 months revealed that her learning skills were affected, mainly pertaining to inattention. She also exhibited disinterest in interacting or carrying out a conversation which, according to mother, was not present before the AIE. Continued speech and language therapy for past one and half years has resulted in marked improvement in attention and pragmatic language skills.

Case 5

A 12-year-old girl presented with fever and altered behaviour which later developed into speech regression, verbal outbursts and involuntary orofacial movements. After initial IV immunotherapy, her assessments revealed inattention, impaired social connection, aphasia and restricted oral movements for speech and feeding. Intervention was started with the goals of improving connection with caregiver, reestablishing interest in activities which were gradually stepped up to work on attention, memory, receptive language and speech pattern. She is the only child in the case series who was able to retrieve all the skills which were affected at the completion of the clinical course and rehabilitation programme at six weeks from initial presentation. Follow-up after three months showed that she could maintain a conversation with intelligible speech and could narrate a personal experience without disruption to language flow. She was later discharged with an education plan to support loss of learning during hospitalization and recovery.

Case 6

A 2 year and 4-month-old boy presented with language loss as the primary reason for medical attention. He also had accompanying behaviour abnormalities, vocal outbursts and orofacial dyskinesia. This was later complicated by language regression, irritability and excessive crying. Reduction in atypical oral movements and irritability were observed after starting immunotherapy. Inattention and word finding difficulties were persisting on completion of the clinical course. Even after two and half years from the AIE, difficulties are noted in his conversational skills, social interaction and ability to engage in structured learning activities. At present, he is continuing speech therapy while attending preschool, with no concerns raised over his cognitive functions.

Characteristics of AIE in the 6 cases are shown in Table 2.

Mean age at presentation was 8.2 ± 4.4 years. Whilst 5 of the 6 patients had NMDAR-antibody testing, none were tested for other autoantibodies. Whilst 5 children had normal language development and age-related cognitive functions prior to onset of encephalitis, one had an isolated delay in expressive language. All 6 were commenced on IV high dose methyl prednisolone and 2g/kg of IV immunoglobulins. Five required subsequent plasma exchanges; second line drugs such as rituximab were required for two patients. Mean duration of follow up for speech rehabilitation was 1.6 ± 0.7 years.

Table 2: Characteristics of autoimmune encephalitis in the 6 patients in this case series

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age at presentation	13 years	12 years	3 years 2 months	7 years	12 years	2 years 4 months
Gender	Female	Female	Male	Female	Female	Male
Duration of illness prior to admission	1 day	3 days	11 days	10 days	7 days	14 days (Speech delay noted from infancy
Total duration of hospital-stay	12 weeks	8 weeks	2 weeks and 2 days	3 weeks	6 weeks	6 weeks
Clinical features	Behavioural disturbances, convulsions, movement disorder, encephalopathy, marked language impairment	Abnormal behaviour, altered sleep pattern, increasing drowsiness, altered consciousness, seizures, dyskinesia	Speech regression, behavioural changes, convulsions, orofacial movements.	Psychosis, frequent convulsions, including status epilepticus movement disorder dystonia	Psychosis (fear, aggression, delusions), orofacial movements, encephalopathy, convulsions, dystonia	Behavioural changes, speech regression, Convulsions, orofacial dyskinesia, no drowsiness
Need for ICU care	Yes (IPPV)	No	No	Yes (IPPV)	Yes	No
Anti-neuronal antibodies	NMDAR-ab negative	Not done	NMDAR-ab negative	NMDAR-ab negative	NMDAR-ab positive	NMDAR-ab negative
Treatment	High dose MPNL, IVIG Plasma exchange	High dose MPNL, IVIG Plasma exchange Rituximab	High dose MPNL, IVIG, plasma exchange	High dose MPNL, IVIG, plasma exchange, Rituximab	High dose MPNL, IVIG, plasma exchange, MMF	High dose MPNL IVIG
Long-term morbidity	Social communication, emotional regulation, learning difficulties, adjustment issues in school	Auditory processing disorder, cognitive deficits, impaired narrative skills in language, learning difficulties	Attention deficit, language impairment, deficits in prosody, echolalia	Epilepsy, inattention, impaired conversational skills. learning difficulties	Gap in some aspects of learning due to long term hospitalization	Delayed speech, attends pre-school. Intervention designed for features of autism spectrum disorder
Duration of follow up	3 years	3 years	2 years	1 year and 6 months	1 year and 3 months	1 year
Relapses	Nil	Nil	Nil	Nil	Nil	Nil
Tumour association	Nil	Nil	Nil	Nil	Nil	Nil

IPPV: Intermittent positive pressure ventilation, MPNL: Methyl prednisolone, NMDAR- N-methyl-D-aspartate receptor

Discussion

This case series focuses on the spectrum of speech and language effects of children presenting with AIE. These are subsequently linked with cognitive and learning difficulties persisting over long-term[3,4,7]. Although all 6 achieved normal motor functions, cognitive and language functions returned to normalcy only in one. Their follow up has shown that comprehensive rehabilitation helps to acquire lost functions if instigated early and repeatedly. Evidence on language dysfunction in AIE is limited. It is highlighted that speech dysfunction is commoner among children and is mainly reported in conjunction with NMDAR-Ab AIE, affecting 57-70% of children[1]. Speech deficits are noticeable in early phase of illness. In 81 children with NMDAR-Ab encephalitis reported by Florance N, *et al*[1], 57% had severe speech deficits, although speech reduction as presenting manifestation was noted only in 3%. The rare situation of increased speech at initial stages, deteriorating over time, has been described in a girl with NMDAR-Ab encephalitis[4]. In another case of cortical aphasia and apraxia which were the main clinical presentation of an NMDAR-Ab encephalitis[7], along with oral apraxia, language difficulties ranged from phonemic paraphasia, anomia, impaired spontaneous speech, receptive aphasia to alexia and agraphia[7].

The other important aspect highlighted in the literature is the impact on cognition and the importance of intensive rehabilitation even after the completion of immunotherapy. Case reports, exclusively focusing on cognitive outcome of children with NMDAR-Ab encephalitis, reveal impairments in attention, verbal fluency, working memory, processing speed and social cognition, highlighting need for close neuropsychological monitoring[8,9.] A case report on neuropsychological outcomes of two children with anti-NMDA-receptor encephalitis, ranging from receptive and expressive aphasia to impaired early executive functions, further emphasized the benefit of comprehensive neuropsychological assessments and well-planned rehabilitation[5].

Conclusion

There is a gap in the understanding of specific communication disorders occurring in AIE and their long-term effect on functional recovery. We believe that the descriptions of our six patients will add to current understanding on the spectrum of speech and language related presentations in AIE.

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