

The Landau-Kleffner syndrome

The Landau-Kleffner syndrome is a rare disorder characterised by an acquired receptive and expressive aphasia and epileptic seizures¹⁻⁴; it is also known as 'a syndrome of acquired aphasia with convulsive disorder'³ or 'acquired aphasia of childhood with epilepsy'.⁵ It is defined on the basis of specific clinical and electroencephalography (EEG) criteria. It is almost certainly under recognised and therefore under diagnosed, an observation which has at least been partly responsible for the recent inception of a specific self help or support group for parents with affected children.

Epidemiology

The incidence and prevalence of Landau-Kleffner syndrome are difficult to determine; since its first description in 1957, almost 200 cases have been reported,⁵ the majority demonstrating a consistent pattern in terms of electro-clinical symptomatology and outcome. Boys appear to be more affected in an approximate ratio of 2:1.

Clinical features

Over 50% of children present between the ages of 3 and 8 years with an apparent loss of auditory verbal understanding (agnosia) and speech,^{5,6} and deafness is frequently the initial considered diagnosis (this is the predominant reason why Landau-Kleffner syndrome is diagnosed late). In the vast majority of children with the syndrome the agnosia/aphasia is acquired, occurring in a previously normal child, although rarely the comprehension and speech difficulties have been considered to have been 'developmental' in onset.⁷ The agnosia is for common, familiar noises (including the barking of a dog, sounding of a car horn, or ringing of a door bell) as well as for the spoken word. Impairment of comprehension and speech may be partial or more commonly total, representing a complete aphasia. The agnosia and aphasia usually develops over days but it may develop over weeks. Rarely, other neuropsychological problems such as apraxia may also develop in Landau-Kleffner syndrome.⁸ Non-verbal intelligence scores are usually within normal limits, emphasising the specific language and non-global nature of the cognitive deficit.

The remaining 40-50% of children present with epileptic seizures,^{5,9} either some weeks before or coincidental with the onset of aphasia. In a significant proportion of cases (20-30%), seizures develop subsequently some months after the onset of the comprehension and speech difficulties. Seizures are reported to occur in 70-75%⁵ of all patients with Landau-Kleffner syndrome, at some point in the evolution of the condition, and are usually complex partial (with focal motor and atypical absence symptomatology), generalised tonic-clonic and atonic ('drop') seizures; tonic and myoclonic seizures are rare.^{5,9,10} Seizures may be infrequent or repeated (nocturnal) with (rarely) episodes of convulsive and non-convulsive status epilepticus.

The final clinical manifestation of Landau-Kleffner syndrome is with a behaviour disturbance, which may occur in almost three quarters of patients with the syndrome, and is frequently severe.^{2,5,11} Explanations for the behavioural difficulties may include a primary functional disinhibition at a limbic or diencephalic level or as a secondary (frustration induced) effect due to loss of comprehension and language, or both. 'Hyperactivity' and apparently

unprovoked outbursts of rage and aggression may also occur; rarely, the child may appear autistic or psychotic¹¹ and risk exclusion or suspension from school. It is this aspect that often leads to an initial diagnosis of a primary conduct disorder and referral to a psychiatrist.

The electroencephalogram

Typical EEG findings include repetitive spikes and spikes and slow waves of high amplitude occurring at 1-3 Hz, unilaterally, bilaterally, or multifocally over the temporal, temporoparietal, or parieto-occipital regions,^{5,6,10} without a clear hemispheric dominance. These findings are more easily demonstrated during sleep onset and slow wave sleep, with the paroxysmal activity becoming more bilateral, symmetrical and continuous, often persisting for many hours. This latter finding is also seen in another epilepsy syndrome termed continuous spike waves or electrical status epilepticus of slow wave sleep,¹² which also shares some of the clinical features of Landau-Kleffner syndrome; whether the two are distinct entities or fall within the spectrum of a common underlying disorder is unclear and is outside the brief of this paper.

In Landau-Kleffner syndrome the relationship between the EEG findings and agnosia/aphasia and seizures is not entirely clear.^{4,13} Changes in comprehension and speech may be reflected in alterations in spike and wave EEG activity but this is not consistent. However, it does appear that the paroxysmal EEG activity may precede the development of clinically witnessed epileptic seizures.

Pathogenesis

The pathogenesis and aetiology of Landau-Kleffner syndrome are unknown, probably complex, and have been reviewed in detail elsewhere.^{4,6,13} The agnosia/aphasia may represent an 'epileptic' phenomenon caused by paroxysmal spike and slow wave activity within the appropriate temporal lobe.^{5,10} However, this may be difficult to accept in the absence of clinically occurring epileptic seizures. An alternative hypothesis is that an underlying brain pathology (of whatever nature) in an area or areas concerned with speech may be responsible both for the comprehension/speech difficulties and abnormal EEG findings and subsequently for the development of epileptic seizures. What precisely is this 'underlying pathology' is also unclear. Children have developed normally and are usually healthy with no preceding illness/infection before the onset of the syndrome and there is no obvious genetic predisposition. Inflammatory and postinfectious causes have been implicated but have not been consistently demonstrated or confirmed by neuroradiological or neuropathological investigations, including cerebrospinal fluid analysis. Cerebral angiography has rarely shown evidence of cerebral arteritis¹⁴ and most recently positron emission tomography has demonstrated non-specific 'metabolic' abnormalities within the temporal lobes of patients with Landau-Kleffner syndrome.¹⁵ It remains unclear as to whether the underlying pathology is simply functional or due to a subtle structural lesion; the available evidence and the natural history of Landau-Kleffner syndrome would tend to suggest the former hypothesis, possibly on the basis of an impaired or dysfunctional 'loop' within the speech cortex: hearing-verbal integration-spoken language.^{5,6,13}

Diagnosis

The diagnosis of Landau-Kleffner syndrome depends largely on being aware that the condition exists, and its usual pattern of presentation. Differential diagnoses include deafness, an acute behavioural or psychiatric disorder (including elective mutism), or epilepsy in which there is a transient postictal dysphasia or aphasia but without the profound agnosia and behavioural dysfunction.⁴ Children are frequently referred initially to an ear, nose, and throat specialist, audiologist,¹⁶ or psychiatrist – with a consequent delay in diagnosis. A significant delay in establishing the correct diagnosis may lead to profound behavioural difficulties with serious consequences and marked parental anxiety. Referral to a paediatric neurologist or child development centre is recommended after a normal audiological or ear, nose, and throat assessment, or both.

Treatment

Clearly, appropriate management depends upon establishing the correct diagnosis. Epileptic seizures usually respond to conventional anticonvulsant treatment, often with a single drug; this clinical response is not necessarily accompanied by normalisation of the EEG findings.^{5 17} In contrast, the language difficulties persist and do not appear to respond to anticonvulsants.^{4 5 17} Recently, vigabatrin has successfully treated both the seizures and aphasia in one child with this disorder.¹⁸ The effect of the newer drugs including lamotrigine and gabapentin is either not known or has not been reported. Corticosteroids (prednisolone or corticotrophin (ACTH) or both) have been used with considerable (but not invariable) success on the assumption that the disorder is due to an acute or subacute encephalitis.^{5 19} However, there are no controlled data, the often fluctuating course of Landau-Kleffner syndrome makes interpretation of 'results' difficult, and adverse effects may be both frequent and severe. Nevertheless many authors currently recommend a course of high dose steroids, even for several months. The most recent therapeutic option is a neurosurgical procedure termed subpial transection.²⁰ This is designed to prevent the cortex from generating paroxysmal activity (by sectioning horizontal fibres) while preserving its physiological function (by sparing vertical fibres). Preliminary results have been encouraging but as with any neurosurgical operation, the risk:benefit issue must be considered carefully.

Finally, one cannot overstate the importance of speech therapy, special education, and rehabilitation. These measures must be introduced early, not just to address the specific and primary language difficulties but also to try and prevent the development of any secondary behavioural disturbance. Limited data suggest that *early* treatment and 'rehabilitation' is more effective.^{3 10}

Prognosis

The outcome of Landau-Kleffner syndrome depends on whether one considers the speech/language component or epilepsy. The epileptic seizures are frequently (but not invariably) controlled by anticonvulsants and tend to remit spontaneously, usually before adulthood.⁵ Very few patients experience seizures beyond the age of 15 or 16 years. In contrast, the prognosis for speech and language is variable and unpredictable; difficulties often persist throughout childhood and into adult life,^{3 17} although complete recovery may also occur in some patients.^{3 21} Not uncommonly the language and behaviour difficulties may fluctuate with frequent remissions and relapses, accompanied by corresponding EEG changes.^{5 6 10} Rarely

the aphasia may last for only a few months before resolving. A number of studies have identified a direct relationship between the age of onset and long term outcome; the younger the child (usually under the age of 5 or 6 years), the worse the prognosis for recovery of comprehension and language.^{3 10} Finally, the later the introduction of speech therapy and educational support, the worse the outcome; this may simply be a reflection of a delayed diagnosis.

Conclusion

Although the Landau-Kleffner syndrome is uncommon, there is a need for an increased awareness of the disorder, particularly among those professionals to whom are commonly referred children with acute or subacute loss of speech and language – hospital and community paediatricians, audiologists, personnel in the ear, nose, and throat department, psychiatrists, and paediatric neurologists. Once considered, the diagnosis may be confirmed by sleeping EEG activity. A short course of corticosteroids (prednisolone rather than corticotrophin) would seem reasonable but the role of the newer antiepileptic drugs requires further evaluation. Speech therapy and educational rehabilitation should be introduced as early as possible and a neurosurgical referral should be considered for those children with persisting aphasia and drug resistant seizures.

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