

LANDAU-KLEFFNER SYNDROME

Landau-Kleffner Syndrome: Course and Correlates with Outcome.

Robinson RO, Baird G, Robinson G, Simonoff E

Developmental Medicine and Child Neurology, 2001;43: 243–247

The presenting characteristics of 18 (11 female, seven male) children with Landau-Kleffner syndrome (LKS) were studied with respect to course and outcome of their condition at a mean length of 67 (SD 46) months' follow up. All had regression of receptive language (mean age of onset 4 years 9 months) and electrical status epilepticus in sleep (ESES). Length of ESES correlated strongly with length of period between onset of illness and onset of recovery ($p < 0.006$) and also with eventual receptive ($p < 0.001$) and expressive ($p < 0.007$) language. Behavior during the acute phase was severely affected in nine children and associated with frontal lobe discharges in awake electroencephalograms (EEGs) ($p < 0.004$). Age at onset was not correlated with outcome. All children had impaired short-term memory at follow up. Three children had language outcome within the normal range. No child with ESES lasting longer than 36 months had normal language outcome. These data lend support for intervention in ending ESES by 36 months using multiple subpial transection (MST) if steroids are ineffective or cause unacceptable side effects.

Multiple Subpial Transection in Landau-Kleffner Syndrome.

Irwin K, Birch V, Lees J, Polkey C, Alarcon G, Binnie C, Smedley M, Baird G, Robinson RO

Developmental Medicine and Child Neurology, 2001;43: 248–252

We have considered multiple subpial transection (MST) as a treatment option for Landau-Kleffner syndrome

(LKS) for the past 6 years. The effect of this technique on language and cognitive ability, behavior, seizures, and EEG abnormalities is analyzed here. Five children (4 males, 1 female; aged 5.5 to 10 years) underwent MST with sufficiently detailed pre- and postoperative data for analysis. Behavior and seizure frequency improved dramatically after surgery in all children. Improvement in language also occurred in all children, although none improved to an age-appropriate level. All five had electrical status epilepticus in sleep (ESES) before surgery, which was eliminated by the procedure. One child has had an extension of his MST due to the recurrence of ESES and accompanying clinical deterioration with good effect. An attempt is made to set the effect of MST against the natural history of the condition. MST is an important treatment modality in LKS, although the timing of this intervention and its effect on final language outcome remains to be defined.

COMMENTARY

Despite its relatively low incidence and prevalence, the Landau-Kleffner Syndrome (LKS) is a neurological disorder that, in the last decade, has generated a great degree of interest, coupled with significant controversy with respect to its diagnostic criteria and treatment. The article by Robinson et al. is therefore, a timely and important contribution, as it again reminds us of the clinical characteristics of this disorder and sheds light on the course and some of the predictive variables of its outcome.

With respect to the clinical phenomena of the 18 children in this study, it is worth emphasizing the following characteristics: (1) the onset of language dysfunction occurs after age appropriate language functions have developed; (2) nonverbal cognitive functions are essentially preserved; (3) behavioral problems may be severe in some of these children (above all in the presence of epileptiform activity involving frontal lobe structures). Yet, this study helped to dispel the frequently held misconception that LKS may be associated with (or causes) autistic symptoms. Careful consideration of such criteria may avoid a false-positive diagnosis of LKS.

The majority of children included in this study failed to recover language function completely. Of notice was the unlikely recovery of language among children with an electrographic persistence of a pattern of electrical status epilepticus in sleep (ESES) for a period longer than three years. This important finding provides the clinician with guidelines to rely upon when considering a surgical option. However, we must keep in perspective that the discouraging outcome in language functions observed in many of these 18 patients is not universal to all children with LKS and may be a function of the referral pattern to tertiary centers of children with more severe forms of pathology. Let us remember that spontaneous recovery of language functions is a well-known phenomenon in some of the children with LKS.

In 1995, Morrell et al. (1) reported on the use of the surgical technique, multiple subpial transection (MST) in 14 children with LKS and in 1999, Grote et al. (2) described the changes in language function measured with neuropsychometric testing in 12 of these 14 patients. Irwin et al. describe the impact of MST on language and behavior of 5 children with LKS. In both patient series MST appeared to yield an early and quite significant improvement in behavior, while recovery of language functions was slower to become apparent. The difference in the timing of improvement between behavior and language functions suggests that behavior problems may represent an expression of a paraictal phenomenon (3). Language deficits, on the other hand, may result from a complex disruption of synaptic connections in language cortex by the constant "bombardment" of epileptic activity, which may require a longer time to "be repaired" (4). Morrell et al. suggested that such repair is only possible within a "window of time" before the stage of plasticity of the language system is over.

The extent of language recovery differed between the two patient series. While four of the 12 children reported by Grote et al. (2) regained completely language functions, none of the five children in the Irwin et al. study did. This difference may be explained by a longer postsurgical follow-up in the Grote et al. study, as he clearly demonstrated a correlation between degree of language improvement and duration of post-surgical follow up. The second cause may reside in an earlier surgical intervention after the start of symptoms in the Grote et al. study, as that study shows an inverse relationship between recovery of receptive language functions and time between onset of symptoms to surgery. This observation seems to be in agreement with the Irwin et al. data and those presented in the companion manuscript by Robinson et al., also reviewed in this issue. Indeed, recovery of language functions either spontaneously or after MST seems to be unlikely after 3 years of electrical status epilepticus in sleep (ESES).

This raises the important question on the timing of surgery. In other words, how long should clinicians wait for a

spontaneous recovery (well known to occur in some children with LKS) before considering a surgical option? The Irwin et al. data and the Robinson et al. data clearly suggest that in the appropriate patient (see below) MST should be carried out before three years from the onset of ESES. After a comprehensive review of the literature, Morrell et al. concluded that persistence of language deficits without any sign of improvement for more than one year is likely to be followed by a lifelong linguistic handicap (4). Thus, it would seem reasonable to consider the possibility of surgery in children with no documented improvement for a period of 12 to 18 months.

It is necessary to emphasize the need to properly select patients for MST, as not every child is candidate for surgery. The ideal patient is one with a classic form of LKS, a well-localized epileptogenic zone unilaterally in intra- and/or perisylvian cortex, without evidence of cross-the-board cognitive deficits (that is, without impairment of nonverbal cognitive functions). Children with bilateral independent sources of epileptic activity, documented by methohexital suppression test or intracarotid amytal test, may require bilateral surgeries, but the timing between the surgeries and outcome of these children is yet to be established. On the other hand, some children, as shown in both case series reviewed here, required a repeat surgical procedure in the same area to completely abolish seizure activity. Finally, it should be emphasized again that MST should not be used for the management of language deficits of children with autistic regression, as the data published in peer reviewed journals seem to suggest only a transient and limited improvement (5).

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References

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