Generalised Epilepsy in Hypothalamic Hamartoma; Evolution and Postoperative Resolution

The following is a summary of an article written by Drs Harvey, Rosenfeld, Freeman, Wrennall, Bailey and Berkovic, published in Neurology in 2003.

In a surgical series of 12 patients with hypothalamic hamartoma and intractable epilepsy, the authors documented a parallel progression of epileptic seizures and EEG abnormalities leading up to surgery.

It was noted that typically, gelastic seizures in this syndrome are not recognized as epileptic events until features other than the brief laughter-like vocalization develop. Whereas gelastic seizures in the 12 patients presented in this series began on average at 6 months of age, complex partial and focal motor features developed on average at 4 years, and tonic seizures on average at 6 years.

At least a third of patients had normal scalp EEG well after their epilepsy was suspected or diagnosed. EEG patterns typical of SGE developed later, in conjunction with tonic seizures. Developmental disability, behavioural disturbance, or both developed in all 12 children.

The authors demonstrated that this triad of refractory generalized seizures, slow SW, and neurobehavioral impairment is potentially reversible after hypothalamic hamartoma resection, with remission of generalized seizures in 11 of 12 cases associated with a marked reduction in interictal SW activity and neurobehavioral improvements in most.

Interestingly, the decrease in interictal SW was not immediate following resection of the hamartoma, and the resolution of the generalized seizures took up to 6 months in some cases. Delayed seizure remission has also been described following other surgical approaches to the treatment of this unusual syndrome. (cf GKS)

Medics are publishing more and more on the origin of seizures in patients with hypothalamic hamartoma. Gelastic seizures are now known to originate in the intrinsically epileptogenic hamartoma. In contrast, the authors point out that there is no evidence that the generalized seizures that develop in this syndrome originate in the hamartoma, and there is some evidence to the contrary; generalized onset of tonic seizures without primary involvement of the hamartoma has been recorded in patients undergoing stereo video-EEG monitoring including depth electrodes inserted within the hamartoma. Nevertheless, increasing reports of the abolition of all seizure types in patients undergoing microsurgical resection, radiofrequency coagulation, or irradiation of hypothalamic hamartomas indicate an intrinsic role for the hamartoma in SGE.

The authors report that their findings, however, add weight to the notion that slow SW is an extraselesional phenomenon, stating that the more important aspect of their intraoperative studies is the observation that cortical and scalp slow SW persisted after resection of the hamartoma. Together with the absence of synchronous scalp and hamartoma discharges, these findings suggest a secondary generator of interictal slow SW activity that is interictally independent of the hamartoma.
The authors hypothesise that the concept of secondary epileptogenesis may provide a framework for understanding how a focal epileptogenic lesion could give rise to the generalized seizures and slow SW that gradually evolved and postoperatively gradually resolved in their patients, drawing a comparison with Morrell’s series. Morrell, in his presentation of patients with cerebral tumors and epilepsy in whom secondary epileptogenesis was suspected, described three stages of this process. The first stage is heralded by the appearance of the mirror focus, whose IED are totally dependent on the primary focus, removal of which results in immediate cessation of the secondary spikes. As the process advances, the secondary site becomes capable of generating seizures and its IED do not temporally coincide with those of the primary focus. In the intermediate stage, removal of the primary focus results in a gradual running down of the secondary focus rather than in the immediate disappearance of IED. Seizures may halt abruptly or continue to decrease in frequency for months to years. If the process is allowed to continue, however, the secondary focus becomes fully autonomous and is irreversibly unaffected by the removal of the primary lesion.

The postoperative clinical course in 11 of 12 of the authors’ series of patients with SGE is said to be analogous to that described by Morrell for the patients he classified as having the intermediate form of secondary epileptogenesis. The lack of an immediate effect of hamartoma resection on interictal SW, the subsequent improvement in scalp EEG recordings, and the delayed resolution of generalized seizures in five patients is also consistent with such a process.

The authors argue that acknowledgment of the potential role of secondary epileptogenesis has implications for the treatment of children with epilepsy associated with hypothalamic hamartomas. They emphasise the argument for undertaking surgical treatment before the stage of irreversibility, conceding that it is debatable whether such a stage exists for this condition. However, they assert that given the demonstrated ineffectiveness of medical treatment through AEDs, intervention before the development of other partial and generalized seizures is desirable, particularly given the fact that the cognitive and behavioural deterioration associated with epilepsy in this syndrome may be largely a result of the seizures and the interictal epileptic disturbance.

Considering, however, that there are patients with hypothalamic hamartoma and chronic epilepsy who do not develop SGE, the authors concede that the selection of children for surgical intervention and the timing of this is a complex issue and is not fully addressed by their study. The SGE features in patients with hypothalamic hamartoma have previously been attributed to either widespread occult cerebral dysgenesis or irreversible cerebral damage. The authors have shown that these SGE features are partly functional in nature and potentially reversible. These observations may be relevant to epilepsy surgery in other children with generalized epileptic encephalopathies and focal cerebral lesions.

SGE – Symptomatic generalised epilepsy
SW – Slow spike-wave
IED – Interictal epileptiform discharges