Intravenous Methylprednisolone Pulse Therapy in a Young Girl with Intractable Absence Seizures

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The medical treatment of epilepsy is effective in the majority of patients, resulting in seizure control and a normal lifestyle. However, about 25% of patients are refractory to treatment with anti-epileptic drugs. In these patients, other therapeutic measures are considered, such as epilepsy surgery, vagal nerve stimulation, ketogenic diet, and drugs rarely used in epilepsy such as steroids and immunoglobulins. Steroids and adrenocortical hormones have been used, particularly in infantile spasms (West syndrome). In addition, there are a few reports on the use of oral steroids in children with other forms of intractable epilepsy, including absence seizures [1,2]. But there are no reports on the use of intravenous steroid pulse therapy in children with refractory absence epilepsy.

We present a young girl with absence seizures resistant to all syndrome-appropriate anti-epileptic drugs, who showed a dramatic clinical and electrophysiological improvement after IV pulse therapy with methylprednisolone.

PATIENT DESCRIPTION

A 7 year old girl with absence seizures was admitted to the pediatric neurology department because of multiple daily clusters of absence seizures. The patient was born after an uncomplicated pregnancy by spontaneous delivery and an uneventful perinatal period. Growth and development were normal and she was in second grade in a regular school. Her medical history included right nephrectomy because of a dysplastic kidney.

Since she was 5 years old her parents noted multiple daily episodes of staring, sometimes associated with rhythmic movements of the eyelids lasting 10–15 seconds. An electroencepalograph study revealed the typical pattern of generalized three per second spike and wave complexes. Therapeutic trials with ethosuximide 20 mg/kg/day, valproic acid 50 mg/kg/day, lamotrigine 5 mg/kg/day and topiramate 5 mg/kg/day failed to control the seizures.

On admission, the physical and neurologic examinations were within normal limits. Treatment with levetiracetam 50 mg/kg/day was begun and a subsequent video-EEG study recorded numerous clinical and electrical epileptic episodes of absence seizures. At that point, an attempt was made to introduce the ketogenic diet. However, the diet was stopped after a week due to poor compliance of the patient and the family.

Subsequently, a 5 day course of IV methylprednisolone 30 mg/kg/day was started, with normal vital signs and blood electrolyte values throughout treatment. A dramatic clinical improvement was observed 2 days after the last dose. The video-EEG study revealed a significant decrease in the amount of epileptiform activity, now noted mostly during sleep. At discharge, the patient was advised to continue with a combination of daily levetiracetam and oral prednisone 2 mg/kg/day for 2 consecutive days each week for another 6 weeks. No adverse effects were reported and the patient continued to be seizure-free during a follow-up period of 8 months.

COMMENT

Adrenocorticotropic hormone and corticosteroids have been used for many years in the treatment of infantile spasms (West syndrome). According to retrospective studies, both drugs are effective and can lead to reduced frequency or cessation of infantile spasms and to normalization of the EEG in 50–75% of patients, usually within a week or two [3]. Several studies report similar efficacy of ACTH and prednisone, although others suggest a better outcome in patients treated with ACTH.

The anticonvulsant mechanism of action of corticosteroids is unknown. ACTH has both endocrine and neuromodulatory properties. Its effects on infantile spasms could be exerted systemically via the brain adrenal axis with suppression of corticotropin-releasing hormone or through a direct anticonvulsant effect [1,4,5].

It was suggested that ACTH affects membrane stabilization and modulates neuronal excitability via the gamma-

EEG = electroencepalograph

ACTH = adrenocorticotropic hormone

aminobutyric acid receptor, while others postulated that ACTH acts on the cholinergic system. The use of corticosteroids in the treatment of other epileptic syndromes beyond infancy has been limited and only a few studies have been reported [1,4,5]. Snead and colleagues [3] described their experience in 64 children with intractable epilepsy other than infantile spasms, treated with either ACTH or prednisone. Most patients had myoclonic seizures. Treatment was successful in 74% of those treated with ACTH and in none of the patients treated with prednisone. These results led to the assumption that ACTH has a direct effect on neuronal function. Hasaerts and Dulac [4] presented a retrospective study of 32 children with secondary generalized epilepsy treated with hydrocortisone 5 mg/kg/day for 1 month, tapered over 6 months. Half of the children demonstrated a significant reduction in seizure frequency and 66% showed improvement in their cognitive abilities.

Verhelst et al. [1] reported their experience with steroids in 32 children with intractable epilepsy, demonstrating a decrease in seizure frequency in 47% of the children, of whom 25% were seizure-free. In this study, no correlation between seizure type and outcome was demonstrated. Reviewing their experience with 15 patients treated with ACTH for intractable generalized seizures, Okumura et al. [5] demonstrated significant improvement in 13 of 15 patients; however, its efficacy was often transient.

In all these studies, the patients were treated for at least several weeks with various regimens of oral corticosteroid preparations, and they continued treatment despite significant adverse events such as increased weight, improved appetite, behavioral disturbances and hypertension. Our patient was resistant to all syndrome-appropriate anti-epileptic drugs and failed to comply with the ketogenic diet.

The rationale for using an IV course of steroids was based on its short duration, anticipation of fewer side effects, and the availability of video-EEG monitoring throughout treatment. Indeed, our patient had no side effects during the 5 day course of treatment, and an immediate improvement, both clinical and electric, was noted. To the best of our knowledge, this is the first report on the use of IV steroids in intractable absence seizures. We suggest that IV methylprednisolone is an effective and safe treatment in children with intractable absence seizures.

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