Infantile spasms (IS) are seizures commonly associated with West syndrome—a severe infantile epileptic encephalopathy often accompanied by poor developmental outcomes. Babies with IS have epilepsy. There are three cases of IS per 10,000 live births in the U.S. each year. Greater than 90 percent of these seizures begin between 3 and 12 months with peak onset at 6 months. Although they often involve sudden vigorous muscle contractions of the neck, arms, legs and trunk, they can also present as mild contractions of the abdominal muscles or subtle movements of the eyes, head or shoulders. The clustering of these seizures is often the key to diagnosis. IS results from a brain abnormality with many different associated conditions that can be structural, metabolic, genetic or of unknown cause. It is not known how such varied conditions lead to IS.

The optimal management strategy, including diagnosis and treatment, is currently unknown. As a result, management may vary among different clinicians. This lack of consensus may negatively impact care and hinder advancement of understanding IS.

The Infantile Spasms Clinic at Nationwide Children’s Hospital is a multidisciplinary team consisting of a pediatric neurologist, nurse practitioner, social worker, developmental psychologist and registered nurses. The team works closely with other services such as Endocrinology, Cardiology, Nephrology and Ophthalmology and has established a standardized management protocol for the diagnosis, treatment and follow-up that is consistent with national expert recommendations. The protocol emphasizes the rapid diagnosis and treatment of IS, the use of first-line therapy and early changes if the initial treatment is deemed ineffective. Here we profile two patients to demonstrate key aspects of clinic protocols, including early changes in treatment after an initial lack of response, as well as diligent follow-up to assure rapid, complete and persistent electroclinical remission of IS.

**Case Study:**

**Infantile Spasms**

**Neurosciences Center at Nationwide Children’s Hospital**

John R. Mytinger, MD, Director of the Infantile Spasms Clinic

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**Patient 1: West Syndrome Due to Periventricular Leukomalacia**

A 6-month-old boy with periventricular leukomalacia and neonatal seizures was referred to the Infantile Spasms Clinic by a developmental specialist for clustering spells that began at 5 months of age. A diagnostic video EEG revealed an infantile epileptic encephalopathy (in this case, consistent with the term hypsarrhythmia) and captured IS. The findings of IS, an infantile epileptic encephalopathy and developmental delay confirmed the diagnosis of West syndrome. Patient was treated with ACTH (150 units/m²/day) for just less than a month. Family reported remission of seizures. A one-hour EEG with sleep performed within three weeks of starting ACTH showed resolution of hypsarrhythmia and a more organized background with some remaining multifocal spikes. Per clinic protocol, patient underwent overnight EEG to confirm electroclinical remission, which showed ongoing subtle IS. Patient was then treated with vigabatrin (150 mg/kg/day). Two weeks later, another overnight EEG revealed remission of clinical IS and fewer multifocal spikes. A one-hour EEG performed within two months was essentially normal without spikes. Rapid and sustained remission from IS and improvement in the EEG is necessary for optimal developmental outcomes. Treatment options include anti-seizure medication such as vigabatrin or hormone therapy with either adrenocorticotropic hormone (ACTH) or high-dose oral corticosteroids. Surgery may be required to treat underlying causes.

**Case Elements: Electroclinical Remission**

Subtle IS may be present on initial presentation or can manifest after the start of treatment. The clustering of IS may also resolve with treatment, leaving behind spasms that only occur singly. The subtle nature of these IS may prevent caregivers from identifying them. The clinic’s protocol includes a minimum one-hour EEG with sleep 14 to 21 days after the start of treatment to assure electrographic improvement. If parents are no longer seeing clinical IS and there is improvement on this EEG, the clinic’s protocol requires hospital admittance for an overnight EEG to confirm electroclinical remission. Our first case (Patient 1 above) exemplifies a circumstance when parents were no longer seeing spasms and there was an improved EEG. However, the overnight study revealed ongoing IS. This led to immediate treatment with vigabatrin which resulted in confirmed electroclinical remission.

**Case Elements: Follow-up**

About a third of IS patients suffer relapse after initial remission, so follow-up is critical. Such was the case for a 5-month-old girl (Patient 2 above) who was referred to the clinic following two months of clustering seizures. Although she initially responded to treatment with ACTH, follow-up EEG indicated relapse. In keeping with clinic protocol, the follow-up EEG was extended to include sleep, which is important as abnormalities may only be present during sleep. The follow-up EEG indicated remission was achieved within 10 days of starting treatment. ACTH was continued for just under one month. After over a month of seizure freedom, IS returned and she was rehospitalized. A functional hemispherectomy was performed to disconnect the abnormal left hemisphere.

**Patient 2: West Syndrome Due to a Large In Utero Middle Cerebral Artery Stroke**

A 5-month-old girl presented to Nationwide Children’s for possible seizures. Diagnostic video EEG revealed frequent multifocal spikes, predominately in the left hemisphere. She demonstrated left-hand preference and an MRI indicated a previously undiagnosed large middle cerebral artery stroke. She was diagnosed with infantile spasms. IS and hypsarrhythmia were confirmed. Electroclinical remission was achieved within two weeks of starting treatment. ACTH was continued for just under one month. After over a month of seizure freedom, IS returned and she was rehospitalized. A functional hemispherectomy was performed to disconnect the abnormal left hemisphere.

Researchers evaluated the time to remission following ACTH treatment among patients treated for IS at Nationwide Children’s from January 2009 to September 2013. Two high-dose ACTH protocols were used during the study period. Prior to September 2012, a long-course (typically 12 weeks) was used, and after this date the protocol was modified to a short-course (typically four weeks). ACTH response was defined as remission of clinical IS sustained for ≥ 28 days and electrographic response was confirmed in most cases by EEG. Of the 41 patients treated with ACTH, 23 (14 in the long-course group and nine in the short-course group) responded to ACTH, with response being determined within two weeks in 22 of 23 patients. The mean time to clinical remission was 5.6 days. There was no difference in the rates of remission, days to remission or rates of relapse between the short- and long-course groups. These findings suggest that, among IS patients, the response to ACTH is determined early in the treatment course and that clinicians should consider an alternative treatment if clinical remission does not occur within two weeks of starting ACTH.

**Case Elements: Early Treatment Changes**

The complex nature of IS means that therapy that works in one patient may be ineffective in another. Some clinicians will continue a therapy for a month or longer, even without signs of improvement. In contrast, the clinic’s protocol requires an early change in treatment if the initial treatment is deemed ineffective. Such was the scenario in our first patient (Patient 1 above) who failed to respond to ACTH. Once ongoing infantile spasms were confirmed, vigabatrin was initiated and resulted in a complete and sustained electroclinical remission. Previous research suggests changing ineffective treatments every two weeks can yield an IS remission rate as high as 96 percent. To study this further, clinical researchers utilized data from an IRB-approved retrospective and prospective observational database created at Nationwide Children’s.