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Case Report

Successful Management with the Ketogenic Diet of an Infant with Aicardi Syndrome: A Case Report

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Abstract

In this report, we present an 11 month female infant with AS whom achieved >90% reduction in seizures and reduction of AEDs following commencement of a ketogenic diet whilst inpatient on PICU for intractable seizures. Although the ketogenic diet is known to have strongly ameliorative effects in infantile spasms, there is little in the literature regarding the successful introduction of the ketogenic diet for AS. This case demonstrates the efficacy of such intervention and suggests the benefit of the ketogenic diet in the management of Aicardi syndrome, but also highlights the possibility of using this diet in other infants with intractable seizures.

Keywords: Ketogenic Diet; Aicardi Syndrome; Seizure Control

Abbreviations

AS: Aicardi syndrome; AED: Anti Epileptic Drug; PICU: Pediatric intensive care unit; EEGs: Electroencephalogram; PEG: Percutaneous endoscopic gastrostomy

Introduction

Aicardi Syndrome (AS) is a rare congenital epileptogenic disorder that is characterised by the triad of infantile spasms, agenesis or incomplete formation of the corpus callosum, and chorioretinal lacunae. Its aetiology is currently unknown. It predominantly affects female, therefore is thought to be an X-linked dominant disorder and likely lethal in males. Infantile spasms are the most common presenting feature of AS. Moreover, pathognomonic ophthalmologic examination findings and characteristic MRI brain changes can reliably confirm the diagnosis of AS. Treatment of seizures remains the mainstay of managing these children and requires Paediatric Neurology input with high level of expertise in treating refractory seizures. Multiple combinations of anti-epileptic drugs are used to optimize seizure control with Vigabatrin usually the drug of choice.

Case Presentation

The 5 month old female was admitted to PICU with known AS, diagnosed by infantile spasms, absent corpus callosum on brain MRI and retinal lacunae. Of note, other comorbidities included congenital stridor, scoliosis, vertebral abnormalities, microcephaly and a right-posterior plagiocephaly. Her seizures presented typically as clusters of asymmetrical extensor spasms with a frequency of 2-4 episodes per day with duration of 2-10 minutes. In addition to this, she was noted to be having frequent apnoeic episodes during sleep, which were clinically suspected to be seizures. She was therefore being treated with frequent doses of her rescue benzodiazepine medication. Serial EEGs demonstrated asymmetrical background changes in keeping with AS, as well as focal seizures arising from both left and right hemispheres.

With regards to respiratory support, she had been transferred in status epilepticus having been intubated and ventilated. She was extubated a month later, and furthermore underwent tracheostomy age 8 months. A Percutaneous Endoscopic Gastrostomy (PEG) inserted at 7 months.

Following discussion with the family and multidisciplinary team, the ketogenic diet was then introduced slowly via PEG. The infant's medication regime on initiation of the diet consisted of five anti-epileptic medications Vigabatrin 150mg/kg/day; Phenytoin 4.5mg/kg/day; Clonazepam 35mg/kg/day; Topiramate 6mg/kg/day and Levetiracetam 50mg/kg/day.

Having been on Infantrini high calorie feeds via gastrostomy, Ketocal (ketogenic balanced formula) was introduced gradually and the Infantrini volume reduced and titrated accordingly. Blood glucose and ketone levels were closely monitored to confirm ketosis whilst ensuring normoglycaemia. On day 6, ketosis had been achieved at ketones 4.6mmol/L on a 2:1 diet of Ketocal. Carbohydrate containing fruit-juice boluses were used to counteract excess ketosis. Ketocal volume was further increased, and on Day 18 she was on ratio of Ketocal 3:1. The stabilised diet consisted of 4 hourly boluses feeds of 105ml Ketocal (10.1g Ketocal 3:1, 2.6ml Calogen, 0.4g Maxijul, 0.7g Optifibre, 95ml water). All feeds were administered through gravity method via her gastrostomy.

Within 2 weeks of starting the ketogenic diet, the seizure frequency had decreased. At the time of discharge 3 months after starting the diet, seizure control had dramatically improved, with an almost complete cessation of cluster seizures. The patient continued to have

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1-2 short-lasting (10-30's) seizures per day lasting 10-30 seconds; however, reassuringly she would often be seizure-free overnight. No rescue medication was required in the 4 weeks prior to discharge. At discharge, her on-going medications were Vigabatrin 150mg/kg/day, Phenytoin 3.9mg/kg/day and Levetiracetam 60mg/kg/day which was significantly reduced compared to her admission medication.

Before commencing the ketogenic diet, polysomnography studies showed the patient was having 2.9 episodes of apnoea and hypopnoea per hour whilst asleep. The majority of these (1.9 per hour) were central apnoeic episodes. After starting the ketogenic diet, this had fallen to 0.2 episodes per hour, representing a significant improvement in the patient's central control of breathing.

Throughout this trial of the ketogenic diet her weight was monitored and plotted on growth chart. By discharge at the age of 11 months, the weight had increased to 7.725kg (2^{nd}-9^{th} centile), having been 3.42kg (<0.4^{th} centile) on transfer. Head circumference, which had been on the 0.9centile for several months prior to admission had increased to 43cm (9^{th} centile) at 11months.

Discussion

Children with Aicardi Syndrome (AS) can be very challenging to manage successfully, requiring a multi-disciplinary approach to care. Seizures are often intractable to antiepileptic drug treatment. In a study of 77 females aged 1 to 25 years, 91% achieved no developmental milestones higher than a 12 months level, with the milestones reached ranging from a 2 to 36 month level [1]. 92% had ongoing seizures, 67% daily. Vigabatrin has been suggested as a potentially efficacious treatment in refractory AS [2]. It has been reported that early treatment with Vigabatrin in the first year of life may lead to cognitive improvement. However, the decision to use Vigabatrin must take into account the risk of potential visual field constriction which can be worrying for families.

The ketogenic diet has been successfully used since the 1920's for controlling seizures in children with refractory epilepsy, although use had declined with the introduction of phenytoin and sodium valproate. It can prove to be a significant undertaking for families in maintaining the diet and change in lifestyle. In addition to this, it requires the expertise of dieticians, specialist nurses, neurologists and gastroenterologists. Recently the use of the ketogenic diet has again increased, and has been demonstrated to have been particularly efficacious in cases of IS (>90% reduction in seizure burden). There have been a few case reports of the use of ketogenic diet in Aicardi Syndrome, with only transient benefit [3].

The ketogenic diet can be initiated by fasting until ketosis is achieved, or, as in this case, by gradually introducing a ketogenic diet starting from full caloric intake. There is some evidence that fasting is preferable when a more immediate response is required. However efficacy is not dependent on this and there may be short-term side effects, particularly hypoglycaemia [4]. We achieved a good effect with slow introduction of the ketogenic diet, with rigorous observation of the patient's blood glucose, growth and level of ketosis.

This case provides evidence that the ketogenic diet should be considered in patients with AS and refractory seizures, as it demonstrates the reduction in seizure burden, the reduction in dose and number of anti-epileptic medication and use of rescue medication. In this age-group, gradual conversion of milk to ketogenic formula can be transitioned relatively easily compared to older children whom require careful monitoring of variety of foods and formulas. With the wider use of the ketogenic diet in these patients, it will become clearer whether the efficacy of the ketogenic diet in AS is similar to that in other seizure disorders characterized by IS.

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