Case Report

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Post Ictal Psychosis in Drug-Resistant Epilepsy Responding to a Ketogenic Diet.

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Abstract

Ketogenic diets mimic the metabolic profile of fasting, altering neuron energetics and stabilizing neuron synaptic function. They have an established role in the treatment of drug-resistant epilepsy(DRE). We present the case of a 30-year-old male with an 18-year history of DRE and postictal psychosis; all attempts at seizure control failed until he was finally commenced on a ketogenic diet, which greatly reduced the seizure frequency. In addition to improved seizure control, his psychosis and anxiety symptomatology dramatically improved, resulting in a better quality of life.

Keywords: ketogenic diet; Symptomatology; Metabolic

Case

Seizure history

JE is a former landscaper with drug-resistant epilepsy (DRE). His father and cousin also have epilepsy; he has no other epilepsy risk factors. His seizure semiology included generalized tonic-clonic (GTC), absence, and atypical seizures. His GTC seizures started at 12 years of age. In his early teens, he developed absence seizures and atypical hyperkinetic seizures associated with bizarre behaviour; the latter were postulated to originate from the frontal lobe, as multiple EEGs over a 12-year period repeatedly demonstrated frontal lobe epileptiform activity. All other investigations (including NMDA antibodies) were unremarkable (see Table 1). From 2005 to 2016, he trailed ten anti-epileptic drugs (AEDs), with minimal response. By 2014, he was experiencing 30-40 absence seizures and 1-2 GTC seizures per day.

Neuropsychiatric symptoms

As his condition progressed, JE developed neuropsychiatric symptoms which were a source of great distress to him and his family. These symptoms were classified into three subtypes: a) post-ictal and inter-ictal psychosis, b) psychotic episodes and aggressive behaviour not related to seizure activity (considered to be a form of epileptic encephalopathy), and c) affective symptoms. In 2012, he began to suffer from delusions. His first brief psychotic episode was in 2014 while admitted to Waikato Hospital for drug-resistant seizures, during which several seizures involving thrashing, screaming, grabbing of his throat, and breath-holding were witnessed. In 2015, he was admitted to a psychiatric ward due to increasingly frequent episodes of agitation and aggression, during which there were psychotic elements - he became paranoid, spoke in a different voice, and injured both himself and others. A psychiatric evaluation concluded that there was evidence of both anxiety and psychosis. Risperidone was introduced, but not tolerated. Quetiapine was effective, but produced vivid nightmares and fatigue, necessitating a switch to Olanzapine. This too wasdiscontinueddue to intolerance of side effects.

JE also suffered from affective symptoms, predominately anxiety. In 2009 he underwent psychology sessions to help alleviate his anxiety. At this time, he also suffered from low mood and suicidal ideation for a few weeks, but this resolved without treatment. The anxiety remained to be a prominent symptom and he often exhibited selective mutism.

Cognitive decline and regressive behaviours

By 2015, JE had developed significant cognitive impairment and regressive behaviours. He was unable to work that year, and by late 2016 he no longer recalled what he had done for work. He required full-time observation and care at home, with at least one family member with him at all times. A 2015 Montreal Cognitive Assessment (MoCA) demonstrated a score of 15/30 with language, memory and visuospatial/executive domains most affected. EEGs performed both in 2015 and 2016 were suggestive of encephalopathy.

Trial of the ketogenic diet

JE was admitted to Waikato Hospital, New Zealand in October 2016 and fasted for 7 days prior to the introduction of a ketogenic diet (fat: protein: carbohydrate ratio of 3:1). The diet

provided 2275kcal/day; 220g fat (87% of total energy intake), 65g protein (11.4%) and 8.4g total carbohydrate (1.5%). Blood ketone (beta-hydroxybutyrate, or BHB) levels were maintained between 2-5 mmol/L. Within weeks, his seizure frequency decreased markedly, to 1 GTC seizure every 4 days, with no further absence or atypical seizures. He tolerated this diet well, with no reported adverse effects. His weight remained stable. Despite this success, his significant cognitive impairment made it unviable to return home. He was discharged to a supported care facility where his seizure control remains comparatively excellent, averaging one brief GTC seizure every fortnight. Only clobazam 5mg at night is now required. His anxiety has improved and his psychosis has resolved. This resolution of psychosis has been maintained solely with KD for the last 10 months.

Discussion

20-40% of patients with newly diagnosed epilepsy have DRE [1], defined as the failure of two appropriate and tolerated anti-epileptic drug schedules of at least 6 months duration [2]. When further drug trials and surgery are no longer feasible, a ketogenic diet may be indicated.In 1921 Dr Rollin Woodyatt and Dr Russell Wilder designed the ketogenic diet after observing that fasting was an effective treatment for epilepsy [1]. Although many anti-epileptic drugs have been developed since then, only 65% of patients achieve adequate seizure control with drug therapy.

A ketogenic diet is a high-fat, adequate-protein, low-carbohydrate diet that forces the body to use fat-derived ketone bodies (particularly BHB) as a primary fuel source. Ketones may exert anti-seizure effects through several possible mechanisms, e.g. enhancing neuron energetics, reducing neuron excitability, and reducing oxidative stress (reference). Four validated ketogenic diets in epilepsy exist: a) classic ketogenic diet (CKD), b) medium-chain triglyceride (MCT) diet, c) modified Atkins diet (MAD), and d) low glycemic index treatment (LGIT) diet. The main distinction between these is the fat: protein: carbohydrate ratio [3,4].

In 2014, Klein et al., reviewed all published ketogenic (CKD or MAD) diet studies in adults with DRE. Across all five studies, 32% of adults treated with the CKD and 28% of adults treated with the MAD achieved a greater than 50% seizure reduction [5]. A large observational study in 2016 showed that after 3 months on the MAD, 36% of patients had a greater than 50% seizure reduction [6].

Post-ictal psychosis is a rare phenomenon characterized by delusions and hallucinations. Patients may become aggressive to protect themselves from a perceived threat [7]. Reducing seizure frequency can improve psychosis and aggression. Interestingly, a ketogenic diet has also been demonstrated to reduce symptomology in anxiety and treatment-resistant schizophrenia in animal and human studies[8,9]. It is now thought that gut microbiota may play a role in several psychiatric diseases, including psychosis. The regulation of gut microbiota on brain function and behaviour is postulated to occur via metabolic, anti-inflammatory and anti-apoptotic mechanisms. Recent studies showing the impact of the ketogenic diet on the microbiota-gut-brain (MGB) axis could account for the benefits seen with our patient's symptomatology [10,11].

Date	Investigation	Findings
2008	Thyroid function, Cortisol, IGF-1, Growth hormone, 72 hour fasting glucose and insulin	No evidence of insulinoma
2012	MRI brain	Unremarkable
2013	SPECT	No focal area of hypo-metabolism detected
2016	MRI brain	No parenchymal change to suggest encephalitis/encephalopathy
2016	CSF NMDA R antibodies	Unremarkable
2016	Serum ceruloplasmin	Normal

Figure 1: Summary of diagnostic tests since 2008 which revealed no metabolic or structural cause for seizures

Conclusion

Early implementation of ketogenic diets in DRE can improve seizure frequency, thus potentially avoid the loss independence experienced by our patient. In addition, this is the first documented case showing resolution of psychosis with a combined antipsychotic and KD approach.

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