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Animal-based ketogenic diet puts severe anorexia nervosa into multi-year remission: A case series

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Background: Anorexia nervosa is a devastating condition that increases risk of death over five-fold and is associated with a high rate of relapse. Considering the growing field of metabolic psychiatry, anorexia can be framed as a 'metabolic-psychiatric' condition that may benefit from treatment with metabolic health interventions with neuromodulatory properties. Ketogenic diets, very low carbohydrate high-fat diets, are one such neuromodulatory intervention with a long history of use in epilepsy and more recently in other systemic, neurological and mental health conditions.

Aim: To describe clinical cases that highlight the potential of ketogenic diets in the treatment of anorexia and the need for further research.

Setting: Patient interviews were conducted via telemedicine.

Methods: Medical interviews and chart reviews were conducted with three patients with severe anorexia. Written informed consent was provided by all participants.

Results: Patients with anorexia, body mass index (BMI) nadirs of 10.7 kg/m^2, 13.0 kg/m^2 and 11.8kg/m^2 and refractory to standard of care therapy, each achieved remission of between 1–5 years to date on a high-fat animal-based ketogenic diet. Patients exhibited not only improvements in weight, with weight gain of over 20 kg each, but also diminution of anxiety and overall enhanced mental well-being.

Conclusion: These cases suggest a ketogenic diet may be useful for some patients with anorexia. Further research is needed.

Contribution: This case series is the first to document treatment of anorexia with unimodal ketogenic diet intervention and raises provocative questions about the role of this neuromodulatory dietary treatment for patients with anorexia, as well as the neurometabolic nature of the disease itself.

Keywords: animal-based diet; anorexia nervosa; carnivore diet; eating disorder; ketogenic diet; mental health.

Introduction

Anorexia nervosa (AN) is a mental health disorder with high morbidity and mortality as well as a high relapse rate. The lifetime prevalence of AN is roughly 4% among women and 0.3% among men.[1] Anorexia nervosa sufferers exhibit standardised mortality ratio of > 5, far higher than any other eating disorder[2,3] and an absolute mortality of 5.6% per decade.[4] Unfortunately, the standard treatment for AN has relatively low efficacy. While a standardised definition of relapse is outstanding, relapse rates in AN can be 50% or more, with the highest risk in the first year and increasing rate of relapse with longer duration follow-ups.[5,6]

Standard nutritional therapy for AN focus on increasing caloric intake in the context of 'unrestrictive' and 'balanced' diets. Otherwise put, limits are not generally placed on the sources of calories, with priority given to weight gain. In some cases, atypical anti-psychotics that promote insulin resistance and metabolic dysfunction and weight gain, such as olanzapine, are prescribed as adjunctive treatment.

When considering patients in life-or-death situations, calorie replenishment at all costs may make sense; however, for those not on the brink of death, there are other factors to consider in setting patients up for long-term success, including patients' relationship with food and their overall metabolic health. Common knowledge posits patients with AN should be discouraged from practicing any food group restrictions, as this may have a negative impact on the psyche

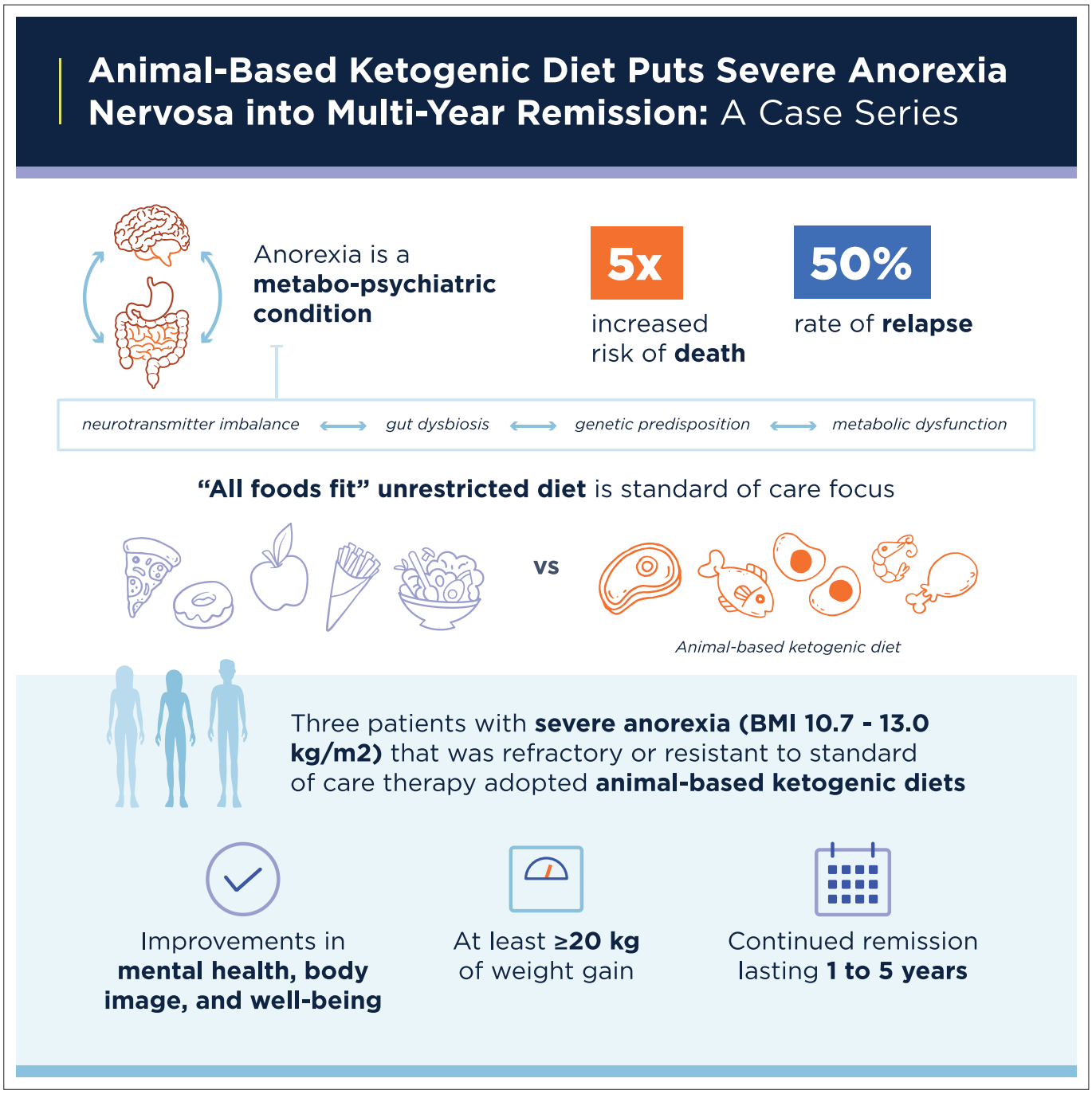


FIGURE 1: Graphical abstract: Animal-Based Ketogenic Diet for Anorexia Nervosa.

of patients predisposed to developing unhealthy relationships with food. As a consequence of this line of thinking, foods rich in sugar, refined carbohydrates and ultra-processed foods are usually not only on the table but sometimes encouraged (see Figure 1).

Ketogenic diets (KDs) lay at the opposite side of the spectrum of liberal-to-restrictive eating patterns, being, by definition, carbohydrate-restricted. It might therefore seem counterintuitive to prescribe a KD for AN, from both psychological and metabolic perspectives: (1) AN is a dietary restriction disorder and KDs are a form of restrictive dieting. (2) AN is characterised by a metabolic state of relatively low fasting glucose and insulin, similar to a KD. However, KDs have demonstrated efficacy in other neurological and mental health disorders, including bulimia nervosa, binge-eating disorder, major depression and schizophrenia,[7,8,9] and their recent clinical adoption by some metabolic psychiatrists suggests KDs have promise for the treatment of a variety of mental health conditions, including eating disorders.[10,11]

Herein, we describe the cases of three patients (pseudonym: Katherine E., Trevor O. and Amelia F.) with body mass index (BMI) nadirs of 10.7 kg/m^2, 13.0 kg/m^2 and 11.8 kg/m^2 and multiple medical and psychiatric comorbidities, who after failing to respond to standard therapy, each self-adopted high-fat animal-based KDs and subsequently experienced

improvements in mental well-being and other comorbidities, along with large increases in weight that have been maintained to date for years.

The possibility that an animal-based KD may have a role in the long-term treatment of AN counters common wisdom regarding nutritional guidance for eating disorders, raises interesting questions about the biopathology of AN and opens doors for further investigation.

Methods

Individual patient cases were identified from those known to the research team from presentation at conferences or by treatment by colleague practitioners. All patients provided written informed consent to have their data published in this report. Patients adopted pseudonyms (Katherine E., Trevor O., Amelia F.) to protect their identities. In addition, participants were required to provide documentation in the form of historic blood work and photographs for use by the research team and to verify elements of their histories. All patients were screened with a five-question standardised survey; (Sick, Control, One, Fat, Food [SCOFF]), for the presence of persistent eating disorder symptoms.

Results (case descriptions)

The following results were obtained from the patients:

Case 1

Katherine E. is a 39-year-old woman who first remembers struggling with body image at age 7. Although not overweight, she recalls being the 'fattest one' among a troop of young ballet dancers, a self-image she carried into high school. By age 16, peers at school nicknamed her 'apple girl' because her diet was restricted to mostly apples and low-fat foods. Over the next several years, Katherine was subject to a series of sexual traumas and abuse, which she attests exacerbated her restrictive eating behaviour because the only thing she could control in her life was her food. By age 24, she weighed 56 kg at 1.73 m tall, with a BMI of 18.7 kg/m^2. Her then boyfriend criticised her body composition, referring to her as 'fluffy' and suggested she try to lose fat and gain muscle. This catalysed what would become an over a decade long struggle with exercise addiction, and, by age 27, her BMI had dropped to 16.0 kg/m^2.

Wanting to become a mother, but having difficulty conceiving, Katherine underwent fertility treatment and three rounds of *in vitro* fertilisation at age 27 to become pregnant. Despite wanting the best for her future child, the weight gain associated with pregnancy was discomforting for Katherine, and she never let the scale read above 59 kg. Within 1 month of delivery, she had reduced her weight back below 50 kg. Capitalising on the momentum of postpartum weight loss, Katherine adopted a vegan diet, which she describes as a 'cultural excuse' to restrict her intake further. It was at age 30, at BMI 14.0 kg/m^2, that she was diagnosed with AN, underwent nutritional counselling and was additionally prescribed bromazepam 6 mg three times daily and lormetazepam 4 mg nightly for comorbid anxiety and insomnia.

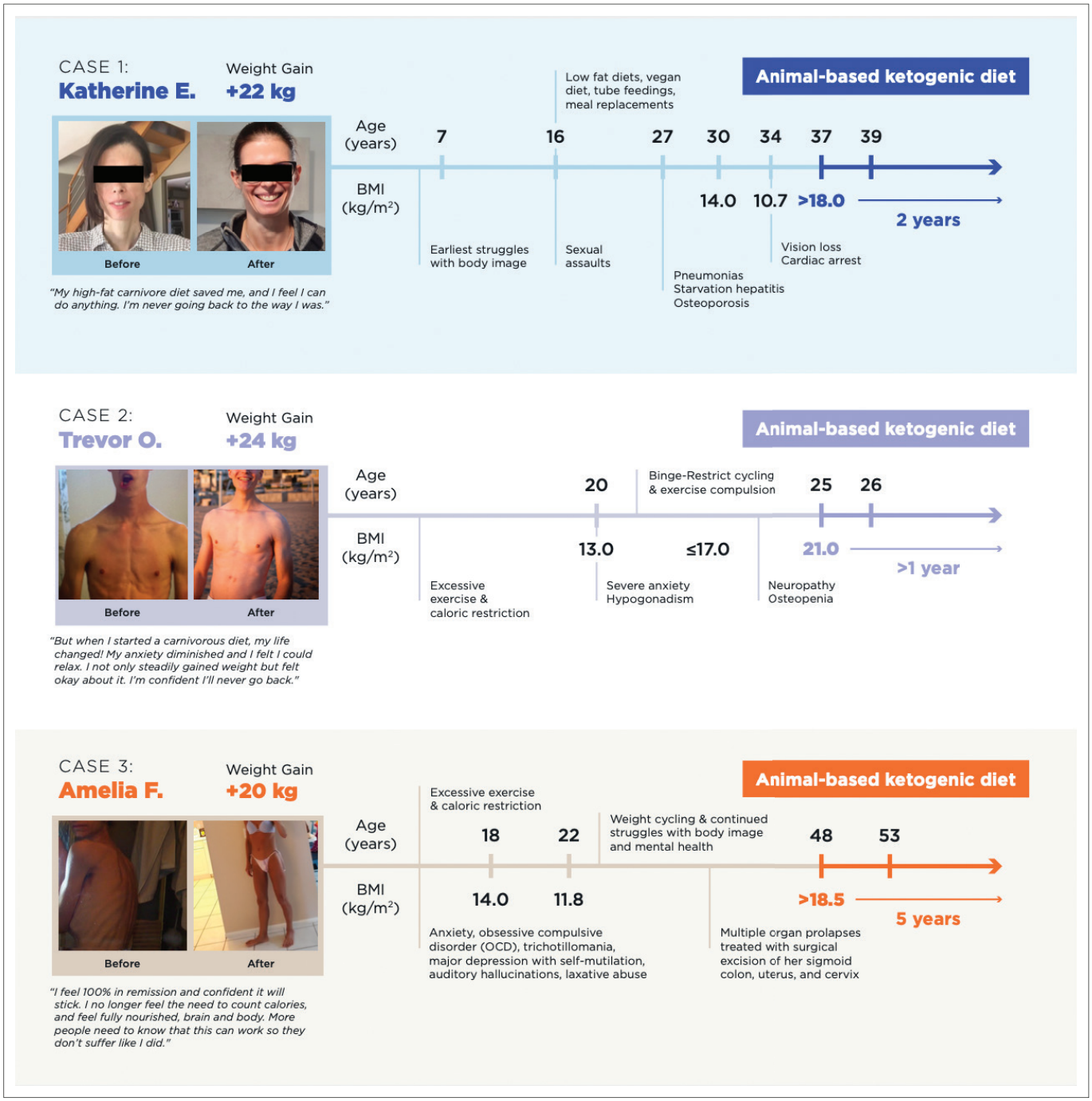
She made efforts to subvert medical prescriptions aimed at weight restoration. When prescribed a feeding tube, she developed a habit of switching the feeding solution with water and when prescribed meal replacement shakes, she emptied the containers and refilled them with water prior to having others witness their consumption. By age 33, Katherine's BMI was 12.0 kg/m^2 and she was suffering from hypokalemia to 2.5 mmol/L – 3.0 mmol/L, despite supplementation with 8 g potassium daily. She was hospitalised for two episodes of pneumonia, starvation-induced hepatitis and temporary vision loss because of orbital fat atrophy. By age 34, Katherine reached her weight nadir at 32 kg, maintaining a BMI of 10.7 kg/m^2 (Figure 2). She reports her dietary intake at this time consisted of 100 calories daily in the form of lettuce dressed in stevia sweetener.

Her second hospitalisation for pneumonia was complicated by cardiac arrest and resuscitation; at this time, Katherine reports realising that the moment of her death was no longer in her control. However, following discharge from a 1-month hospitalisation at an eating disorders inpatient unit, she still struggled with restrictive eating and maintained a near fat-free diet consisting of lettuce, fat-free yogurt, egg whites, a small amount of white fish and up to 8 L of Diet Coke and 60 pieces of sugar-free gum daily. She reports, 'I was making sure I was eating enough not to die.'

This pattern of eating continued until age 37, a pivotal year for Katherine, when she discovered blogs and videos by credentialed healthcare practitioners on experimental treatment of mental health disorders with KDs. Through exposure to these online educational materials, and reflections on her future with her son and motherhood, Katherine adopted under her own volition a high-fat animal-based KD. She reports, 'this solved all my issues… all of them!' On her new high-fat KD, she experienced a 'mental calm and clarity' and reduced anxiety around food. This precipitated a positive feedback cycle of mental well-being and physical restoration. Her caloric intake steadily increased, without any sequalae of refeeding syndrome, and she gained 9 kg in 4 months. She reports:

> 'When I was eating the fat, my body felt amazingly good. My brain was saying keep going, and I couldn't help but listen.' (Patient Katherine E., 39-year-old-woman)

Her diet focuses on eating entirely animal based foods, including fatty beef and lamb, fatty fish, bacon, egg yolks and organ meat (thymus, heart, bone marrow). Over time,



Note: Patients body mass index by age are marked with vertical lines, corresponding to annotations below each timeline. Time on an animal-based ketogenic diet and in remission is noted.

FIGURE 2: Patients' timelines.

she reports that her discomfort with eating a higher calorie diet dissipated, as she realised how well she functioned on the diet. Katherine is now 39 and, for the past 2 years, she reports her weight has been stable at ~54 kg, 22 kg above her lowest weight. She consumes approximately 2000 calories – 2500 calories per day, although she no longer counts calories fastidiously and only mentally notes approximate consumption to ensure intake of a minimum threshold of > 2000 calories.

Bone density scan conducted on April 2022 revealed osteoporosis with T-score –2.7. The latest complete blood count, comprehensive metabolic panel, lipid panel, iron studies, thyroid and liver function tests from November 2022 were unremarkable, and she is being followed by endocrinology every 4 months and by psychiatry monthly. Katherine reports no intrusive thoughts or issues with anxiety, no exercise compulsion and discontinued her benzodiazepines as she no longer suffers from anxiety or insomnia. She now works full-time as a civil engineer, has full custody of her son and a new litter of puppies, and reports pleasure in life and optimism for her future.

> 'My high-fat carnivore diet saved me, and I feel I can do anything. I'm never going back to the way I was.' (Patient Katherine E., 39-year-old-woman)

Case 2

Trevor O. is a 26-year-old man who describes his childhood as ideal. He grew up in a household with caring parents who practiced a non-restrictive approach to eating and permitted Trevor and his younger brother to eat anything they wanted, which constituted a balanced standard American diet. Throughout high school, Trevor reports no issues with food or weight, maintaining a slim physique, 55 kg at 1.75 m tall (BMI 18.0 kg/m^2) and remaining physically active and socially engaged with golf and track. At the end of high-school and transitioning into college, Trevor started taking nutrition courses, cut out junk food and began spending increasing amounts of time in the gym with an intent to build muscle and cut fat, with an emphasis on getting 'ripped.'

Over the course of his first year of college, he worked out 2 h daily and additionally made sure to get at least 15000 steps. His weight dropped to 39.9 kg by age 20 (BMI 13.0 kg/m^2). At this point, his dietary intake consisted of lean proteins (egg white, tuna fish, lean turkey) and low-calorie vegetables, with an intake of 800 calories daily. He was diagnosed by his primary care provider with AN and anxiety, treated with escitalopram (later with the addition of clonazepam) and referred to psychiatry for cognitive behavioural therapy and a nutrition team, who practiced an 'all foods fit' approach and encouraged Trevor to consume 'normal' foods such as pizza and milkshakes.

Being aware that his current weight was detrimental to his health and wanting to comply with his care providers, Trevor attempted to calorie replete. However, his unrestricted eating pattern exacerbated his anxiety and placed him in a binge-restrict cycle: some days he'd consume more than 3500 calories, including 10 servings of oatmeal, 14 pancakes with toppings and pints of ice cream as snacks. However, he'd subsequently 'panic' and feel he was gaining fat with frequent body checks and then self-restricting. This pattern continued until age 24 (BMI ~17.0 kg/m^2), but his anxiety worsened. He reports moving compulsively to burn calories; he would perform exercise snacks, including random planks and stair runs. He refused to sit and would eat alone on the second floor so that he would have an excuse to run up and down the stairs to grab utensils that he forgot intentionally. He also developed osteopenia, hypogonadism (January 2021: total testosterone 118 ng/dL, free testosterone 11.4 pg/mL) and peripheral neuropathy of unclear aetiology.

At age 25, Trevor chose to adopt a KD based on internet readings and social media recommendations, with 75% calories from fat and targeting blood ketones of > 1.0 mM, which he tracked on a blood meter. He reports '[An animal based KD] changed my life completely,' with complete cessation of anxious thoughts around food and exercise. A routine day of eating includes six or more eggs fried in butter with raw milk for breakfast and fatty fish and/or fatty meat with tallow, ghee or butter for dinner. His weight increased to 64 kg, BMI 21.0 kg/m^2, which he has maintained for over a year with a less compulsive exercise pattern of weightlifting 3 days weekly. He has discontinued his anti-anxiety medications and continues to report greatly improved anxiety.

His hypogonadism resolved, with total testosterone increasing from 118 ng/dL to 671 ng/dL (free: 11.4 pg/mL to 114 pg/mL) between January 2021 and May 2023. His peripheral neuropathy also resolved, and he is being followed by a nutritionist specialising in KDs.

Case 3

Amelia F. is a 53-year-old woman, who began struggling with restrictive eating and comorbid mental health disorders in early adolescence. At age 3, her father left her and her mother but would intermittently re-appear and disappear from her life, each time making promises to Amelia that he would ultimately fail to keep. This left her with a self-described sense of abandonment, 'unlovability' and a lack of control that contributed to her restrictive eating as 'what I put in my mouth was the one thing I could control.' By age 18, she was diagnosed with AN, at 43 kg and 1.75 m tall (BMI 14.0 kg/m^2) with comorbid anxiety, obsessive compulsive disorder (OCD), trichotillomania, major depression with self-mutilation and auditory hallucinations that she described as incessant voices telling her:

> 'You are worthless, you don't deserve to eat, can't eat that, nobody will love you because you're fat.' (Patient Amelia F., 53-year-old-woman)

Throughout college, Amelia was resistant to treatment by six separate psychotherapists and dietitians. Pharmacotherapy consisted of fluoxetine, venlafaxine, quetiapine. She suffered from exercise compulsion, laxative abuse and consumed < 500 calories daily exclusively from rice cakes and fruit. By age 22, Amelia's BMI was 11.8 kg/m^2 and she dropped out of college to focus on her health recovery.

She tried to eat better and comply with a dietitian's advice, emphasising a 'there are no bad foods' approach to caloric replenishment. Amelia struggled to make progress, still restricting herself to < 1000 calories until, at age 23, she met her to-be husband. With his support, she was able to gain weight to a BMI of 17.0 kg/m^2, regained her menses and had two healthy children. However, she still struggled with anxiety, OCD and relapsed, returning to a BMI of 11.8 kg/m^2 in her late 30s. Despite what she describes as a supportive family environment and a desire to change, she maintained her weight and eating habits for over a decade; her course was complicated with multiple organ prolapses treated with surgical excision of her sigmoid colon, uterus and cervix. At age 48, through reading and internet research, she became intellectually curious about animal-based KDs through the works of various physicians specialising in KDs. She progressively started to titrate in

animal proteins to her diet. She describes the shift as an emotional epiphany:

> 'I don't know how else to describe it but when I ate those three bites of that steak, [it was as if] receptors lit up in my brain and I cried tears of joy. I felt a calm joy that I'd never experienced, and I was all in.' (Patient Amelia F., 53-year-old-woman)

She reports:

> '[*T*]he more I increased my meat and fat intake, the more free I felt. The voices that were screaming in my head were now in another room with the door closed and locked.' (Patient Amelia F., 53-year-old-woman)

That year, her BMI increased to 18.5 kg/m^2, while consuming an average of 3000 calories daily almost exclusively from fatty red meat, fish and pure animal fat sources. She avoids vegetables primarily because they cause gastrointestinal distress and strength trains daily for 20 min. She also reported complete resolution of anxiety, OCD, trichotillomania and depression and has discontinued all medications. Amelia has remained in remission for almost 5 years.

Of note, all three patients scored 0/5 on SCOFF screening for eating disorder at time of interviews.

Discussion

To date, there has been one prior case report on KD for AN,[12] establishing a precedent for this report. However, while remission was achieved, the patient in this prior report underwent multi-modal treatment with ketamine infusion and her BMI nadir was 16.1 kg/m^2. Herein, we presented three cases of patients who underwent unimodal treatment for severe life-threatening AN with BMI 10.7 kg/m^2, 13.0 kg/m^2 and 11.8 kg/m^2 and who subsequently gained weight and reported improvements in anxiety and all other psychiatric comorbidities and who have been living comfortably in remission for years.

The impressive response of these patients to a high-fat animal-based KD, taken in the context of the broader literature on ketosis for mental health conditions, provokes questions as to whether there something unique about this diet (appropriately formulated with sufficient caloric intake) that confers particular benefits to some patients with AN. Ketogenic diets have a century-long history for use in epilepsy and have more recently been applied clinically in other neurological and psychological conditions, with some impressive results.[10] For example, in a recent trial of 31 patients with schizophrenia, bipolar disorder, major depressive disorder, all patients experienced improvements.[13] And, considering genetic, metabolic and microbiome signatures associated with AN, it has been proposed that AN should be framed as a 'metabo-psychiatric' condition in which endocrinological and metabolic abnormalities are not simple epiphenomenon but aetiologies.[14,15]

Anorexia nervosa has a relatively high hereditability, with estimates ranging from 0.5 to 0.8 and genome-wide association studies identifying loci for genes in metabolic pathways, such as ghrelin, AgRP and lipids, as well as a protective effect of elevated fasting insulin in Mendelian randomisation.[16] In addition, functional neuroimaging studies have noticed alterations in dopamine and serotonin signalling, such as increased $5HT_{1A}$ and diminished $5HT_{2A}$ signalling (subject reviewed in:[15,17]). Acknowledging AN as a metabo-neuro-psychiatric disorder and that ketone bodies are potent signalling molecules in the brain that provide therapeutic benefit to other neurological conditions, provides foundational biological plausibility for the therapeutic use of KD in AN.

That said, if a KD is therapeutic in AN, the underlying mechanism would likely be multifactorial: KD may restore neurotransmitter balance and alter neurometabolism,[10] reduce inflammation and neuroinflammation[18] or alter the microbiome and gastrointestinal homeostasis.[19,20] Furthermore, KD can alter insulin sensitivity systemically and centrally in the brain, although how this relates to its therapeutic effect in mental health disorders is not entirely clear. Alternative contributing factors may include that some patients with restrictive eating patterns might suffer from sugar addiction with a standard American mixed diet eating pattern and pharmacological interventions (e.g. olanzapine) potentially exacerbating these symptoms and causing them to feel a sense of loss of control, contributing to anxiety and relapse. The sense of control provided by an animal-based KD, therefore, may have a psychological benefit in so far as it allows patients to retain a sense of restriction and control while also allowing them to nourish their body. Furthermore, restrictive eating disorders are associated with microbiome dysbiosis[21] and irritable bowel syndrome,[22] the symptoms of which may theoretically be ameliorated by reduction of fermentable dietary content, with alleviation of gastrointestinal discomfort facilitating sustainable nutrient replenishment. The utility of KD for eating disorders deserves further careful study and raises interesting questions about the mechanisms by which this pattern of eating could be used to treat a diversity of mental health conditions, from sugar-addiction and obesity and binge-eating to severe food restriction and anorexia. In brief, these cases of patients adopting animal-based KD and reporting stunning remission of severe anorexia provides inspiration for further therapeutic and mechanistic investigation.

Patients' perspectives (quotes)

> 'My son has seen me through a lot. I remember when I was at my worst on a feeding tube and too weak to walk, he used to sit by my bed and stick the hose from his toy firetruck up his nose to mimic his mommy. Now, I'm looking forward to bringing him to a trampoline park for his eleventh birthday and jumping alongside him! A ketogenic carnivore diet cured me – mind and body. Eating this way gives a calmness and clarity of mind I can't even describe. I'm so grateful to be here today and wanted to share my story because I know there are others out there like me who can benefit from this lifestyle.' (Patient Katherine E., 39-year-old-woman)

'I grew up eating whatever I wanted and then decided to better myself by cutting out junk food and focusing on eating a healthy balanced diet. My intention was to build muscle and improve health, but I got caught in a terrible cycle and my life started falling apart. Trying to reverse my anorexia with a "all-foods-fit" diet just made my anxiety much worse and, even though I gained weight, I felt horrible, mentally and physically. But when I started a carnivorous diet, my life changed! My anxiety diminished and I felt I could relax. I not only steadily gained weight, but felt okay about it. I'm confident I'll never go back, which it not something I thought I'd could say before an animal-based keto diet.' (Patient Trevor O., 26-year-old-man)

'Anorexia was an over three decades long struggle for me. It defined me and caused me so much shame. I was told I'd never be completely better, that there would always be those voices in my head telling me I shouldn't eat and that I could only partially quiet them. All my physicians and dietitians promoted an "all foods are good" approach to my treatment, and that never really helped what was going on inside, and only made the anxiety worse. A carnivore diet cured me. I feel 100% in remission and confident it will stick. I no longer feel the need to count calories, and feel fully nourished, brain and body. More people need to know that this can work so they don't suffer like I did.' (Patient Amelia, 53-year-old-woman)

Limitations

The patients presented in this report each self-selected to adopt their animal-based KD; thus, there is inherent selection bias. As the report was conducted retrospectively, while we are able to present data collected clinically, for example, BMI and baseline and follow-up sex steroids, we do not have research-level metabolic data, such as microbiome data or transcriptomics or functional magnetic resonance imaging (fRMI), to report in this manuscript. Further large-scale research is required to elucidate possible neuro and metabolic aetiologies of AN. It is also not clear to what degree ketosis was beneficial in the success of these patients, as opposed to nutrient replenishment or psychological factors associated with the dietary change. Further research is certainly warranted.

Conclusion

The KD is a low-carbohydrate high-fat diet that has historically been used to treat treatment-resistant epilepsy. Over the past several years, there has been growing interest in using a KD for the treatment of mental health conditions, including eating disorders. These cases of patients who used high-fat animal-based KDs for the effective treatment of severe life-threatening anorexia nervosa contrast with common practice and raises provocative questions about the role of this lifestyle in the care of other patients with anorexia nervosa.

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Competing interests

N.G.N. declares he stands to receive royalties from his cookbook on a Mediterranean Ketogenic Diet; however, he donates all proceeds to nutrition education and research efforts. M.H. stands to receive royalties from her book, The Dietician's Dilemma. Other authors declare the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Authors' contributions

N.G.N. conducted patient history, consolidated data and drafted the report. M.H. helped with conducting histories and collecting data. F.E.F. provided guidance and editorial commentary.

Ethical considerations

These patient cases were collected retrospectively with the full written informed consent of each patient interviewed. Pseudonyms were adopted to protect patient identity. Harvard Medical School IRB (IRB24-0433) determined that this submission did not require a full IRB approval as defined by Department of Health and Human Services (DHHS) regulations or FDA regulations.

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Data availability

All publicly available data are provided in the manuscript. Please contact the corresponding author (N.G.N.) with further questions.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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