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Case Report

Prolonged Maintenance of Remission with Crohn Disease Exclusion Diet (CDED) in Two Siblings with Crohn Disease

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Abstract

Dietary and nutritional interventions have been shown to have roles in managing active Crohn disease (CD), with exclusive enteral nutrition (EEN) being recommended as the preferred initial treatment in children following diagnosis. In recent years, other nutritional interventions such as the Crohn's disease exclusion diet (CDED) have been considered and evaluated for induction therapy. To date, the long-term benefits of CDED have not been established. This report highlights the outcomes of the prolonged use of CDED in two siblings with CD.

Keywords

Crohn's disease; pediatrics; inflammatory bowel disease; diet therapy; Crohn's disease exclusion diet

1. Introduction

While the precise pathogenesis of Crohn disease (CD), one type of Inflammatory Bowel Disease (IBD), is unknown, dietary factors are a key component along with the intestinal microbiome, and host immune responses [1]. Dietary and nutritional interventions have also been shown to have roles in the management of active CD, with exclusive enteral nutrition [2] being recommended as the preferred initial treatment in children following diagnosis [2-4].

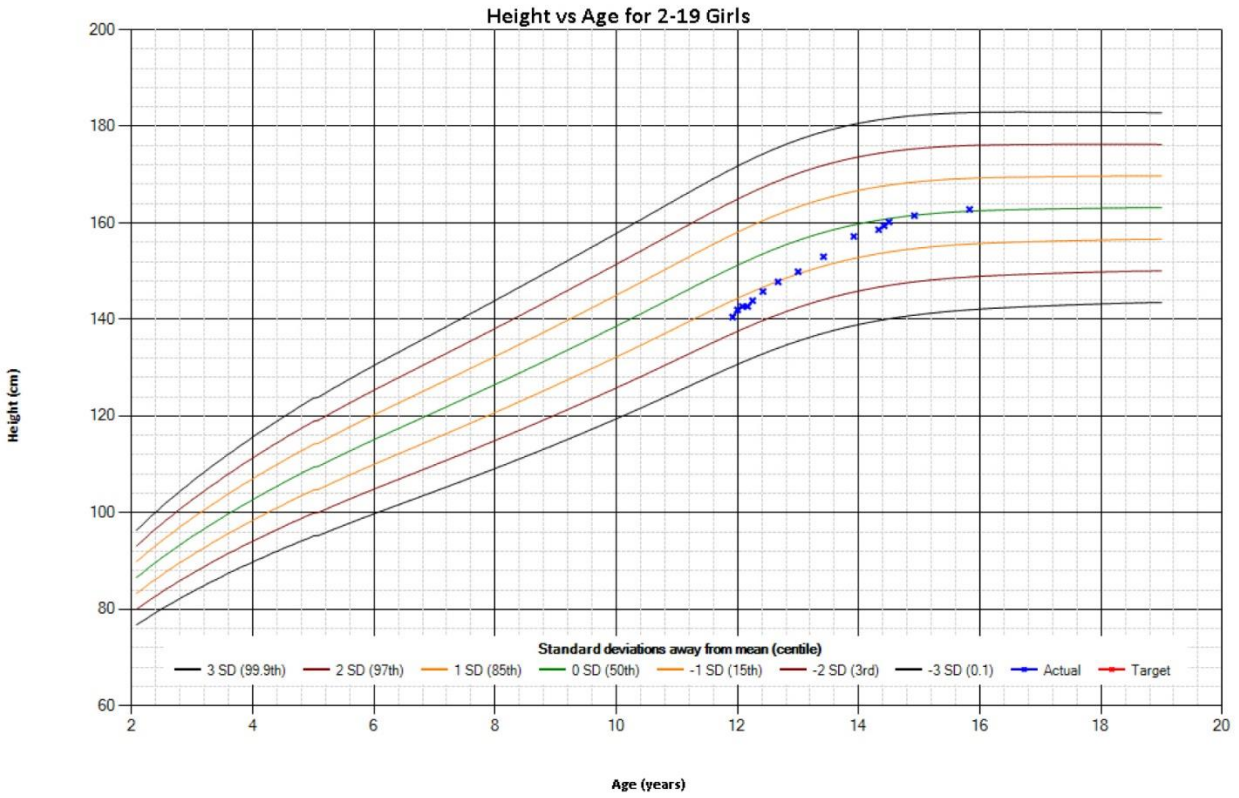
EEN is associated with high rates of clinical remission [5]. Furthermore, it has also been shown to lead to higher rates of mucosal healing than other induction therapies, such as corticosteroids. Whilst EEN has many benefits, it does require a prolonged period (typically up to eight weeks) of exclusion of solid foods and ingestion of liquid formulae alone [2]. Consequently, acceptance of the intervention and adherence during therapy may compromise its potential efficacy.

Whilst EEN continues to have a key role in children and adolescents with active CD, other nutritional interventions have been considered and evaluated in recent years. These are characterized using solid foods, with restrictions on the type and range of foods consumed. One such restrictive dietary intervention is the Crohn Disease Exclusion Diet (CDED) [6-8]. This approach involves excluding nutritional components that are considered to have pro-inflammatory or other adverse effects on the gut, with phased relaxation of the restrictions over several weeks. Prospective controlled short-term trials have indicated that CDED is as effective as EEN in remission induction in children with mildly to moderately active CD [6-8]. To date, the long-term benefits of CDED have not been established. This report highlights the outcomes of the prolonged use of CDED in two siblings with CD.

Ethical approval for this case study was approved by the University of Otago Human Ethics Committee H17/146. Written informed consent has been obtained from the patient to publish this paper.

2. Description of Cases

The first child (Patient A) presented at 8 years of age with a 2-3-week history of mouth ulcers, weight loss, intermittent fevers, and intermittent haematochezia. Before this, she had been well, with a maternal history of CD. The initial examination was unremarkable, other than several oral aphthous ulcers. Her BMI z score was -0.09 at diagnosis, suggesting appropriate growth (**Figure 1**).



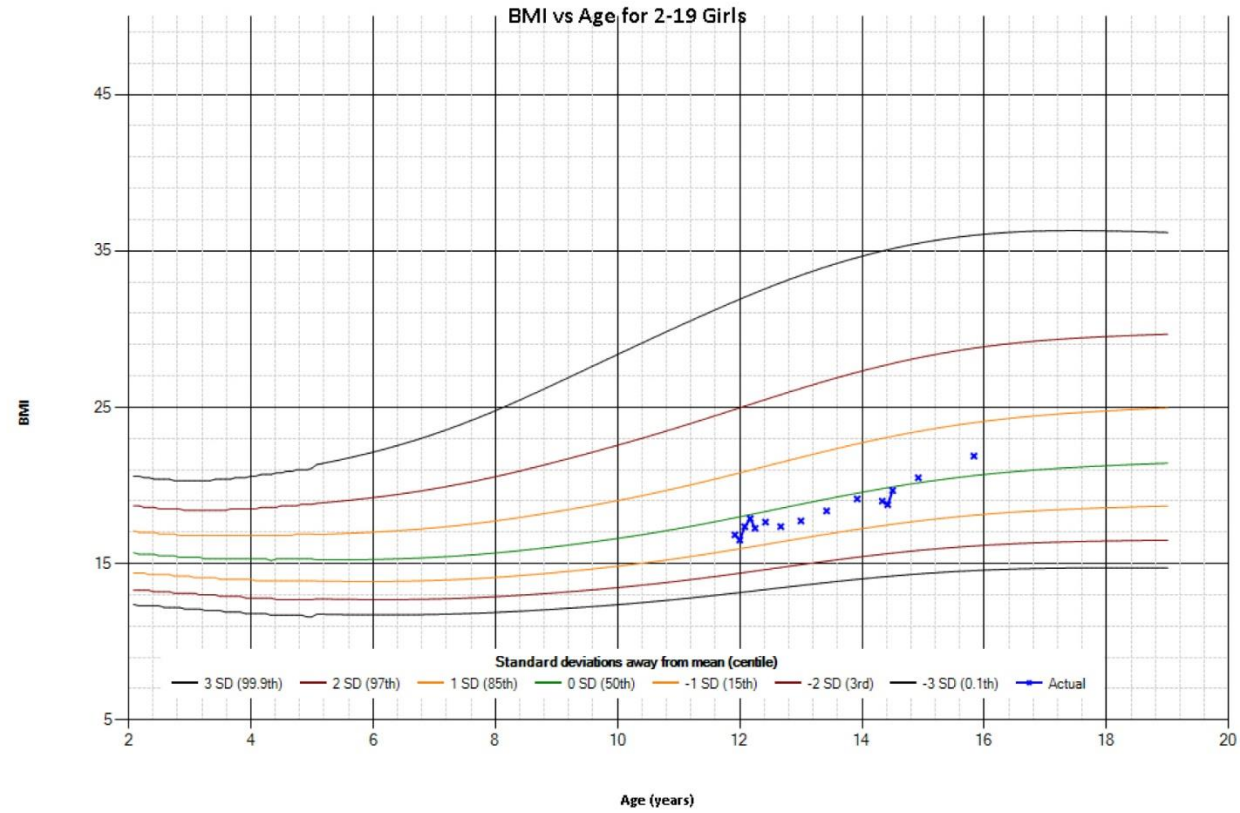


Figure 1 Anthropometric graphs of Height-For-Age and BMI-For-Age for Patient A using the World Health Organisation growth charts for girls aged 2-19 [9].

Initial investigations showed mildly abnormal serum inflammatory markers with fecal calprotectin measured at 51 μg/g (normal range <50 μg/g). Other routine blood tests were regular. She proceeded to have an upper gastrointestinal (GI) endoscopy and ileo-colonoscopy. Patchy aphthoid ulcers were seen in the antrum and colon, with extensive ulceration involving the ileocecal valve and the terminal ileum. The histologic findings from mucosal biopsies included mild active chronic gastritis (with no granulomata) and mild active chronic ileitis and caecitis. Magnetic resonance enterography (MRE) showed a 15 cm segment of terminal ileal wall thickening, with no other small bowel involvement.

Following the above investigations, a diagnosis of CD was made. She was commenced on eight weeks of Exclusive Enteral Nutrition (EEN) to induce remission. Given the familial interest in managing disease control with diet, she then commenced CDED as ongoing maintenance therapy in conjunction with a maintenance enteral nutrition (MEN) volume of 50% of estimated energy requirements (EER).

After the normalization of abnormal serum inflammatory markers, these have remained normal for the subsequent eight years (**Figure 2**). Furthermore, repeated measurements of fecal calprotectin have also been standard throughout (**Figure 3**). Serial imaging with ultrasound of her terminal ileum demonstrated resolution of wall thickening by 6 months, with no recurrence of abnormalities. In conjunction with these assessments, she had excellent catch-up weight gain in the first 8 months after diagnosis, with persistently satisfactory growth since (**Figure 1**).

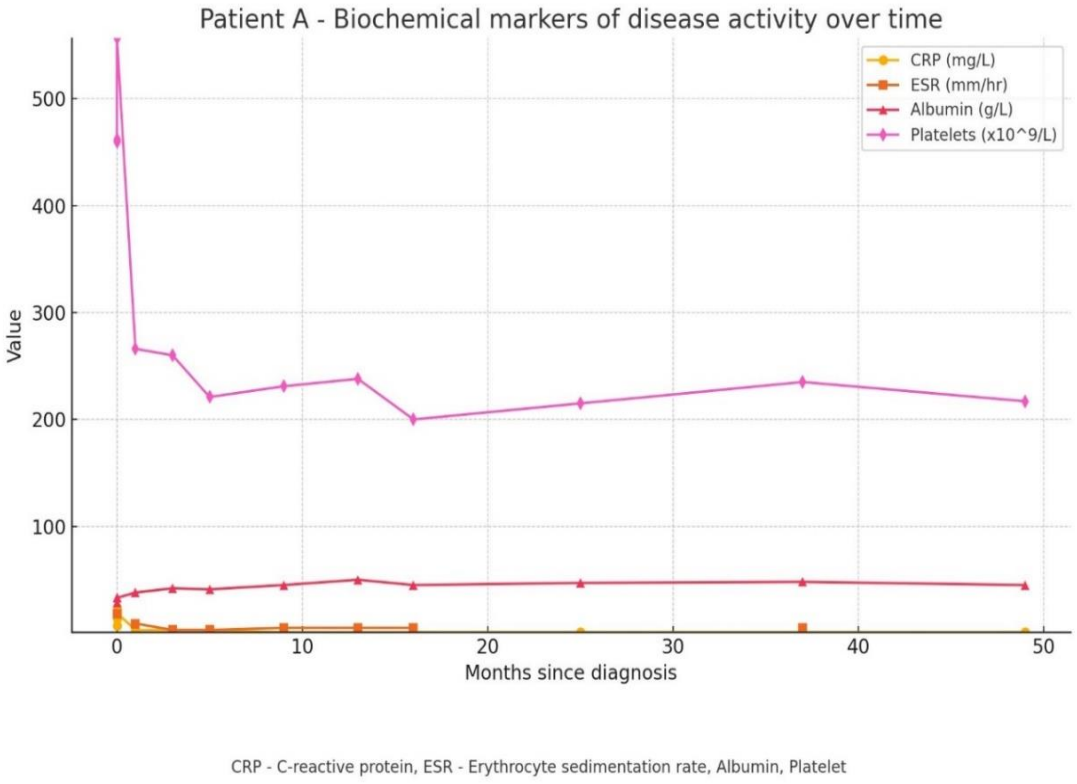


Figure 2 Biochemical markers of disease for Patient A.

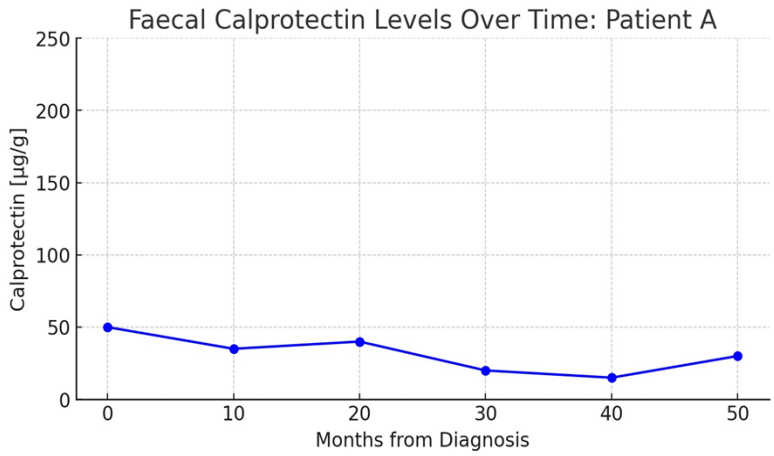


Figure 3 Faecal calprotectin levels over time for Patient A.

In summary, she has remained on CDED along with MEN as her sole intervention for eight years since diagnosis. Furthermore, she has remained well over this time, with excellent symptomatic and biochemical remission.

Patient B was seen in the pediatric gastroenterology clinic at age 11 years, shortly after her younger sister was diagnosed with CD. At presentation, she reported a history of abdominal pain, lethargy and anorexia over approximately one month, with vague abdominal discomfort and fatigue for several months prior. She was passing 3-4 soft, formed bowel motions per day, with no blood or mucous. She also had a largely unremarkable medical background, other than a history of reflux in infancy and allergies to nuts and bee stings. Patient B was taking an over-the-counter probiotic and a supplement to help with the management of stress. Her physical examination at diagnosis was unremarkable, but anthropometric data showed a weight loss of 1.5-2 kg.

Although serum inflammatory markers were within normal limits (**Figure 4**), her fecal calprotectin was raised (150 µg/g). Her nutritional blood was unremarkable. Endoscopically, the only finding was patchy ulceration in the left colon; granulomatous ileitis was also demonstrated histologically. Subsequent MRE showed mild limited wall thickening in the terminal ileum with some associated lymphadenopathy.

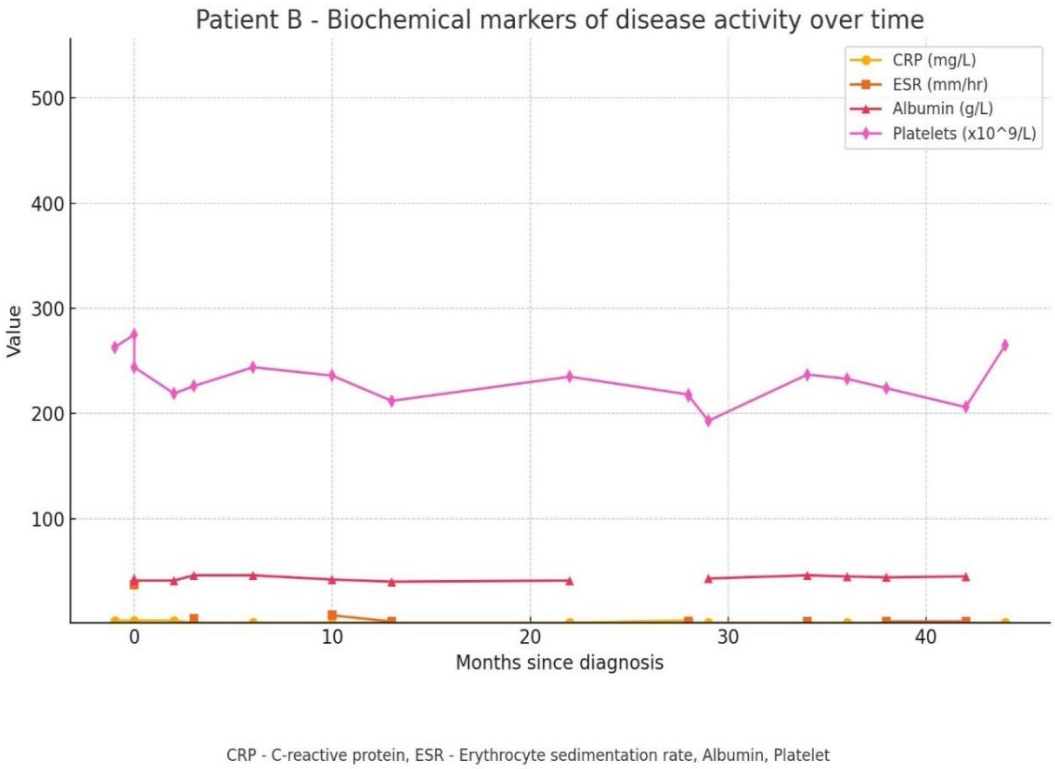


Figure 4 Biochemical markers of disease for Patient B.

Patient B was also given a diagnosis of CD and commenced eight weeks of EEN to induce remission. Following EEN, Patient B also commenced CDED with MEN and has remained on this as sole maintenance therapy for the eight years since. In the first year after diagnosis, she had one mild exacerbation of symptoms with an associated increase in fecal calprotectin, which was managed with a four-week course of EEN with good response. Subsequently, however, calprotectin levels have been repeatedly normal (**Figure 5**). Furthermore, repeat ultrasound imaging of her small bowel demonstrated resolution of ileal wall thickening. Over the time since diagnosis, she has grown satisfactorily (**Figure 6**) and progressed through puberty.

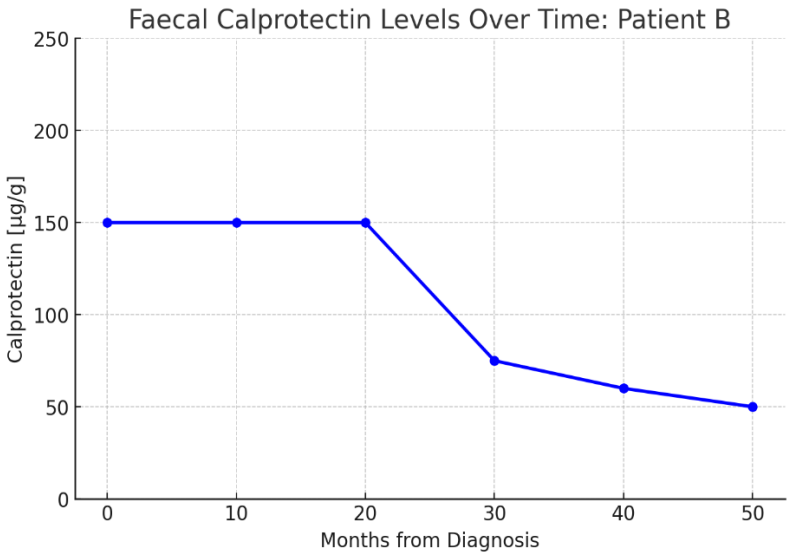


Figure 5 Faecal calprotectin levels over time for Patient B

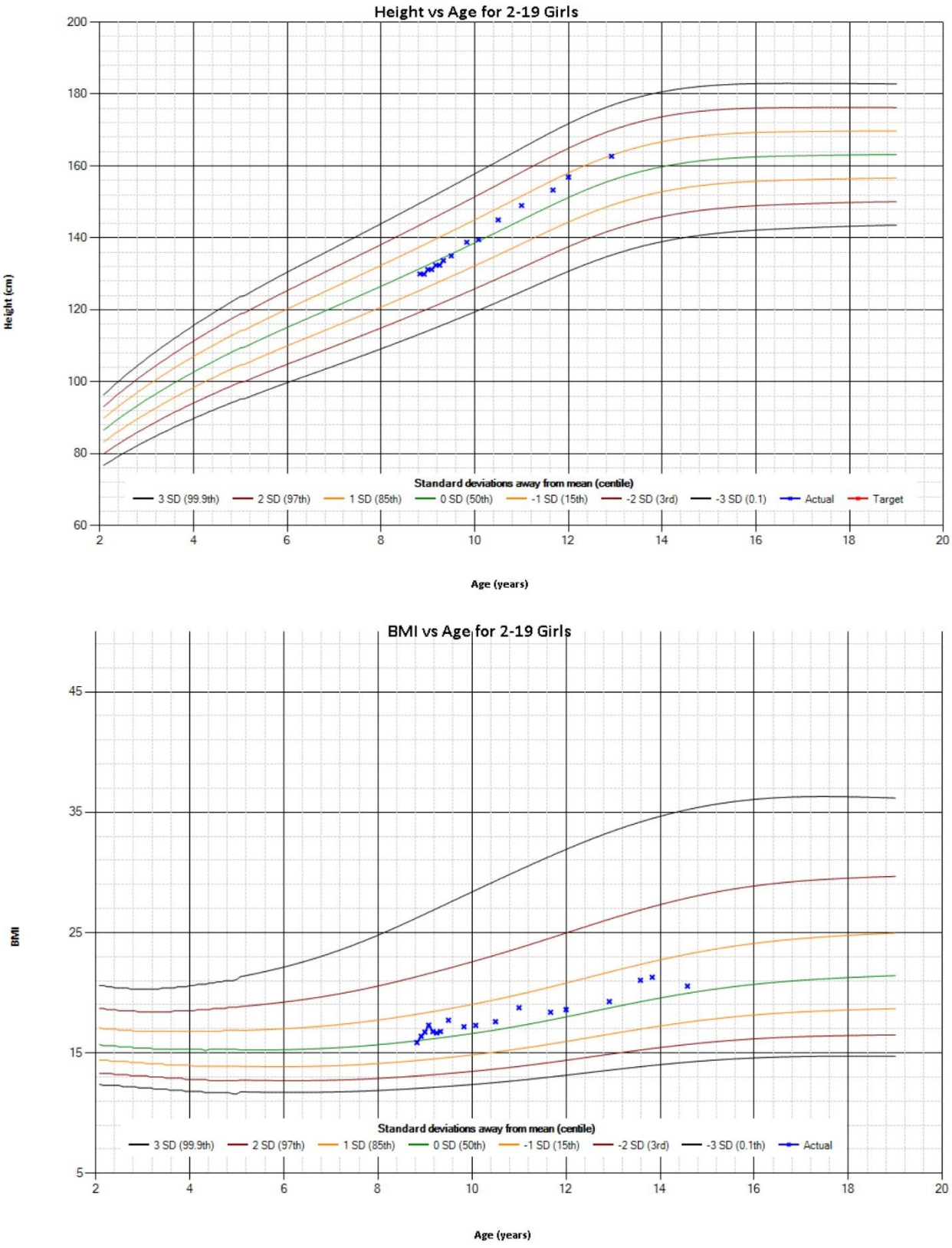


Figure 6 Anthropometric graphs of Height-For-Age and BMI-For-Age for Patient B using the World Health Organisation growth charts for girls aged 2-19 [9].

3. Discussion

The two siblings illustrated in this report were diagnosed within a few months, were both treated with EEN with successful induction of remission and have both remained on CDED to date. Furthermore, both have thrived with normal growth and development over this time.

The CDED is a structured dietary intervention with three distinct phases to reduce inflammation and manage symptoms in individuals with CD [8]. Phase 1 focuses on inducing remission during the first six weeks, emphasizing specific whole foods while excluding processed foods, additives, and specific inflammatory triggers, often combined with Partial Enteral Nutrition (PEN). Phase 2, beginning after six weeks, gradually reintroduces more foods while reducing reliance on formula, promoting dietary diversity within safe limits. Phase 3, the maintenance phase, is designed to sustain disease activity control by continuing to avoid high-risk foods while allowing a broader, balanced diet to support long-term gut health and nutritional needs.

The underlying concepts leading to the development of the CDED approach were outlined in a review published in 2014 [7]. This report detailed the potential adverse impacts of various food components or additives on the gut. Animal and *in vitro* data were outlined, showing that these elements were associated with disruption of mucosal barrier function, promotion of inflammation, and/or alterations in the intestinal microbiome. After this, the first reports of the use of CDED were published. The first of these showed a reduction of disease activity or induction of remission in children and young adults with active CD [7]. The second report showed the benefits of CDED when used as an adjunct alongside biological agents in children/young adults with CD [6].

The present case study demonstrated a significant reduction in fecal calprotectin (FCP) levels in two children with active CD following the implementation of the CDED. These findings are consistent with those reported by Matuszczyk et al. [10], who observed that CDED combined with PEN resulted in the normalization of FCP levels in approximately one-third of children, indicating successful induction of remission. Additionally, their study highlighted the importance of extending the induction phase of CDED and PEN beyond 12 weeks to achieve the full therapeutic effect. These results support the role of dietary interventions as adjunctive strategies to pharmacological treatments in reducing inflammation and promoting mucosal healing and support the need for further research to refine the duration and composition of nutritional protocols to maximize clinical outcomes.

The evidence from existing literature highlights the significant role of dietary modifications in managing CD, particularly through approaches such as EEN and the CDED [11]. These strategies have effectively reduced inflammation, achieved clinical remission, and promoted mucosal healing in select individuals. These interventions can serve as effective adjuncts to medical therapy by tailoring nutrient intake and limiting pro-inflammatory dietary components. Future research should consider these approaches' comparative effectiveness and mechanisms of action, offering a more comprehensive understanding of nutritional strategies in CD management.

More recently, the potential benefits of CDED were evaluated prospectively compared to EEN [12]. Children with mild-moderately active CD were treated with EEN or CDED over 8 weeks. There was no difference between the efficacy of either diet treatment ($P = 0.469$). The children with CDED had superior weight gains ($P = 0.001$) and higher BMI z-score ($P = 0.002$).

To date, the role of the CDED in terms of maintenance of remission beyond the first few months after diagnosis has not been assessed. Therefore, adherence to healthy eating guidelines should be

recommended to children and their families in the absence of more robust studies that determine the efficacy of maintenance CD diet therapies. Whilst EEN has not been considered as a long-term treatment option (as it would require ongoing avoidance of solid foods), MEN has been demonstrated to help in the maintenance of remission and with optimization of growth [13, 14]. Concerns have been raised about the long-term benefits of a Specific Carbohydrate Diet (SCD), another restrictive nutritional therapy for CD [15].

One limitation of this study is that the small sample size restricts the generalizability of the results. To draw conclusions applicable to a broader population, further research involving larger, controlled trials would be essential. This would provide more robust data to validate and expand upon the observations noted in this case study. Further, prospective controlled evaluations could also enable focused evaluations of the impact of these interventions on the intestinal microbiome.

Potential adverse effects of prolonged use of CDED could include food-related anxiety and social disruptions. The siblings outlined in this case report live together with their mother (who also has CD and has also adopted the CDED) in a setting where their dietary choices are consistent and normalized.

Restrictive dietary interventions could also be associated with compromised growth or nutrition, especially without monitoring and support from an experienced dietitian. The siblings in this report have typical growth trajectories with no concerns about growth or wellbeing. Both have had regular dietetic reviews over time. Both girls also have ongoing MEN, which will protect them against micronutrient deficiency.

While the siblings in this case demonstrated normal growth and no evident nutritional deficiencies, restrictive diets can carry risks such as food-related anxiety, disordered eating patterns, or social challenges related to meal preparation and consumption. These psychological impacts are especially relevant in individuals with IBD, where the disease itself is often associated with increased anxiety, depression, and a diminished quality of life [16]. Addressing these potential psychological and nutritional challenges is critical for ensuring the long-term safety and sustainability of dietary interventions like CDED. Future research should focus on strategies to mitigate these risks and support the overall well-being of individuals adhering to restrictive therapeutic diets.

A further potential adverse effect of persistent dietary restrictions could be modulation of the intestinal microbiome. Many studies have shown the impact of EEN on the microbiome [17, 18]. However, there are not yet published data that have delineated the short—or long-term effects of CDED on the microbiome. This will be an important area of future endeavor.

Finally, another potential consequence of CDED is clinical improvement without maintenance of mucosal healing. Neither of the two current cases has had repeat endoscopic assessment since diagnosis, but both have had serial assessments of blood markers, calprotectin, and radiological imaging.

Author Contributions

Grace Douglas: Methodology, writing – original draft, formal analysis, writing – review and editing. Andrew S Day: Conceptualization, Methodology, Supervision, writing – review and editing. Stephanie C Brown: Conceptualization, writing – review and editing. Each author has approved the submitted version. Furthermore, each author agrees to be personally accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of

the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature.

Competing Interests

The authors have declared that no competing interests exist.

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