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Case Report

Subcutaneous golimumab to treat a biological naïve chronically active ulcerative colitis child. A case report

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ABSTRACT

Introduction: Ulcerative colitis is an immune-mediated disease that carries challenges in pediatrics since it's frequently severe and extensive. Current pediatric ulcerative colitis guidelines offer a weak recommendation regarding the usage and the dosage of golimumab in low-weight children. We present a case of an off-label, unrecommended dose of subcutaneous golimumab to treat low-weight chronic active ulcerative colitis child.

Case presentation: A 10-year-old Syrian girl, anti-TNF naïve, chronically active ulcerative colitis was weighs 25 kg, standing 142 cm tall, body surface area (BSA) of 0.993 m^2, past medications included oral prednisone and mesalamine, no prior surgery. We used golimumab 200 mg, 100 mg at weeks 0, 2 as induction, then 50 mg every four weeks for about two years.

Clinical discussion: The recommendation regarding the use of subcutaneous golimumab in pediatrics is weak since is based on an open-label pharmacokinetics cohort. It is available in 100 mg/1 ml, 50 mg/0.5 ml as a smart SmartJect, or in 45 mg/0.45 ml in VarioJect which provides golimumab from 10 mg to 45 mg in increments of 5 mg/0.05 ml. Golimumab Varioject is in short supply, and unavailable in several regions including Syria. The recommended golimumab maintenance dose always requires two injectors, which adds another burden.

Conclusion: This case demonstrated that golimumab 200 mg, 100 mg at week 0, 2 as an induction then 50 mg every four weeks was efficacious and safe in<45 kg children, there were no side effects or adverse events during two years therapy period.

1. Introduction

Ulcerative colitis is distinguished by diffuse mucosal inflammation that is restricted to the colon. The most common symptom is bloody diarrhea and may be associated with abdominal pain, urgency, or tenesmus. Clinical suspicion, appropriate colonoscopy findings, biopsy histological findings, and negative stool examinations for infection should be used to make the diagnosis [1]. Corticosteroids,5-ASA, azathioprine are important treatment options [1–4], and If the treatment failed then anti-TNFα is considered [1–4]. Golimumab is a human IgG1 tumor necrosis factor-alpha (TNFα) antagonist [5]. The latest pediatric ulcerative colitis treatment guidelines recommended off-label use of golimumab if infliximab loss of response or intolerance, rather than as an initial treatment [6]. We present a case of an off-label, unrecommended dose of subcutaneous golimumab to treat a 10-year-old Syrian girl, 25 kg anti-TNFα naïve, chronically active ulcerative colitis [6]. She started subcutaneous golimumab 200 mg, 100 mg at week 0, 2 as an induction then 50 mg every four weeks as first anti-TNFα treatment when she was ten years old, and continued it for about two years (122 weeks) under normal living conditions. Subcutaneous golimumab achieved clinical and endoscopic remission without any adverse events. This case report has been reported in line with the SCARE criteria 2020 [7].

2. Case presentation

A 10-year-old Syrian girl steroid-dependent ulcerative colitis referred to the hospital for anti-TNFα treatment follow-up. She weighs 25 kg and stands 142 cm tall, with a body mass index (BMI) of 12.4 kg/m^2 and a body surface area (BSA) of 0.993 m^2 calculated using the Mosteller formula, no prior surgery or medical family history. Her past medications included oral prednisone 1 mg/kg up to 40 mg in severe acute colitis, then tapering, and mesalamine 60–80 mg/kg/day up to 4.8 g daily, azathioprine was not available at that time [6]. The infections

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screening, as recommended before the use of biological therapies such as latent tuberculosis, hepatitis B, and C viruses, came back negative [6]. She presented mild abdominal pain, up to 5 times nocturnal bloody diarrhea, her blood tests revealed anemia and an increase in C-reactive protein (CRP). Stool tests, including routine stool cultures, Clostridium difficile toxin, Cryptosporidium testing, and microscopy for ova and parasites, all came back negative. Multiple large ulcerations were discovered during a colonoscopy Fig. 1, and colon biopsies were negative for Clostridium difficile infection and Cytomegalovirus. She recorded 9 points on the Mayo score and 40 points on the pediatric ulcerative colitis activity index (PUCAI) [8]. We started subcutaneous golimumab with a loading dose of 200 mg at week 0, followed by 100 mg at week 2, then 50 mg every 4 weeks. She achieved clinical remission at the end of the induction in the sixth week. She continued the treatment for two years (122 weeks) with no complications or adverse effects. After two years, she weights 33 kg and 147 cm tall (BMI = 15.3 kg/m^2, BSA = 1.183 m^2). She experienced intermittent minor abdominal pain, an abdominal ultrasound was normal, and laboratory tests such as a complete blood count, CRP, and fecal calprotectin were all within normal limits. A colonoscopy revealed a lack of vascular pattern Fig. 2, she scored 1 point on the Mayo score and 5 points on the PUCAI. We relied on evaluating her during treatment on PUCAI and CRP, every month when of her golimumab injection and calprotectin every three months and the results were normal [6]. Table 1 compares the patient's tests before starting golimumab to week 122 after starting golimumab.

3. Discussion

European Medicines Agency (EMA) and the American Food and Drug Administration (FDA) have approved only infliximab and adalimumab as anti-TNFα agents for the treatment of pediatric UC [6]. While the paediatric ulcerative colitis guideline allows for golimumab only after infliximab loss of response [6]. The dose of Golimumab is based on the results of two studies, open-label cohort, pharmacokinetics phase (weeks 0–14), and PURSUIT PEDS PK Long-Term cohort [9,10]. In those studies, anti-TNFα naïve children with moderate-to-severely active UC children received golimumab induction doses based on weight (<45 kg [90/45 mg/m^2], ≥45 kg [200/100 mg]) at weeks 0 and 2 according to weight. Children who responded to treatment were followed up on for two years, with a maintenance dose administered every four weeks [10]. Golimumab showed a clinical benefit and safety in biologically naïve UC pediatric patients, but the drug levels in the subgroup of children weighing <45 kg were numerically lower than those ≥45 kg, which means in practice, a high dose of golimumab is preferred [9–11]. The previous studies had determined the golimumab dose in low-weight children <45 kg with 90 mg/m^2 for induction and 45 mg/m^2 for maintenance [9,10]. While management of paediatric ulcerative colitis guideline recommended the dose of golimumab in <45 kg children as 115 mg/m^2 for induction and 60 mg/m^2 for maintenance [12]. The 60 mg maintenance dose of SC golimumab will require two injectors each time at least one of them golimumab varioject which is in short supply, and unavailable in several regions, also no data on golimumab level for such dose is available, while auto-injector aims to facilitate patient self-injection [13]. Golimumab is also available in vials for infusion for very specific indications such as rheumatoid arthritis, active psoriatic arthritis, active ankylosing spondylitis, and active polyarticular juvenile idiopathic arthritis [14] Furthermore, clinical studies do not support the recommendation to treat low-weight children with 115/60 mg of golimumab. The GO-LEVEL study proposed using therapeutic drug monitoring to optimize golimumab dosing, with therapeutic thresholds of 3.8 g/mL at week 6 and 2.4 g/mL during maintenance [15]. This is also impractical, as these tests do not exist in many developing countries,

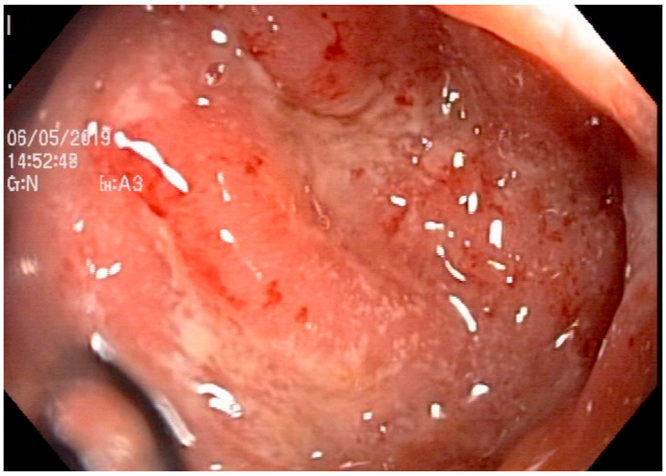

Fig. 1. The end of the ascending colon and cecum before starting treatment.

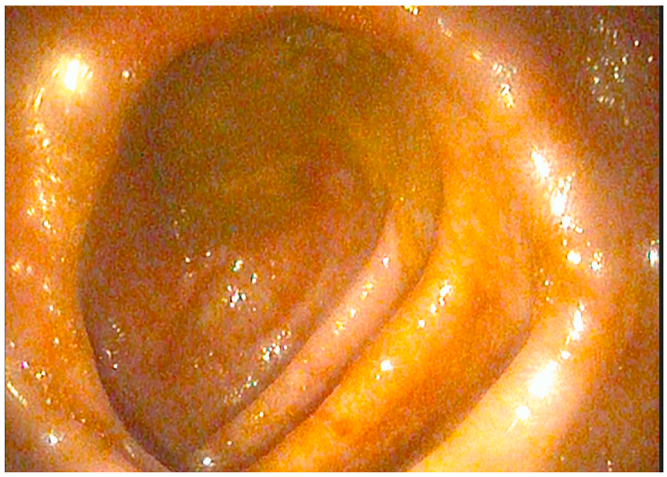

Fig. 2. Same area after two years treatment.

Table 1
Compares the patient's tests prior to starting golimumab to week 122 after starting golimumab.

Test	Before golimumab	After last evaluation	Units	Normal Value
WBC	14100	6300	mm^3	4500–10500
CRP	28	3	mg/l	0–5
Fecal calprotectin	488	54	mg/kg	Up to 120
Red blood cells	4.17	4.30	mm^3	(3.7–4.9) × 10^6
Hemoglobin	10.6	12.70	g/dl	11–14.3
MCHC	35.5	33.42	%	32–36%
MCV	71.7	88.37	fl	80–94
MCH	25.5	29.53	pg	25–31
Platelets	628	134	mm^3	(130-450) × 10^3
ALT/SGPT	14	13	U/L	5–40
AST/SGOT	17	15	U/L	5–40
Gamma G.T	23	27	mg/dl	8–61
Calcium	9.31	9.25	mg/dl	8.8–10.4
Sodium	142	138	mmol/l	134–146
Potassium	4.27	4.3	mmol/l	3.5–5.0
Iron(Fe)	27	71	ug/dl	50–170

ALT = alanine aminotransferase, AST = aspartate aminotransferase, CRP = C-reactive protein, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, SGOT = serum glutamate oxaloacetate transaminase, SGPT = serum glutamate pyruvate transaminase.

including Syria. The immunoassays for measuring serum levels of golimumab and golimumab antibodies were comparable in quality, but the quantitative results were not, emphasizing the importance of using the same assay to consistently monitor a patient's treatment [16]. We previously used golimumab with 200/100 then 50 mg every four weeks to treat acute severe ulcerative colitis low-weight child, which helped him to achieve clinical and endoscopic remission [17]. This case demonstrated that golimumab with 200 mg, 100 mg at week 0, 2 then 50 mg every four weeks may be safe and effective in the treatment of pediatric chronic active ulcerative colitis in low weight children. Further studies are needed to determine the preferred dose, especially in low-weight children.

Ethical approval

This case report did not require review by the Ethics Committee.

Sources of funding

None to declare.

Consent

Written informed consent was obtained from the patient/patient guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

N/A.

Golimumab was studied in an open-label pharmacokinetic cohort of 35 children with moderate-severe UC.

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Author contribution

Marouf Alhalabi established the conceptualization, wrote the main manuscript text, prepared (Figure 1 and Fig. 2, Table 1). Ahmad Abbas edited and revised. All authors had reviewed and approved the final manuscript.

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Declaration of competing interest

None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103456.

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Abbreviations

UC: ulcerative colitis
IBD: inflammatory bowel disease
Anti-TNFα: tumor necrosis factor alpha inhibitors
PK: Pharmacokinetics
SC: Subcutaneous
CRP: C-reactive proteinx'
E. coliEscherichia coli:
PUCAI: pediatric ulcerative colitis activity index