Case Report

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Teduglutide in Enterocolitis Secondary to Graft-Versus-Host Disease Post-Bone Transplant: Case Report

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Abstract

Background: Gastrointestinal graft-versus-host disease (GVHD) is one of the most severe complications of hematopoietic stem cell transplantation (HSCT), particularly in pediatric patients. It is frequently associated with treatment refractoriness and prolonged dependence on parenteral nutrition. Teduglutide, a GLP-2 analog, has shown promise in intestinal mucosal regeneration, but its use in GVHD remains limited. This case report describes the clinical experience with teduglutide in a pediatric patient with refractory GVHD-associated enterocolitis. **Methods:** We report the case of a 3-year-old child with primary immunodeficiency (Hyper-IgM Syndrome – CD40L deficiency) who underwent haploidentical HSCT and subsequently developed grade III gastrointestinal GVHD. The patient presented with severe chronic diarrhea, rectal prolapse, extensive intestinal inflammation, and nutritional failure despite standard immunosuppressive therapy. Teduglutide was initiated on a compassionate basis at a dose of 0.9 mg subcutaneously once daily. **Results:** Following initiation of teduglutide, the patient showed sustained improvement in stool consistency and frequency, reduced signs of intestinal inflammation, nutritional stabilization, and resolution of rectal prolapse episodes. Clinical response was maintained until the patient's death due to pulmonary infectious complications unrelated to gastrointestinal involvement. **Conclusions:** The positive intestinal response observed in this case supports the potential role of teduglutide as an adjunctive therapy for mucosal recovery in refractory GI-GVHD. Although encouraging, its use in this setting warrants further investigation through controlled studies, particularly in pediatric populations.

Keywords: Refractory enterocolitis; Hematopoietic Stem Cell Transplantation; Pediatric chronic diarrhea; Teduglutide

1. Introduction

Graft-versus-host disease (GVHD) is a common and potentially severe complication of bone marrow transplantation (BMT), characterized by an immune-mediated attack of donor cells against the recipient's tissues. Among its clinical manifestations, approximately 70% of cases involve the gastrointestinal (GI) tract, especially in pediatric patients [1,2]. In these cases, intestinal GVHD can lead to severe enterocolitis, resulting in malabsorption and prolonged dependence on parenteral nutrition (PN), which significantly increases the morbidity and mortality of these patients [3,4].

Intestinal injury in GVHD is driven by complex immunological mechanisms, leading to epithelial destruction, loss of barrier function, and exacerbation of the inflammatory response, which worsens the clinical condition and hinders nutritional recovery [5]. Historically, the overall 2-year survival rate after the onset of acute GVHD with GI symptoms in stages 3 or 4 was approximately 25% [6,7]. Moreover, GI involvement in acute GVHD has been identified as a major risk factor for steroid-refractory disease [7,8].

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In cases of refractoriness to conventional therapies, new therapeutic approaches have been explored to promote mucosal repair and restoration of intestinal function. One of these is teduglutide, a glucagon-like peptide-2 (GLP-2) analog, which has been successfully used in the treatment of short bowel syndrome due to its regenerative effects on the intestinal mucosa, thereby enhancing nutrient absorption and reducing dependence on parenteral nutrition (PN) [9]. Recent studies have also demonstrated its potential as an adjunct therapy in other conditions of functional intestinal failure, such as GVHD-associated refractory enterocolitis, although clinical experience in pediatric populations remains limited [10,11].

This case report describes the clinical experience with teduglutide in a pediatric patient with enterocolitis secondary to GVHD post-BMT, highlighting the observed effects, clinical outcome, and potential applicability of this promising therapy in refractory contexts.

2. Detailed Case Description

A 3-year-old boy diagnosed with Hyper-IgM Syndrome (CD40L deficiency) underwent a haploidentical hematopoietic stem cell transplantation (HSCT) from his father. He was eutrophic and in good clinical condition prior to transplantation. Post-BMT, he developed grade I cutaneous GVHD, treated with methylprednisolone, and presented with diarrhea, abdominal distension, and persistent pain despite morphine administration. He developed feeding refusal and, due to intestinal involvement, was started on PN. He subsequently developed cholestasis. Abdominal ultrasound revealed colonic wall thickening, intestinal pneumatosis, and bowel distension, suggestive of inflammatory colitis. His clinical condition worsened, with fever and bloody diarrhea. Laboratory tests showed significant deterioration, including jaundice, elevated liver enzymes, and serum albumin of 2.6 mg/dL. Upper GI endoscopy and colonoscopy confirmed grade III GI GVHD, with ulcerative pancolitis (Figure 1 and Figure 2).

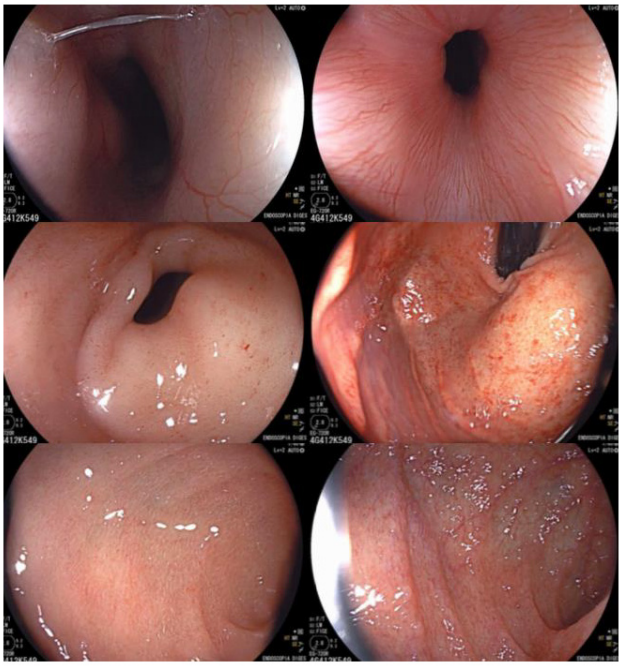

Figure 1. Upper GI endoscopy findings: Intense hyperemia throughout the stomach without other lesions.

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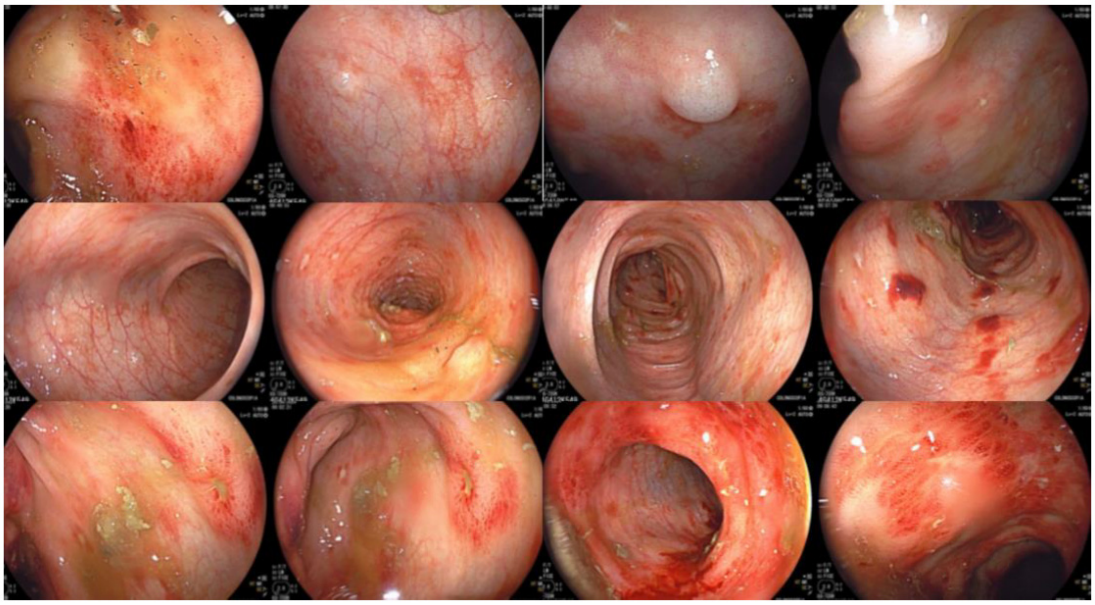

Figure 2. Colonoscopy findings: Pancolitis with ulcers, hyperemia and aphthous lesions. Biopsies confirmed severe inflammation and lesions consistent with GVHD in the stomach, duodenum, and colon (Figure 3).

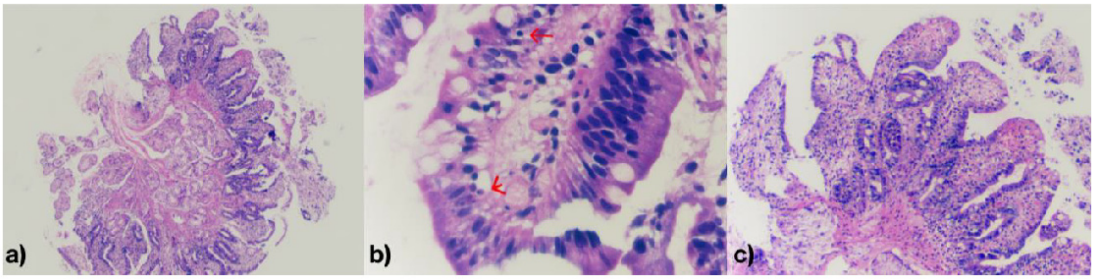

Figure 3. Biopsy findings: a) Duodenal mucosa with partial flattening of villi, erosion, and epithelial detachment; b) Intraepithelial lymphocytes (long arrow) and apoptotic bodies (short arrow); c) Detachment of the surface epithelium and intraepithelial lymphocytes.

He remained on PN with poor oral intake and underwent gastrostomy. He developed *Clostridium difficile* infection (CDI), treated with oral vancomycin. Despite multiple therapies (corticosteroids, immunosuppressants, antibiotics, and intensive support), he continued to experience persistent diarrhea, including episodes of rectal prolapse, tenesmus, and hematochezia. Secretory diarrhea was documented with fecal sodium of 120 mEq/L. Teduglutide was initiated at 0.05 mg/kg/day subcutaneously, and by the second week, stool consistency and frequency improved, despite ongoing clinical deterioration. The response was sustained, with some days without bowel movements. He later developed respiratory deterioration, bloodstream infection, and necrotizing pneumonia, requiring middle lobe lobectomy. Pulmonary biopsy revealed invasive aspergillosis. He progressed to bronchopulmonary fistula, acute respiratory distress syndrome (ARDS), and death.

3. Discussion

GVHD remains one of the leading causes of morbidity and mortality following bone marrow transplantation, classically divided into acute and chronic forms. Recently, classification has shifted toward clinical phenotype rather than time of onset. Acute GVHD was defined by onset within the first 100 days post-HSCT, although, currently, clinical manifestations, not the time of symptom onset after HSCT, determine whether GVHD is acute or chronic [12]. Acute GVHD is a reaction of the

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donor's immune cells against the host's tissues, with the three main tissues affected being the skin, liver, and gastrointestinal tract [13]. The modified Glucksberg-Seattle criteria are widely used and provide a stage and grade (grade 0–IV) for each organ and its degree of involvement. Those with grade III/IV GVHD tend to have a poor overall outcome [14].

Acute intestinal GVHD is among the most feared complications, particularly in pediatric patients, due to the high risk of infection, malnutrition, and prolonged dependence on PN, as observed in this case [1–3]. The patient presented a severe clinical course, refractory to conventional therapies, progressing to chronic enterocolitis with inflammatory, malabsorptive, and secretory features—typical of grade III intestinal GVHD [4]. He also developed CDI. The literature describes that patients undergoing HSCT typically have more risk factors for this infection during treatment and an increased risk of CDI compared to the general population [16].

The pathophysiology of intestinal GVHD involves activation of donor T lymphocytes, release of inflammatory cytokines, and direct damage to the intestinal epithelium, impairing barrier function, increasing bacterial translocation, and perpetuating inflammation [4,5]. In this case, intestinal GVHD progressed with increasing severity despite immunosuppressive and antibiotic therapies. The diagnosis was possible after performing upper digestive endoscopy with biopsies, which corroborates studies demonstrating that endoscopy has high diagnostic accuracy and plays a significant role in the early diagnosis and treatment of intestinal GVHD in patients undergoing bone marrow transplantation, but histological evaluation of the gastrointestinal mucosa is necessary to confirm a more precise diagnosis [17].

The clinical and endoscopic manifestations (ulcerative pancolitis, rectal prolapse, frequent bloody bowel movements) and histological findings of GVHD grade III reflect the intensity of mucosal damage, reaffirming that the integrity of the epithelial barrier is central to disease control [5]. In this context, therapies that promote mucosal repair gain relevance. Teduglutide, a GLP-2 analogue, has shown promising effects in stimulating intestinal mucosal regeneration. Its action includes increased enterocyte proliferation, reduced intestinal motility and secretion, and increased absorption of water, electrolytes, and nutrients [10].

Although primarily indicated for short bowel syndrome, emerging data suggest benefits in severe, persistent intestinal inflammation. Recent studies support this perspective. Ramos et al.[11] reported clinical improvement and reduced PN dependence in children and young adults with refractory intestinal GVHD treated with teduglutide. Brehm et al. [15], in a multicenter study, also documented significant clinical responses in adults with severe intestinal GVHD after treatment failure, demonstrating improvement in intestinal absorption and recovery of bowel function.

In the present case, teduglutide administration was associated with sustained improvement in bowel habits, with more formed stools, reduced frequency, and occasional absence of bowel movements—outcomes not achieved with other treatments. These findings support the hypothesis that, beyond immunological control, mucosal repair may be a crucial therapeutic component in refractory GVHD. Despite intestinal clinical improvement, the patient succumbed to severe infectious respiratory complications. Notably, the intestinal benefits of teduglutide persisted until the final phase of hospitalization, reinforcing its potential direct effect on the GI mucosa, independent of systemic condition.

4. Conclusions

This case highlights the emerging role of teduglutide as an adjunctive therapy in selected cases of intestinal GVHD, particularly in patients who are refractory and dependent on intensive nutritional support. Although the clinical outcome was marked by death due to systemic complications unrelated to the gastrointestinal tract, the maintenance of intestinal benefits until the final stages of hospitalization highlights the relevance of mucosal repair as a complementary therapeutic component. The reported experience contributes to the understanding of the applicability of teduglutide as a promising adjunctive option in challenging clinical situations. However, further

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studies—especially in pediatric populations—are essential to establish its efficacy, safety, and long-term impact.

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Informed Consent Statement: Written informed consent has been obtained from the parent's legal guardian to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to patient privacy.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ARDS	**Acute respiratory distress syndrome**
BMT	Bone Marrow Transplant
CDI	*Clostridium difficile* infection
GLP-2	Glucagon-like peptide 2
GVHD	Graft-versus-host disease
HSCT	Hematopoietic stem cell transplantation
PN	Parenteral nutrition
SC	Subcutaneous

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