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OCTREOTIDE AS A BRIDGE TO ANTI-TNF THERAPY IN SEVERE FISTULIZING CROHN'S DISEASE COMPLICATED BY A CLINICALLY HIGH-OUTPUT ENTEROCUTANEOUS FISTULA: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Introduction: Fistulizing Crohn's disease is a severe phenotype of inflammatory bowel disease and may be complicated by enterocutaneous fistulas, which are associated with substantial morbidity due to sepsis, fluid and electrolyte disturbances, skin damage, and severe malnutrition. Anti-tumour necrosis factor agents, particularly infliximab, represent a cornerstone of medical therapy for fistulizing Crohn's disease. However, their initiation may need to be temporarily deferred in patients with septic risk, uncontrolled fistula output, or profound nutritional impairment.

Case report: We report the case of a 54-year-old man with severe stenosing and fistulizing ileocolonic Crohn's disease, classified as A3L3B3P0 according to the Montreal classification, complicated by a long-standing -clinically high-output- enterocutaneous fistula. On admission, he had severe malnutrition, with a body mass index of 13.8 kg/m^2, hypoalbuminemia at 24 g/L, hyponatremia, elevated C-reactive protein, and multiple complex fistulous tracts on abdominopelvic computed tomography, without a drainable deep collection.

Because immediate infliximab therapy was considered unsafe, a multidisciplinary -bridging strategy- was initiated, combining nutritional optimization, local wound care, correction of deficiencies, and subcutaneous octreotide at a dose of 100 µg every 8 hours for one month. This approach was associated with a marked reduction in fistula output, from six to seven pouch changes per day to one daily change, progressive improvement of skin lesions, weight gain without edema, increased serum albumin, and decreased systemic inflammation. These improvements allowed subsequent initiation of infliximab therapy.

Conclusion: This case suggests that octreotide may be useful as -adjunctive antisecretory bridge therapy- in selected patients with Crohn's disease-associated clinically high-output enterocutaneous fistulas when biologic therapy must be delayed. Its role should not be interpreted as definitive fistula therapy, but rather as part of a broader strategy aimed at reducing fistula output, improving nutritional and inflammatory status, and creating safer conditions for disease-modifying treatment.

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KEYWORDS

Crohn's disease, enterocutaneous fistula, octreotide, somatostatin analogues, bridging therapy

LEARNING POINTS

- This case highlights the potential role of octreotide as adjunctive antisecretory bridge therapy in Crohn's disease-associated clinically high-output enterocutaneous fistulas when immediate biologic therapy is considered unsafe because of severe malnutrition, major inflammatory burden, or septic risk.
- This observation emphasizes the importance of multidisciplinary stabilization before biologic therapy, including nutritional optimization, correction of metabolic and electrolyte abnormalities, local wound care, and inflammatory control in fragile patients with complicated fistulizing Crohn's disease.
- This case demonstrates that a conservative strategy integrating octreotide may achieve substantial reduction in fistula output, improvement of nutritional and biological status, and creation of safer conditions for subsequent disease-modifying therapy initiation.

INTRODUCTION

Crohn's disease is a chronic inflammatory bowel disease characterized by segmental transmural inflammation, which may lead to stricturing and penetrating complications[1,2]. During the disease course, approximately 20–40% of patients develop a penetrating phenotype, including internal or external fistulas[1,2]. Enterocutaneous fistulas are abnormal communications between the gastrointestinal tract and the skin. In Crohn's disease, they may occur spontaneously as a consequence of penetrating disease or develop after abdominal surgery. Although uncommon, they are associated with substantial morbidity, mainly related to chronic external drainage, sepsis, fluid and electrolyte disturbances, skin injury, and severe malnutrition[1,2].

Management requires a multidisciplinary strategy focused on sepsis control, drainage of collections when present, correction of fluid and electrolyte abnormalities, skin protection, reduction of fistula output, anatomical assessment, and nutritional optimization[2,3]. Anti-tumour necrosis factor (TNF) therapy, particularly infliximab, remains a key treatment for fistulizing Crohn's disease, but its initiation may need to be temporarily deferred in patients with septic risk or profound nutritional impairment[3].

Somatostatin analogues, especially octreotide, reduce gastrointestinal secretions and may rapidly decrease fistula output. Most available evidence concerns postoperative or mixed enterocutaneous fistulas, while data in Crohn's disease remain limited to small series and case reports[4,5]. Therefore, octreotide should be considered -adjunctive bridging therapy- rather than definitive fistula treatment.

We report a case of severe stenosing and fistulizing ileocolonic Crohn's disease complicated by a -clinically high-output- enterocutaneous fistula, in which octreotide was used to reduce fistula output, improve nutritional status, and allow subsequent initiation of infliximab.

CASE DESCRIPTION

A 54-year-old Moroccan man with a history of pulmonary tuberculosis successfully treated in 2014, right femoral fracture managed by osteosynthesis, and cholecystectomy for acute cholecystitis in 2021 was followed for Crohn's disease diagnosed in 2006.

At diagnosis, he underwent surgery for intestinal obstruction, consisting of a right hemicolectomy with terminal ileal resection and ileotransverse anastomosis. The postoperative course was complicated by an anastomotic leak on postoperative day 8, requiring reoperation with repair of a transverse colonic leak and creation of a terminal ileostomy. In 2025, he developed peritonitis secondary to an iatrogenic post-colonoscopy small-bowel perforation, requiring peritoneal lavage and drainage, with closure of a small-bowel-to-abdominal-wall fistula.

Regarding medical therapy, he had received oral 5-aminosalicylates for four years, with poor adherence, before discontinuing both follow-up and maintenance treatment in 2010. A previous colonoscopy showed macroscopically normal small-bowel mucosa and erythematous congestive rectosigmoiditis with areas of mucosal sparing.

The current episode began two years before admission, with progressive development of an enterocutaneous fistula in the right iliac fossa, draining purulent and enteric fluid, associated with a second fistulous opening on the midline laparotomy scar. The fistula was clinically high-output, requiring six to seven pouch changes per day. The patient also reported diffuse abdominal pain and intermittent obstructive symptoms.

On admission, he was severely malnourished, with a World Health Organization performance status of 1, a weight of 45 kg, a body mass index of 13.8 kg/m^2, and a Nutritional Risk Index of 62. Abdominal examination revealed four fistulous openings in the right iliac fossa with purulent discharge *(Fig. 1)*, as well as a fistulous opening on the midline laparotomy scar with surrounding inflammatory skin changes *(Fig. 2)*. An ostomy pouch was present in the left iliac fossa.

Laboratory investigations showed elevated inflammatory

markers, with C-reactive protein at 110 mg/l, platelet count at 467 $\times 10^9$/l, and white blood cell count at 8.5 $\times 10^9$/l. Procalcitonin was 0.11 ng/ml. The patient also had normocytic normochromic anaemia, with haemoglobin at 11.4 g/dl, severe hypoalbuminemia at 24 g/l, hyponatremia at 126 mmol/l, and preserved renal function. Nutritional assessment showed vitamin D deficiency at 9.6 ng/ml and low ferritin at 19.31 ng/ml. Microbiological cultures were negative.

Contrast-enhanced abdominopelvic computed tomography scan showed inflammatory ileal wall thickening with stenotic segments and upstream bowel dilatation, associated with multiple entero-enteric and ileosigmoid fistulous tracts. It also confirmed an enterocutaneous fistula *(Fig. 3)* in the right iliac fossa, with marked perilesional fat stranding but no drainable deep collection.

Because of severe malnutrition, clinically high-output fistula drainage, elevated inflammatory markers, and septic risk, immediate initiation of infliximab was temporarily deferred. A multidisciplinary conservative strategy was initiated, combining local wound care with a zinc-based barrier ointment, thromboprophylaxis, correction of vitamin and trace element deficiencies, and subcutaneous octreotide at a dose of 100 µg every 8 hours for one month. Nutritional support included Modulen® IBD, enteral nutrition, a high-calorie, high-protein, low-fat, low-residue diet, and supplemental parenteral nutrition with Oliclinomel®.

After one month, the patient's condition improved markedly. He gained 14 kg, increasing from 45 kg to 59 kg, without oedema or clinical signs of fluid overload. Fistula output decreased from six to seven pouch changes per day to one daily pouch change, and the surrounding skin lesions progressively healed *(Fig. 4)*. Laboratory tests also improved, with C-reactive protein decreasing to 12 mg/l, platelet count to 412 $\times 10^9$/l, and serum albumin increasing to 32 g/l. Renal function and serum electrolytes normalized. After clinical, nutritional, and inflammatory stabilization, the patient received the first induction dose of infliximab at 5 mg/kg as disease-modifying therapy for Crohn's disease.

DISCUSSION

Crohn's disease is characterized by chronic transmural inflammation, which may lead to stricturing and penetrating complications. The penetrating phenotype is observed in approximately 20–40% of patients during the disease course and is one of the most severe patterns of Crohn's disease[1,2]. Fistulas may be perianal, entero-enteric, enterovesical, rectovaginal, or enterocutaneous. Among these, enterocutaneous fistulas are relatively uncommon but remain particularly challenging because they combine ongoing intestinal inflammation, external enteric losses, septic risk, skin injury, and nutritional depletion[1,2].

An enterocutaneous fistula is defined as an abnormal communication between the gastrointestinal tract and the skin, resulting in external drainage of enteric contents. In Crohn's disease, it may occur spontaneously as a consequence of transmural inflammation and penetrating disease, or develop after abdominal surgery[1,2]. Its prognosis depends on fistula anatomy, output, distal obstruction, active sepsis, nutritional status, and underlying inflammatory activity. High-output fistulas expose patients to fluid and electrolyte depletion, dehydration, renal dysfunction, severe malnutrition, skin injury, prolonged hospitalization, and impaired quality of life[1,2].

Management requires a multidisciplinary approach involving gastroenterologists, colorectal surgeons, radiologists, nutrition specialists, wound-care nurses, and, when necessary, infectious disease specialists. Initial management should focus on sepsis control, drainage of collections when present, correction of fluid and electrolyte disorders, skin protection, anatomical assessment, reduction of fistula output, and nutritional rehabilitation[2,3].

Nutritional optimization is a cornerstone of management. Patients with high-output enterocutaneous fistulas are at high risk of protein-energy malnutrition because of enteric

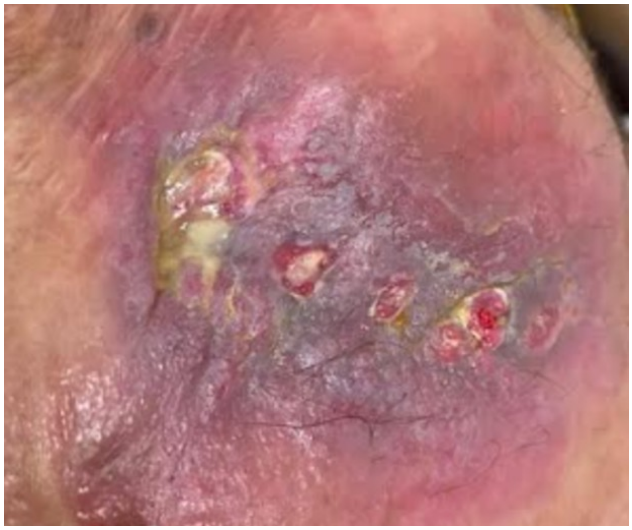


Figure 1. *Baseline multiple fistulous openings in the right iliac fossa.*

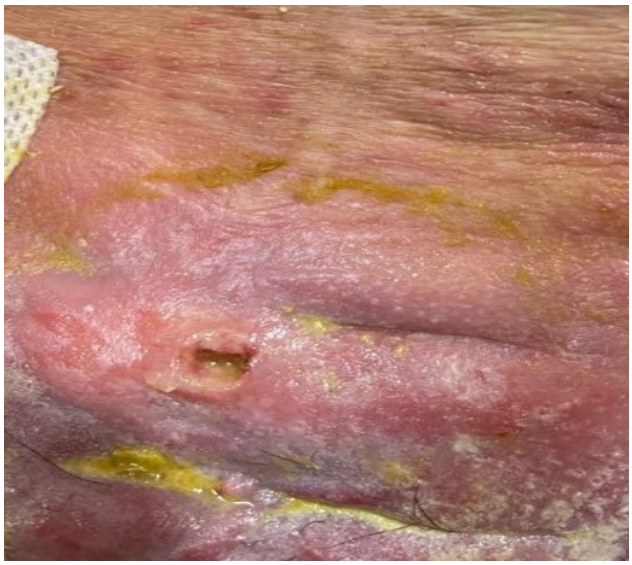


Figure 2. *Midline laparotomy-scar fistula after local cleansing, before initiation of octreotide therapy.*



Figure 3. Contrast-enhanced abdominopelvic CT scan showing an enterocutaneous fistulous tract in the right iliac fossa.



Figure 4. Improved midline laparotomy-scar fistula after one month of octreotide-based conservative management.

losses, reduced oral intake, systemic inflammation, and hypercatabolism. Enteral nutrition should be preferred whenever feasible because of its trophic effect on the intestinal mucosa, while supplemental or total parenteral nutrition may be required when enteral intake is insufficient or fistula output remains excessive. Correction of micronutrient deficiencies, trace element depletion, and hypoalbuminemia is essential before definitive medical or surgical treatment can be safely considered[2].

Somatostatin is an endogenous peptide hormone with broad inhibitory effects on the gastrointestinal tract. It reduces gastric, pancreatic, biliary, and intestinal secretions, decreases intestinal motility, and may reduce splanchnic blood flow. Octreotide, marketed as Sandostatin®, is a synthetic somatostatin analogue with a longer half-life and more convenient administration. These pharmacological properties provide the rationale for its use in enterocutaneous fistulas, mainly as an antisecretory agent aimed at reducing fistula output and facilitating fluid, electrolyte, and nutritional stabilization[4].

Most available evidence for somatostatin and its analogues comes from postoperative or mixed gastrointestinal fistula populations rather than Crohn's disease-specific enterocutaneous fistulas. In these settings, somatostatin-based therapies have been associated with reduction of fistula output and, in some studies, shorter time to closure and shorter hospital stay. However, their effect on definitive spontaneous closure remains inconsistent, and no clear mortality benefit has been demonstrated[5–7]. Therefore, these agents should be considered as adjunctive output-reducing therapy, not definitive fistula-closing treatment.

A major unresolved issue concerns the optimal dosing regimen of somatostatin analogues in Crohn's disease-associated enterocutaneous fistulas. In postoperative or mixed gastrointestinal fistula populations, octreotide is commonly administered subcutaneously, often at doses ranging from 100 µg three times daily to higher regimens, or by continuous intravenous infusion depending on fistula output and clinical severity. However, no validated dose, duration, or response-based adjustment strategy has been established specifically for Crohn's disease-associated enterocutaneous fistulas. The few available reports used heterogeneous regimens, including the early clinical experience reported by Al-Karawi et al.[8] and the higher-dose regimen described in Lavy's pilot study[9].

The report by Lavy and Yasin is particularly relevant to the present case, as it remains one of the few Crohn's disease-specific publications describing octreotide use for enterocutaneous fistulas[9]. In this pilot study, five patients with Crohn's disease-associated enterocutaneous fistulas were treated with octreotide 300 µg subcutaneously four times daily for eight weeks. Fistula closure was achieved in four of the five patients; however, recurrence with subsequent surgery occurred in some cases, highlighting both the potential benefit and the limitations of this approach[9]. These findings support the use of octreotide as an adjunctive output-reducing therapy in selected patients. In this context, our observation adds to this limited literature by illustrating the use of octreotide as a short-term antisecretory bridge before anti-TNF therapy, integrated into a broader multidisciplinary strategy aimed at improving nutritional, inflammatory, and clinical stability before infliximab initiation.

The available Crohn-specific cases, together with the present observation, are summarized in *Table 1*. However, this table should be interpreted as a descriptive summary of limited published experience rather than as evidence supporting a standardized octreotide regimen in Crohn's disease-associated enterocutaneous fistulas. In the present case, octreotide 100 µg every 8 hours was selected by extrapolation from general enterocutaneous fistula management rather than from disease-specific dosing evidence. Therefore, octreotide dosing in this setting should be individualized, short-term, clinically monitored, and reassessed according to fistula output, nutritional response, tolerance, and the possibility of initiating definitive Crohn's disease therapy.

Current guidelines and expert reviews emphasize that surgery has a central role in complicated Crohn's

Source	Patient/disease phenotype	Initial fistula output	Drug and dose	Duration	Response after treatment	Final outcome
Al-Karawi and Ahmed[8]	24-year-old female with Crohn's disease and recurrent enterocutaneous fistulas	High-volume fistula discharge	Octreotide 50 µg SC once daily, gradually increased to 50 µg SC three times daily	Not clearly specified	Gradual reduction in fistula discharge; fistulas began to close after the first week	Clinical improvement, with no further recurrence reported during follow-up
Lavy and Yasin[9]	17-year-old female with terminal ileal Crohn's disease; enterocutaneous fistula after abscess drainage	Not reported	Octreotide 300 µg SC four times daily	8 weeks	Fistula closure after 4 weeks	Secondary reopening after upper gastrointestinal series; surgery required
Lavy and Yasin[9]	50-year-old male with long-standing Crohn's disease; postoperative enterocutaneous fistula	Not reported	Octreotide 300 µg SC four times daily	8 weeks	Fistula closure after 5 weeks	Sustained closure at 24 months
Lavy and Yasin[9]	40-year-old male with diffuse Crohn's disease; spontaneous enterocutaneous fistula	Not reported	Octreotide 300 µg SC four times daily	8 weeks	Fistula closure after 3 weeks	Sustained closure at 19 months
Lavy and Yasin[9]	37-year-old male with ileal Crohn's disease; ileocutaneous fistula after abscess drainage	Not reported	Octreotide 300 µg SC four times daily	8 weeks	Fistula closure within 2 weeks	Fistula recurrence after 1 year; surgery subsequently performed
Lavy and Yasin[9]	45-year-old male with Crohn's disease involving the terminal ileum and rectum; cologluteal fistula	Not reported	Octreotide 300 µg SC four times daily	8 weeks	Fistula closure after 6 weeks	Sustained closure at 12 months
Present case	54-year-old male with severe stenosing and fistulizing ileocolonic Crohn's disease complicated by a clinically high-output enterocutaneous fistula	Clinically high-output fistula requiring six to seven pouch changes per day	Octreotide 100 µg SC every 8 hours	1 month	Marked reduction in fistula output to one pouch change per day, with improvement of skin lesions	Nutritional and inflammatory improvement, allowing subsequent initiation of infliximab

Table 1. *Published Crohn's disease-associated enterocutaneous fistulas treated with somatostatin analogues.*

disease-associated fistulas, particularly in the presence of peritonitis, perforation, haemorrhage, uncontrolled abdominal sepsis, undrained abscess, or failure of conservative management[2]. However, outside emergency settings, surgery should preferably be delayed until sepsis is controlled, nutritional status is improved, electrolyte disturbances are corrected, and inflammatory activity is better controlled. In severely malnourished or clinically fragile patients, premature surgery may carry substantial morbidity; therefore, a bridging strategy aimed at stabilization is clinically relevant when no immediate surgical indication exists[2,3].

Anti-TNF agents, particularly infliximab, remain the best-established biologic therapy for fistulizing Crohn's disease. In the GETAID cohort, Amiot et al. reported complete closure of enterocutaneous fistulas in approximately one-third of patients treated with anti-TNF therapy 10]. In clinical practice, the role of anti-TNF therapy in this setting is not to replace urgent surgery when surgery is mandatory, but to control active Crohn's disease, promote fistula healing when anatomically feasible, and potentially avoid or delay surgery in selected fragile patients after adequate stabilization[10].

In the present case, octreotide was used as part of a broader multidisciplinary conservative strategy, not as definitive fistula therapy but as bridge therapy before disease-modifying treatment. The patient had multiple adverse prognostic factors, including multiple fistulous tracts, clinically high-output drainage requiring six to seven pouch changes per day, severe malnutrition with a body mass index of 13.8 kg/m^2, marked hypoalbuminemia, hyponatremia, elevated inflammatory markers, complex ileal and ileosigmoid fistulas on computed tomography, and septic risk. Hypoalbuminemia and poor nutritional status are well-recognized adverse prognostic factors in enterocutaneous fistulas[2]. Immediate infliximab therapy was therefore temporarily deferred.

After one month of combined management, including wound care, thromboprophylaxis, correction of vitamin and trace element deficiencies, enteral nutrition, supplemental parenteral nutrition, and octreotide, the patient showed marked clinical and biological improvement. Fistula output decreased substantially, skin lesions improved, body weight increased without oedema, serum albumin rose, serum electrolytes normalized, and C-reactive protein decreased. This stabilization created safer conditions for the initiation of infliximab as disease-modifying therapy, with the aim of controlling the underlying Crohn's disease and avoiding immediate surgery in a severely fragile patient.

The main value of this observation is therefore not to suggest that octreotide can replace anti-TNF therapy or surgery, but to support its potential role as adjunctive antisecretory bridging therapy in carefully selected patients

with Crohn's disease-associated clinically high-output enterocutaneous fistulas. By reducing enteric losses and improving the nutritional and inflammatory environment, octreotide may help create more favourable conditions for subsequent biologic therapy or delayed surgery when indicated.

This case has several limitations. As a single observation, it cannot establish causality. The favourable outcome likely resulted from the combined effect of multidisciplinary care, nutritional support, local wound management, correction of deficiencies, and octreotide. In addition, fistula output was assessed clinically by pouch-change frequency rather than quantified in ml/day. The dose of octreotide used in this case was also selected by extrapolation from general enterocutaneous fistula practice, because no Crohn's-specific dosing recommendations are available. Further studies are required to define the optimal indications, dose, duration, and true clinical impact of somatostatin analogues in Crohn's disease-associated enterocutaneous fistulas.

CONCLUSION

Octreotide may represent a useful adjunctive antisecretory bridge therapy in selected patients with Crohn's disease-associated clinically high-output enterocutaneous fistulas when immediate biologic therapy is unsafe because of septic risk, severe malnutrition, or major clinical instability. In the present case, octreotide was associated with marked reduction in fistula output, improvement of skin lesions, nutritional recovery, and biological stabilization, allowing subsequent initiation of infliximab. However, octreotide should not be considered a substitute for definitive Crohn's disease therapy or surgery when surgery is mandatory. Its role is best understood as part of a multidisciplinary stabilization strategy aimed at creating safer conditions for anti-TNF therapy or delayed surgical management.

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