

## Nintedanib Induced Colitis Treated Effectively with Budesonide

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<b>Supplemental Video</b>	<a href="#">Supplemental Video</a>
<b>Category</b>	Medicine & Medical Subspecialties

### Abstract

#### Introduction:

Nintedanib, a tyrosine kinase inhibitor, displays antifibrotic activity via blockade of three receptors (PDGFR, VEGFR, and FGFR). This drug was initially developed as an anti-tumor agent but was later recognized for its unique antifibrotic activity. It is mainly cleared by liver metabolism, with most of the metabolites being excreted in the feces (feces 93.4%, urine <1%). The most common adverse effect associated with nintedanib is diarrhea (62%), which has led to a permanent dose reduction in 11% of patients and discontinuation in 5%. Here we report a case of nintedanib induced diarrhea with complete clinical resolution after treatment with oral budesonide.

#### Case Presentation

A 68-year-old male with a past medical history of interstitial pulmonary fibrosis (IPF) and chronic diarrhea for 3 years was admitted to the hospital with the chief complaint of hematochezia and worsening diarrhea. He denied any abdominal pain or nausea. In the past 3 years, he was taking nintedanib (150 mg twice daily) for IPF. For his diarrhea, he was maintained on cholestyramine twice a day and other antidiarrheals, but his diarrhea persisted and worsened. A colonoscopy performed 2 years ago showed non-specific moderate diffuse colitis.

The physical examination and vital signs were unremarkable. His blood work, including complete blood count (CBC) and comprehensive metabolic panel (CMP), was within normal limits. His CRP was mildly elevated. Repeat colonoscopy revealed diffuse areas of erythematous, friable, and granular mucosa throughout the entire colon, similar to the previous endoscopic findings. Histopathology showed acute superficial inflammation, and expansion of lamina propria by lymphoplasmacytic infiltrate, raising the possibility of nintedanib induced colitis. As it was more pertinent to continue with nintedanib for his IPF, we elected to treat his colitis with budesonide. He was started on 9 mg oral budesonide with the plan to slowly taper it to the minimum effective dose. His diarrhea gradually improved, and at his follow up visit about 4 months later, it had completely resolved.

Final diagnosis: Nintedanib-induced diarrhea/colitis

#### Management:

The mechanism of nintedanib-induced diarrhea/colitis remains unknown. One of the proposed mechanisms involves direct inflammation of the intestinal epithelium induced by nintedanib decomposition products. Nintedanib is primarily cleared via liver metabolism, with most of the metabolites being excreted in the feces. This inflammation, like that of inflammatory bowel disease, may respond to corticosteroid treatment resulting in the improvement of diarrhea.

In our patient, stopping this medication was not a viable option since it was very effective in reducing disease progression. We used budesonide, a glucocorticoid with high first-pass metabolism, as its systemic side effects would be less severe as compared with conventional glucocorticoids. The patient had complete clinical remission in less than three months.

**Learning Objectives**

Diarrhea and colitis are a well known common side effect of nintedanib and often lead to the discontinuation of this medication. In patients with nintedanib induced colitis/diarrhea who are resistant to oral antidiarrheal medications, budesonide could be a viable option to cure this common side effect. Further research is needed to help standardize its use and prevent IPF treatment interruption.