



# Non-selective Beta-Blockers in Retroperitoneal Fibrosis: Possible Role in Symptom Exacerbation – A Case Report

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## Abstract

**Introduction:** Retroperitoneal fibrosis (RPF) is a rare fibroinflammatory disorder characterized by progressive deposition of dense collagenous tissue within the retroperitoneal space, encasing vascular and visceral structures. Although most cases are idiopathic, certain pharmacological agents have been implicated in symptom exacerbation. This case report describes an acute deterioration of gastrointestinal function following initiation of a non-selective beta-adrenergic blocker in a patient with otherwise stable disease.

**Case Presentation:** A 45-year-old Caucasian woman with dyslipidemia and chronic sinus tachycardia underwent exploratory laparotomy for suspected peritoneal malignancy. Histopathological examination confirmed extensive fibrotic deposition with chronic inflammatory infiltrates and excluded neoplasia, establishing a diagnosis of RPF. During three years of surveillance with serial laboratory testing and magnetic resonance imaging, the disease remained quiescent. To optimize heart rate control, therapy with a beta-1-selective antagonist was replaced by propranolol 40 mg twice daily, a non-selective beta-adrenergic blocker. Within days, she developed severe crampy abdominal pain, marked distension, and altered bowel habits, despite stable imaging findings. The close temporal relationship, together with the established role of beta-2 receptors in intestinal smooth muscle relaxation, implicated non-selective blockade in aggravating colonic dysmotility against a background of fibrotic compression. Dietary modifications and low-dose antispasmodics provided only marginal relief.

**Conclusion:** This case highlights that non-selective beta-blockers may exacerbate gastrointestinal symptoms in RPF by impairing smooth muscle relaxation. In patients with colonic involvement, beta-1-selective agents should be preferred, with careful consideration of cardiovascular benefits versus gastrointestinal risks.

## INTRODUCTION

The association between RPF and beta-blocker therapy has been reported only once in the literature, and no robust scientific evidence currently supports this correlation. Nevertheless, in the present case, a patient with RPF experienced a marked exacerbation of previously latent symptoms following the initiation of a non-selective beta-blocker.

## CASE

A 45-year-old woman with a history of dyslipidemia and tachycardia, initially treated with bisoprolol (Cardicor®) 1.25 mg once daily, underwent urgent exploratory laparotomy in 2013 after imaging suggested multiple metastatic lesions involving the abdominal viscera. She presented with nonspecific abdominal discomfort, bloating, and unintentional weight loss. Intraoperatively, a bilateral salpingectomy and peritoneal inspection were performed. Multiple fibrotic masses and dense adhesions were observed, particularly in the retroperitoneal region and around the intestines.

Histopathological examination of the biopsied tissue demonstrated chronic inflammatory infiltrates and dense fibrosis, consistent with idiopathic RPF, thereby excluding the initial suspicion of peritoneal carcinomatosis. Complete surgical excision was not feasible due to extensive involvement of the abdominal viscera and retroperitoneal structures, leaving residual disease.

In the subsequent years, the patient underwent serial follow-up, including laboratory testing (inflammatory markers, autoimmune panel, and serum IgG4), genetic evaluations, and magnetic resonance imaging (MRI). These assessments confirmed the diagnosis of idiopathic RPF with stable residual disease.

During the most recent year, she experienced recurrent episodes of symptomatic tachycardia. A cardiologic evaluation excluded structural heart disease and identified inappropriate sinus tachycardia as the most likely cause. Consequently, her treatment was modified from bisoprolol to a non-selective beta-blocker (propranolol 40 mg twice daily), which provided partial symptom control.

During the same period, she presented to the emergency department on three separate occasions with crampy abdominal pain. These episodes were attributed to persistent fibrotic involvement of the colon, as confirmed by imaging, which showed stable but extensive disease without evidence of progression or malignancy. Symptom exacerbations were managed conservatively with analgesics and supportive therapy.

## DISCUSSION

Retroperitoneal fibrosis (RPF) is a rare but clinically significant disorder characterized by the proliferation of fibroinflammatory tissue within the retroperitoneal space. This pathological tissue frequently encases the abdominal aorta, iliac vessels, and adjacent structures such as the ureters, lymphatics, and, less commonly but notably, segments of the gastrointestinal tract including the colon. RPF may be idiopathic or secondary to drugs, infections, malignancies, or surgical interventions. Idiopathic RPF is increasingly regarded as an immune-mediated condition

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and, in a subset of patients, part of the spectrum of IgG4-related disease. Cytokines such as TGF- $\beta$ , IL-6, and other proinflammatory mediators play central roles in disease propagation and tissue fibrosis [1-3].

Most clinical management efforts focus on urinary tract obstruction resulting from ureteral involvement. However, compression or functional impairment of the colon is an underrecognized but important source of morbidity. Anatomically, the descending and sigmoid colon are within the potential field of fibrotic encasement. When fibrosis extends laterally and posteriorly, these colonic segments may become compressed, displaced, or inflamed, producing symptoms such as abdominal bloating, pain, altered bowel habits, and, in some cases, pseudo-obstruction [4].

In this context, the pharmacological effects of non-selective  $\beta$ -blockers (NSBBs) such as propranolol and carvedilol warrant careful consideration. NSBBs block both  $\beta_1$ - and  $\beta_2$ -adrenergic receptors. While  $\beta_1$ -receptors are predominantly cardiac,  $\beta_2$ -receptors are widely expressed in gastrointestinal smooth muscle, where they promote relaxation and peristalsis. Their inhibition increases smooth muscle tone, reduces motility, and slows colonic transit. Although usually negligible in healthy individuals, this effect can become clinically significant in RPF, where pre-existing mechanical and inflammatory compromise already impairs colonic function [5,6].

The combination of extrinsic fibrotic compression and intrinsic pharmacologic inhibition of smooth muscle relaxation may compound symptoms such as constipation, cramping, and postprandial bloating. This overlap can mimic or exacerbate colonic pseudo-obstruction, particularly in cases of extensive fibrosis or vascular encasement causing subtle mesenteric ischemia. Moreover,  $\beta_2$ -receptor blockade may impair splanchnic vasodilation and reduce mucosal perfusion, potentially increasing the risk of localized ischemic injury in compromised bowel segments [7].

Paradoxically, preclinical studies suggest that some NSBBs, particularly carvedilol, may exert antifibrotic and anti-inflammatory effects. In models of chemically induced colitis, carvedilol has been shown to inhibit TGF- $\beta$ 1 expression, suppress NF- $\kappa$ B activation, and downregulate  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), all key mediators of intestinal fibrosis and myofibroblast activation [8]. These findings raise the possibility that NSBBs could attenuate fibrotic progression in chronic inflammatory conditions. However, extrapolation to retroperitoneal tissues remains speculative, given the distinct embryological origins and microenvironments of the colon and retroperitoneum.

Taken together, these complex and sometimes contradictory effects suggest that the role of NSBBs in patients with RPF and gastrointestinal involvement should be individualized. While their cardiovascular and hepatic indications remain valid, clinicians should consider  $\beta_1$ -selective alternatives (e.g., bisoprolol, atenolol) in patients with gastrointestinal symptoms, particularly those consistent with hypomotility or mechanical bowel dysfunction.

## CONCLUSION

The use of non-selective  $\beta$ -blockers in patients with RPF requires careful consideration, particularly in those with colonic involvement. By inhibiting  $\beta_2$ -mediated smooth muscle relaxation, these agents may exacerbate symptoms of colonic dysmotility, compounding the mechanical and inflammatory disruption already imposed by fibrosis. Although experimental data suggest potential antifibrotic properties of NSBBs, such effects may be clinically negligible—or even offset—by their adverse influence on gastrointestinal motility. Further studies are warranted to clarify this interaction and to guide pharmacologic decision-making in the management of patients with RPF presenting with prominent abdominal symptoms. Overall, in those patients presenting colonic involvement use beta-1-selective agents in RPF patients with colonic involvement.

## DECLARATION

### Consent for publication

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

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