Retractile Mesenteritis Presenting with Malabsorption Syndrome. Successful Treatment with Oral Pentoxifylline

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Abstract
Retractile mesenteritis is a rare benign inflammatory disease of the mesentery. Computed tomographic findings usually suggest the diagnosis, which is confirmed by surgical biopsies. Conservative treatment is empirical, based on corticosteroids, colchicine, immunosuppressive agents and progesterone. Surgical resection is sometimes attempted for definitive therapy, although the surgical approach is often limited. This report describes a 62-year old man with histologically proven retractile mesenteritis presenting with malabsorption syndrome, who presented pulmonary tuberculosis after initial therapy with corticosteroids. He was subsequently treated with oral pentoxifylline (800 mg/day), with substantial clinical and radiological improvement.

Keywords
Retractile mesenteritis - malabsorption syndrome - pentoxifylline

Introduction
Retractile mesenteritis is a rare inflammatory condition of unknown cause, in which the fat of the mesentery is finally replaced by fibrotic tissue. The process usually involves the mesentery of the small bowel, but can occasionally involve the mesocolon and in rare occasions the peripancreatic region, omentum, retroperitoneum and pelvis [1]. The etiology of this disorder is unknown: the use of drugs, infection, autoimmunity, trauma, malignancy, prior abdominal surgery and local ischemia have been suggested as possible causative factors [1-4].

Until now, no conventional treatment has been recognized. Surgery with resection of the accessible involved segments is frequently necessary, but complete excision is often not possible because of vascular involvement [3]. Treatment options include steroids, colchicine, immunosuppressive agents, tamoxifen or progesterone [2]. According to recent studies, pentoxifylline has promising results in a variety of fibromatous and inflammatory conditions [5-8].

We describe the case of a patient with histologically proven retractile mesenteritis presenting with malabsorption syndrome, who manifested pulmonary tuberculosis after initial therapy with corticosteroids. He was subsequently treated with pentoxifylline with good clinical and radiological response. The current knowledge about the mechanisms of antifibrotic and antiinflammatory activity of pentoxifylline is also discussed.

Case Report
A 62-year-old male was admitted to our department for weight loss, vague abdominal pain and large steatorrheic stools over the last 18 months. He underwent in his past medical history three abdominal operations. Thirty years ago he had been operated on for leiomyoma of the cardia. Ten years ago he had been operated on twice, for complete rectal prolapse and obstructive ileus. He did not take any medication. On examination he was pale and afebrile, had severe weight loss, abdominal distention with visible peristalsis and increased bowel sounds. There were no palpable masses or signs of peritonitis. Chest x-rays were normal. Plain abdominal x-rays and abdominal ultrasound showed dilated small intestinal loops with multiple air-fluid levels. The most relevant laboratory data were haemoglobin 9.8 g/dL, white blood cell count 8,900/mL, platelet count 346,000/mL, erythrocyte sedimentation rate 5 mm/1hr, total serum protein 4.2 g/dL, serum albumin 1.7 g/dL, cholesterol 71 mg/dL, prothrombin time 21.3 sec (normal range 10.7 – 13.6 sec), international normalizing ratio 2.60 (normal range 0.85 – 1.15). Ferritin, folic acid and vitamin B12 serum levels were within normal limits. The liver function

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tests and urinalysis were normal. Endomysial antibodies were negative, as well as a detailed immunological investigation.

After admission, parenteral nutrition was started. Gastroscopy revealed a normal esophago-gastric anastomosis. Culture of properly collected proximal small intestinal aspirate evidenced E. coli exceeding 10^8 microorganisms/ml. Treatment with appropriate oral antibiotics was given. Colonoscopy showed an anastomotic stricture at 7 cm from the anus, which allowed the passage of the endoscope. The rest of the bowel was normal. CT scan revealed diffuse thickening of the mesentery encasing mesenteric vessels and displacing adjacent small bowel loops. The proximal small bowel loops were dilated, while the distal ones were congested. There was a vague soft tissue mass in the root of the mesentery. The liver, kidneys and pancreas were normal and no lymphadenopathy was demonstrated.

Over the next few days the abdominal pain and obstructive symptoms worsened. Based on the clinical and radiological suspicion of either peritoneal symptoms or retractile mesenteritis, the patient underwent a laparoscopy which revealed dilated small intestinal loops and a mesenteric mass causing partial intestinal obstruction. Partial excision of the mesenteric mass with the adjacent intestine was performed. The histological examination of the mesenteric mass revealed fibrosis with areas of sclerosing fibrosis of the mesentery (Fig. 1). The mucosa pathology of the resected specimen is shown in Fig. 2. The final diagnosis was retractile mesenteritis with malabsorption syndrome, attributed to bacterial overgrowth.

A week later the abdominal pain and obstructive signs were still present. The patient started therapy with oral prednisolone 40 mg/day. Two months after admission, the patient was discharged with clinically and biochemically improved malabsorption. One month later he was readmitted because of fever and cough. The tuberculosis skin test was positive. Chest x-ray revealed right apical pulmonary infiltrates. Pulmonary tuberculosis was strongly suspected and prednisolone was gradually tapered. A 9-month antituberculous regimen was initiated, awaiting results of the sputum culture, which proved positive. At the same time, oral pentoxifylline was initiated at a dose of 400 mg b.d. and was continued for one year.

A follow-up CT scan showed normal intestinal loops and diffuse thickening of the mesentery, but no evidence of mass. The patient was free of abdominal pain, with normalization of the biochemical parameters of malabsorption, and he had gained 5 kilos. No side effects of the drug were recorded. One year later he was still asymptomatic and in good general condition.

**Discussion**

Retractile mesenteritis is an uncommon, idiopathic, benign process that primarily affects the mesentery, being characterized by variable degrees of fatty necrosis, chronic inflammation and fibrosis. If inflammation and fatty necrosis predominate, the process is termed mesenteric panniculitis, and when fibrosis predominates, like herein, retractile mesenteritis [3].

In most patients there is no evidence of predisposing factors but in some cases, as in our patient, there is a past history of abdominal surgery [4]. The disease may be totally asymptomatic, being incidentally discovered on the CT scan. The signs and symptoms may be related to inflammation or to a mass effect on adjacent organs, especially on the intestinal loops. The main symptoms at presentation include abdominal pain, vomiting, constipation or diarrhea, anorexia, weight loss, fatigue, fever, ascites and pleural or pericardial effusion, while half of the patients may present with a poorly defined abdominal mass [1-4].

The diagnosis can be supported by clinical and radiological characteristics, but definite diagnosis can only be based on histological findings. On CT scans it is usually visualized as a heterogeneous mass with large component

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**Fig. 1** Histological aspect of the surgical specimen of the mesentery showing fibrosis, with areas of sclerosing fibrosis, mild and chronic inflammation with no identifiable foci of fat necrosis. Cellular atypia or remarkable mitotic activity were not observed (H&E; x200).

**Fig. 2** Histological aspect of the resected specimen of the small bowel. The mucosa shows focal villous atrophy with crypt hyperplasia, mild acute inflammation with neutrophils infiltrating the superficial intestinal epithelium. Neutrophils, few plasma cells and macrophages were also noted in the inflamed lamina propria (H&E; x100).
of fat and interposed linear bands with soft tissue density in
cases of mesenteric panniculitis, or as a homogeneous mass
of soft tissue density in cases of retractile mesenteritis [1,4].
Angiography, MRI and positron emission tomography (PET)
have also been used to detect this clinical entity [9].

Most surgical procedures are performed to divert
obstructed intestinal segments or to excise a mesenteric mass
with the adjacent intestine. When the disease is localized,
excision of the mesenteric mass is sometimes possible, but in
many cases only surgical biopsy can be obtained [2, 3]. Our
patient was unsuitable for complete surgical treatment, but
histological examination of the surgical specimens confirmed
the diagnosis. There is no specific medical treatment and
the pharmacological therapy is mainly empirical, based
on antiinflammatory and immunosuppressive agents.
Corticosteroids alone or in combination with colchicine or
azathioprine have shown beneficial effects in some patients
[10]. Antibiotics, cyclophosphamide, emetine, irradiation,
tamoxifen and progesterone have also been used [2, 3].

Pentoxifylline is a hemorrheologic methylxanthine
derivative available on the market for 30 years, with
intensive interest in the treatment of chronic inflammatory
and fibrotic conditions. Many studies have demonstrated the
efficacy of pentoxifylline in improving blood perfusion
and consequently tissue oxygenation [11]. Pentoxifylline
modulates the cytokines that influence inflammation and
fibrosis, provoking healing of soft tissue necrosis and
decreasing fibrosis [5, 6]. It was initially used for the
treatment of peripheral arterial occlusive disease and
intermittent claudication and it was recently tested with
beneficial effects in many diseases including chronic kidney
disease, liver cirrhosis, steatohepatitis, radiation induced
fibrosis, ischemic heart disease, severe acute respiratory
syndrome, organ transplantation, myelodysplastic syndrome,
pancreatic necrosis, Peyronie’s disease, necrobiosis lipoidica
diabeticorum and in patients suffering from AIDS [5-8, 11-13].

The exact mechanism of antifibrotic activity of
pentoxifylline is still unclear, but the results of many
studies indicate that more than one pathway is responsible.
Studies on the inhibitory effects of pentoxifylline on basic
pathobiocemical mechanisms of fibrogenesis showed a
reduction of the biosynthetic activities of fibroblasts as
well as the synthesis of collagen, glycosaminoglycans,
and fibronectin [6]. Pentoxifylline downregulates the in
vivo expression of fibroblast growth factor-2 (FGF-2)
and transforming growth factor-β1 (TGF-β1), inhibits
interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α)
and diminishes the platelet derived growth factor (PDGF),
cytokines that stimulate proliferation and biosynthetic
activities of fibroblasts [14, 15]. Moreover, it decreases
fibroblast collagen synthesis, suppresses types I and III
procollagen gene transcription, through downregulation
of nuclear factor-1 (NF-1) [6]. Pentoxifylline is also a potent
antiinflammatory agent capable of reducing inflammation
by acting on various targets, including the synthesis of
proinflammatory cytokines and chemokines, such as
TNF-α, intercellular adhesion molecule-1, IL-1β, IL-6
and interferon-γ, as well as the growth and activation
of inflammatory mononuclear cells and lymphocytes.
In addition, pentoxifylline downregulates the major
histocompatibility complex class II antigen expression [5].

To our knowledge, the present case is the first report
of the successful use of pentoxifylline in a patient with
retractile mesenteritis. The negligible side effects of the drug
suggest that pentoxifylline might be a useful alternative in
the treatment of retractile mesenteritis. Further trials should
explore this pharmacological agent in retractile mesenteritis
and other fibromatous disorders.

Conflicts of interest
Authors declare that they have no competing interests.

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