A Clinical Review of Mesenteric Panniculitis

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Abstract: Mesenteric panniculitis (MP) is a benign condition characterized by chronic inflammation and fibrosis of adipose tissue mainly of the small bowel mesentery. MP is commonly detected incidentally on cross-sectional imaging of the abdomen and can be asymptomatic in up to nearly half of patients. The most frequent clinical symptom reported is abdominal pain, followed by bloating/distention, diarrhea, constipation, vomiting, anorexia, weight loss, fever, malaise, and nausea. On computed tomography, MP is seen as a mass-like area of increased fat attenuation within the small bowel mesentery, usually located in the left upper quadrant of the abdomen. This mass-like area envelops mesenteric vessels and displaces adjacent bowel segments. Lymph nodes are frequently seen within the area of mesenteric abnormality. One of the most common differential diagnoses of MP is lymphoma, and positron emission tomography/computed tomography may be performed if there is suspicion of a concurrent underlying malignancy. Because of the benign nature of MP, treatment decisions should be guided by severity of symptoms and presence of complications. First-line medical treatment is prednisone and tamoxifen. Surgery is reserved for cases of recurrent bowel obstruction. This article provides a review of MP, including its epidemiology, pathophysiology, clinical presentation, imaging findings, and treatment.
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**Epidemiology**

The prevalence of MP has been reported to range from 0.16% to 7.8% based upon radiologic criteria from several large computed tomography (CT) scan databases. The most common indications for CT scans are evaluation of suspected malignancy (50%-70% of cases), followed by evaluation of abdominal pain, infection, vascular disease, and inflammatory bowel disease. The wide variation in the prevalence of MP depends upon the methodology of the studies and the CT criteria for diagnosis. The lowest reported prevalence (0.16%) came from a retrospective study that based its outcomes on a keyword search of CT databases. In contrast, a prospective study that evaluated 613 patients based on 3 of 5 classic CT scan signs reported the highest prevalence of MP (7.8%). In this study, the indication to undergo a scan was evaluation of various neoplastic (27%) or nonneoplastic conditions (73%). The diagnostic signs used were the presence of a mass effect on neighboring structures, mesenteric fat tissue of inhomogeneous higher attenuation than adjacent retroperitoneal or mesocolonic fat, small soft tissue nodes, a hypoattenuated fatty halo sign, and a hyperattenuating pseudocapsule that may surround the mass-like lesion.

Epidemiologic data based upon studies that report histopathologic diagnosis confirmation are limited. One study sought to obtain information about the frequency and nature of alterations in MP based upon histopathologic analysis; in the mesentery of 712 consecutive autopsies during a 6-month period, the prevalence of MP was 1.26%. Additionally, prospective analysis of 7620 CT scans evaluated from 1995 to 1998 has described a 0.6% prevalence of the disease. In this study, CT criteria for diagnosis were a solitary well-defined mass composed of inhomogeneous fatty tissue with attenuation values higher than those of the retroperitoneal fat at the root of the small bowel mesentery, engulfment of superior mesenteric vessels without vascular involvement, and no evidence of invasion of the adjacent small bowel loops even if displaced. Although there is variation in the frequency of MP reported among the series, the disease is considered to be one of low prevalence overall.

Regarding demographics, most cases occur during the fifth to seventh decades of life, although pediatric cases have been reported. There is a 2:1 male to female predominance in most studies, however, several prospective studies have shown a higher female prevalence. No clear racial associations have been made, but that could be because most studies have been conducted in White-predominant populations.

**Pathophysiology**

Although several hypotheses have been suggested, the underlying cause of MP remains unclear. Several case series have suggested potential etiologies, such as previous abdominal surgery, trauma, autoimmune diseases, chronic infection, or malignancies. However, most of these associations have been made in case reports and case series with no paired matched analysis and thus lack statistical significance.

In 1974, Kipfer and colleagues reported that 30% of patients with MP in their series presented with malignancy, with lymphoma being the most common neoplasm. Since then, several studies have reported a similar association, with an estimated range of 17% to 38% in case-screening series with no matched control groups. A more recent case-control study has demonstrated that the odds of finding a neoplasm in patients with MP does not increase when cases and controls are matched for age, sex, abdominal diameter, and CT protocol. A recent systematic review aiming to clarify this issue included 4 case-control studies with a total of 415 patients. There was no statistical difference in the odds of malignancy between patients with MP and the matched control group. However, van Putte-Katier and colleagues reported a significantly higher risk of cancer, especially prostate carcinoma in men with MP, compared with a control group. In this study, 94 (2.5%) patients with MP were identified from consecutive abdominal CT examinations of 3820 patients. MP was present in 48.9% of patients with malignancy, which was higher than in age- and sex-matched control patients (n=188; 46.3%). The most frequent neoplasm in patients with MP was prostate cancer (in 12 patients), followed by colorectal carcinoma (in 7 patients); extra-abdominal non-Hodgkin lymphoma (in 4 patients); urothelial cell carcinoma and breast carcinoma (in 3 patients each); stomach carcinoma, esophageal carcinoma, and skin malignancy (in 2 patients each); and Hodgkin lymphoma, renal cell carcinoma, cancer of the duodenum, and seminoma testis (in 1 patient each). This study also showed a higher risk of developing cancer at 5-year follow-up, although 33% of patients died because of coexisting malignancy or were lost to follow-up during that time, thus limiting the interpretation of these results.

The histologic changes observed in the mesentery of patients with MP are a mixture of scattered lymphoplasmacytic infiltration, focal fibrosis, fat necrosis, and lipid-laden macrophages, which together lead to thickening and retraction of the mesentery with preservation of vessels, intestine, and/or lymph nodes. The understanding of the pathophysiology of MP remains limited. The presence of resident macrophages has been reported in mesenteric adipose tissue. It has been proposed that...
the transformation of local macrophages to foam cells might occur in MP similar to the process in the context of atherosclerosis, accompanied by upregulation of peroxisome proliferator-activated receptor-γ and scavenger receptor expression; although these data are speculative, they have been suggested as potential added molecular pathways linked to the pathophysiology of the disease.29,30 In line with this hypothesis, a study that analyzed 3698 consecutive CT scans from patients with MP paired to a matched cohort showed that metabolic syndrome, urogenital diseases, and vascular diseases were significantly more common in patients with MP than in those without the disease. Metabolic syndrome was present in 45% of patients with MP and 31.8% of the matched control group, urogenital diseases were found in 22.5% of patients with MP and 12.7% of the control group (P-value range .012-.036). This difference was caused by coronary artery disease in the case of vascular diseases (P=.012), urolithiasis in the case of urogenital diseases (P=.021), and criteria other than hypertension in the case of metabolic syndrome (P=.021). No significant differences were found in the history of abdominal surgery, gastrointestinal disease, or autoimmune disease between these 2 groups.31 More data are needed to support these associations.

Also, MP has been proposed to be a progressive inflammatory process, starting from mesenteric lipodystrophy to retractile mesenteritis, triggered by a wide variety of stimuli, such as thermal or chemical injuries, vasculitis, avitaminosis, autoimmune disease, pancreatitis, bile or urine leakage, hypersensitivity reactions, and even bacterial infections. However, there is scarce evidence to demonstrate histologic progression of the disease.32

**Clinical Presentation**

According to radiologic series, MP can be asymptomatic in 16% to 40% of patients1-25 and is most commonly detected incidentally on cross-sectional imaging of the abdomen.24 A definitive diagnosis of MP can only be made by histology. However, biopsies are not routinely justified based upon MP’s benign and predominately asymptomatic clinical presentation.33,34
Symptoms are nonspecific and can be attributed to concomitant diseases.33 Based upon the largest published clinical series, abdominal pain (the most frequent clinical symptom) is present in 54% to 78% of patients with MP, bloating and distention in 9% to 26%, diarrhea in 19% to 25%, constipation in 10%, vomiting in 18%, anorexia in 13%, weight loss in 23%, fever in 26%, and malaise and nausea in 5%.18 Approximately half of patients have normal physical examination findings, although 20% to 30% of patients may have a palpable abdominal mass or abdominal tenderness on examination.14 Figure 1 displays a proposed diagnostic algorithm for MP.

Although MP usually presents with a benign disease course, complications can occur because of the mass effect on adjacent structures causing bowel, lymphatic, or vascular obstruction. A large series of patients with MP (n=92) found that 28% presented with small bowel obstruction, 14% had chylous ascites, and 3% had superior mesenteric vein thrombosis. Over a 21-month follow-up period, there were 18 deaths, with 17% occurring from complications attributable to MP or its treatment. Although the overall prognosis of MP is good, this study found that MP was associated with significant morbidity in nearly 20% of patients.35

**Laboratory Tests**

Laboratory tests for the diagnosis of MP are nonspecific. Mild leukocytosis and elevation in inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein have been reported in up to 80% of cases8 and can be utilized to monitor response to treatment. Anemia and hypalbuminemia have been reported in 16% and 5% of cases, respectively, and may be present as nonspecific findings associated with the disease.18

**Imaging**

As previously mentioned, MP is usually diagnosed incidentally on imaging performed for unrelated indications. On CT, MP presents as a mass-like area of increased fat attenuation within the small bowel mesentery, usually located in the left upper quadrant of the abdomen, although it may also involve the peripancreatic region and porta hepatis. This mass-like area envelops the

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Figure 2. Axial contrast-enhanced computed tomography image of a 70-year-old man with mesenteric panniculitis showing a mass-like area of increased fat attenuation (arrows) within the mesentery that displaces adjacent segments of bowel.
mesenteric vessels and displaces the adjacent bowel segments (Figure 2). Lymph nodes are often seen within the area of mesenteric abnormality and are usually less than 1 centimeter in size. Two radiologic signs of MP have been described in the literature.\textsuperscript{36,37} The tumoral pseudocapsule sign, which can be seen in 50% of patients with MP, refers to the thin (usually <3 mm in thickness) curvilinear band of soft tissue that encases the mesenteric mass-like area and separates it from the normal mesentery (Figure 3). The fat halo sign refers to the preservation of normal fat density surrounding the enveloped mesenteric vessels and can be seen in 75% of patients with MP (Figure 4).\textsuperscript{38,39}

**Pathology**

The gross findings that have been described in MP are variable. A single mass has been described in up to 69% of cases, multiple discrete masses in 18% to 25%, and diffuse mesenteric thickening in 13%.\textsuperscript{14}

Although biopsies are not routinely justified based upon MP’s mostly benign and predominately asymptomatic clinical presentation, recent published series have reported biopsy results that were obtained to exclude an underlying malignancy and confirm the diagnosis. These biopsy results were obtained through laparoscopy (43.1%), laparotomy (41.2%), or CT-guided needle aspiration (16.7%). Tissue was taken from the mesentery (97.1%), lymph nodes only (7.8%), or both (4.9%). The most common histopathologic features were fat necrosis (77.7%), fibrosis (68.0%), chronic inflammation (50.5%), calcifications (24.3%), and acute inflammation (19.4%).\textsuperscript{40}

**Figure 3.** Axial noncontrast computed tomography image of a 64-year-old man with mesenteric panniculitis showing a mass-like area of increased fat attenuation within the mesentery with a thin peripheral curvilinear band of soft tissue (arrows), referred to as a tumoral pseudocapsule sign.
Differential Diagnosis

As mentioned, one of the most common differential diagnoses of MP is lymphoma. Other differential diagnoses are inflammatory pseudotumors, desmoid tumors, infections, or pancreatitis. Mesenteric edema should also be considered as a differential diagnosis, and can be caused by several conditions, such as cirrhosis, hypoalbuminemia, and heart failure. Infectious causes that can affect the mesentery, such as tuberculosis, should also be considered. Histopathologic evaluation with biopsies is the most accurate approach to safely rule out malignancy when the latter is highly suspected. PET/CT represents an alternative to help differentiate between MP and lymphoma. Measurement of fluorodeoxyglucose uptake has been reported as a marker of lymphoma within surrounding MP, even in the presence of small lymphoma nodules.

Treatment

Considering the benign nature of MP, therapeutic decisions should be guided by the severity of symptoms and presence of complications. Asymptomatic patients who present with MP as an incidental finding do not need to be started on treatment. As described in a case series with successful treatment outcomes, which was published by Akram and colleagues, medical treatment should be offered to patients with persistent symptoms not explained by another etiology.

In this case series, which is the largest one published to date, medical treatment of tamoxifen twice daily and a prednisone taper over 3 months was administered in 20 patients. Of these, 12 (60%) responded to therapy within 12 to 16 weeks, with 6 patients (30%) having persistent symptoms and 2 patients (10%) showing disease progression.

A recently published retrospective study by Cortés and colleagues that determined the long-term management outcomes of 103 patients with biopsy-proven MP concluded that prednisone plus colchicine has a similar efficacy to prednisone plus tamoxifen for the initial treatment and 14-month follow-up of MP. In this series, 52.4% of patients received no treatment, and 4.9% underwent surgery. Among 42.7% of patients on medical therapy, the most common initial regimens were prednisone plus tamoxifen (41.9%), prednisone alone (23.3%), and prednisone plus colchicine (11.6%), with 55.6%, 57.2%, and 60% of patients improving, respectively, with no significant difference in response rates \( (P = 0.85) \). At least half of the patients responded to prednisone plus tamoxifen, prednisone plus colchicine, or prednisone alone at 6.0, 7.2, and 8.4 months, respectively. At a median follow-up of 45.6 months, 65.4% of patients were receiving medical therapy. Of those receiving tamoxifen-based, corticosteroid-based, or corticosteroid-sparing regimens, 100%, 87.5%, and 77.8%, respectively, had improved by their last follow-up appointment \( (P = 0.15) \). However, the quality of data from this study was limited by the large number of patients who were lost to follow-up and the low number of patients included in the colchicine and prednisone group (5 patients), limiting the wide applicability of these results.

Alternatively, other agents have been described for the treatment of MP, especially in patients who do not initially respond to conventional treatment regimens. These nonconventional medications include pentoxifylline, raloxifene, immunomodulators (azathioprine, methotrexate, 6-mercaptopurine), cyclophosphamide, sulfasalazine, thalidomide, lenalidomide, and monoclonal antibodies (infliximab, rituximab). In the aforementioned series by Cortés and colleagues, the proportion of patients on alternative agents increased to 30.8% by the fourth follow-up appointment. Half of these patients were on azathioprine as part of their regimens. The response rates were 100% for azathioprine alone, 100% for prednisone plus azathioprine, 100% for prednisone plus thalidomide, 50% for prednisone plus raloxifene, and 0% for pentoxifylline alone at an average of 6.1, 11.4, 22.0, 5.1, and 14.2 months, respectively.

Few case reports have been published on biologic therapy in patients with MP. As an example, a 45-year-old patient with longstanding history of MP, confirmed...
by pathology, who had failed several treatment options, including corticosteroids, tamoxifen, methotrexate, colchicine, and azathioprine, had an initial good response to infliximab. However, this patient developed mesenteric large B-cell lymphoma 6 months after initiation of tumor necrosis factor inhibitor treatment. For that, he was then transitioned to ustekinumab (Stelara, Janssen) with good clinical response and no recurrence after 24-month follow-up. Medical treatments for MP are summarized in the Table.

### Medical Treatment Options

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<td>Tamoxifen 10 mg twice daily plus prednisone 40 mg daily with a taper completed over 3 months</td>
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<td>Prednisone 40 mg daily and colchicine 0.6 mg daily (although further research is needed to confirm preliminary findings)</td>
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<td>Other potential alternatives that have been described but require further research: immunomodulators (azathioprine, methotrexate, 6-mercaptopurine), pentoxifylline, raloxifene, cyclophosphamide, sulfasalazine, thalidomide, lenalidomide, monoclonal antibodies (infliximab, rituximab)</td>
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### Surgery

Given the self-limited course of this condition, it would appear reasonable to avoid surgical intervention beyond diagnostic sampling. In one recent series, only 5 of 103 (4.9%) patients were treated surgically, which included bowel resection or lysis of adhesions for the management of small bowel obstruction. In a study that included 92 patients followed for 20 months, surgery was performed in 20 of 44 (45%) patients. Among these, 12 of 20 (60%) had only surgery, whereas the other 8 (40%) received additional medical therapy after surgery. The most common indication for surgical intervention was the development of intractable bowel obstruction. In a significant number of these patients, the mass itself was primarily unresectable, and bowel resection was subsequently required. Among 20 patients who underwent any surgical intervention, only 2 of 20 (10%) responded to surgery alone, and 4 of 20 (20%) responded after receiving additional medical therapy.

### Conclusion

MP is an uncommon benign condition characterized by chronic inflammation and fibrosis of the adipose tissue mainly of the small bowel mesentery. It can be asymptomatic in up to 40% of cases, and most cases are detected incidentally on cross-sectional imaging of the abdomen. Benign and malignant urogenital disorders have been associated with MP, although the etiology of this disease remains unclear. MP usually presents with a benign course, but complications can occur as a consequence of the mass effect on adjacent structures causing bowel, lymphatic, or vascular obstruction. First-line medical treatment for symptomatic patients is tamoxifen and prednisone. This article provides an overview of MP and aims to raise awareness and contribute to a better understanding and management of the disease.

**Disclosures**

*The authors have no relevant conflicts of interest to disclose.*

**References**