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REVIEW ARTICLE

Mesenteric panniculitis: a clinical conundrum

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ABSTRACT:

Mesenteric panniculitis is encountered frequently during abdominopelvic CT scanning, often as an incidental finding. The observation is problematic because an association with malignancy has been raised in the literature. This review will describe the CT appearances and examine the available evidence regarding the significance of this finding. Ultimately, the literature remains unclear regarding how these patients should be managed, if at all.

INTRODUCTION

Mesenteric panniculitis (MP) describes inflammation of mesenteric fat, which is manifest on abdominopelvic CT scanning as a circumscribed region of increased attenuation, often described as a "hazy" or "misty mesentery".[1] MP is usually encountered incidentally when performing CT scanning for a variety of indications. Because MP is predominantly a radiological diagnosis, referring clinicians have rarely heard of it and therefore turn to the reporting radiologist for guidance. However, appropriate guidance is problematic because there is a widely held belief that mesenteric panniculitis may herald abdominal lymphoma, although the evidence for this is weak and haphazard.[2] In the authors' experience, a common outcome is for the patient to undergo repeated interval scanning over several years, with little, if any, change in imaging appearances. Ultimately, the referring clinician often abandons follow-up. This article aims to review what is known currently about MP and its significance.

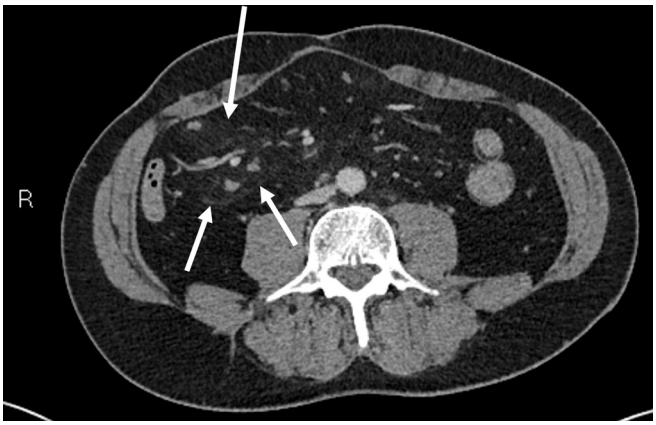
BACKGROUND AND AETIOLOGY

Panniculitis is derived from the Latin word panniculus, meaning "lobule", and describes inflammation of a thin layer of subcutaneous adipose tissue.[3] The phrase "mesenteric panniculitis" was originally coined to describe non-specific inflammation within the small bowel mesentery in seven patients presenting with abdominal pain.[4] This was due to the histological similarities between the findings and those seen in Weber-Christian disease, a disorder in which there is severe inflammation of subcutaneous fat, *i.e.* the panniculus.[4] Although recognised at the time as an awkward misnomer, "panniculitis" remains the most used term to describe the process.[4] However, a variety of terms have been used including mesenteric lipodystrophy, mesenteric sclerosis, and sclerosing mesenteritis.[2]

Mesenteric panniculitis has been described as "rare",[5] with a reported prevalence of between 0.16 and 3.4%, and a male:female predominance of 2 to 3:1 (5–7). The true incidence, however, is difficult to ascertain as systematic review has found no available robust studies that have accrued a consecutive, unselected group of patients prospectively, nor reported the denominator.[2] Aetiology is unknown, but several causative factors have been postulated. One theory postulates that MP is a response to previous abdominal trauma or surgery.[5–7] Association between MP and other inflammatory conditions and vasculitides has also been described and is discussed in further detail below.[5,7] It has also been suggested that there are two distinct pathological entities: one in which fat necrosis predominates, *i.e.* mesenteric panniculitis, and a second, rarer entity where fibrosis and retraction are the primary histological finding, *i.e.* retractile mesenteritis.[5,6] It is also unknown whether the most subtle radiological manifestations simply represent mesenteric congestion, *i.e.* without fat necrosis at all, since these are rarely subject to surgery.

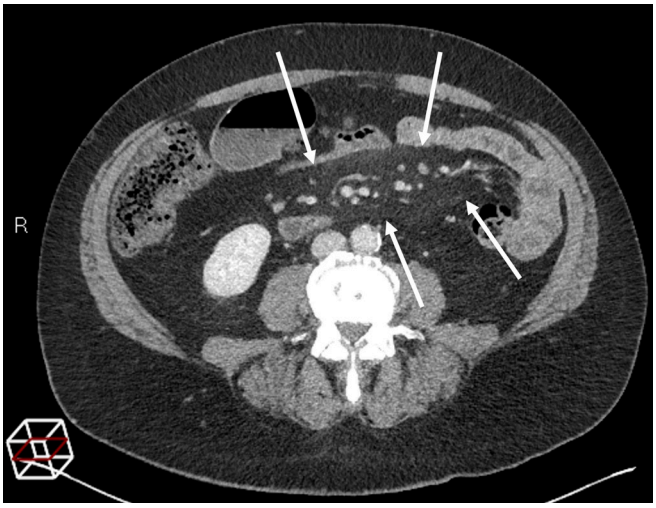
The authors believe that MP is effectively a "dustbin diagnosis" representing the radiological manifestation of a range of different pathologies. Alternatively, in their paper of 1997, Emory et al, suggested that the various

Figure 1. Axial CT slice of a case of "mild" mesenteric panniculitis showing focally increased attenuation of mesenteric fat (white arrows) and encapsulated nodes.



representations embodied a single entity presenting as different histological variants, and recommended "sclerosing mesenteritis" as the most appropriate umbrella term.[8] This theory is supported further by Coulier et al who divided the evolution of mesenteric panniculitis into three distinct stages[6] : in Stage 1, mesenteric fat is replaced by foamy macrophages, with little to no inflammatory changes on imaging.[6] This phase is termed "mesenteric lipodystrophy" and is usually asymptomatic.[6] Stage 2 is characterised by inflammation, with lymphatic dilatation and increased macrophage infiltration, and is termed "mesenteric panniculitis".[6] The final stage is "retractile mesenteritis", which is characterised by collagen deposition, fibrosis, and discrete mass formation.[6] Interestingly, the authors and their colleagues have never witnessed progression from MP to retractile mesenteritis. A 2014 study of 94 patients with MP showed that none progressed to fibrosis over the 5-year period following diagnosis, suggesting that progression is far from inevitable and raising the possibility that MP does not represent a spectrum of the same pathology but rather a collection of different aetiologies.[9] Rather than progression to fibrosis, it is the alleged progression to (or association with) malignancy that excites radiologists' attention (see later sections).

Figure 2. Axial CT slice of a case of "moderate" mesenteric panniculitis showing focally increased attenuation of mesenteric fat (white arrows), this time exhibiting a degree of mass effect on surrounding small bowel loops and increased numbers of nodes compared to a mild case.



Clinical presentation

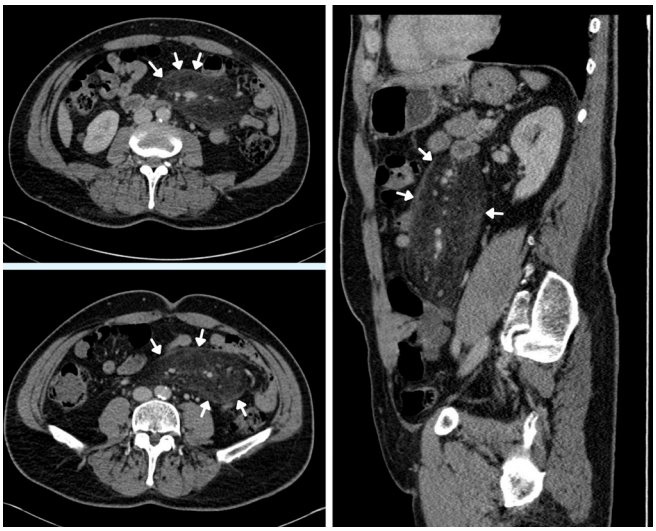
Currently, the vast majority of MP cases are asymptomatic, diagnosed during CT scanning performed for other indications.[3,5] It is likely that the incidence is rising due to relatively unconstrained use of abdominopelvic CT scanning over recent years. When MP does present with symptoms, it is unclear whether it is the prime cause of symptoms (unless the imaging features are very florid and fibrotic) or merely an epiphenomenon associated with an alternative primary underlying diagnosis. The most frequently reported symptoms are localised abdominal pain and a low-grade fever.[4] Diarrhoea, constipation, nausea and vomiting, and even pleural effusions have also been reported, and an abdominopelvic mass may be palpable.[10] In cases of retractile mesenteritis, where fibrosis dominates, patients may present with symptoms of bowel obstruction or even ischaemia, with nausea, vomiting, or constipation.[3,5] Accordingly, there are no specific symptoms and a myriad of other pathologies which need to be excluded in patients in whom symptoms are marked.

Diagnosis

MP is effectively an imaging diagnosis that is mostly made, as stated already, by incidental detection on CT scanning performed ostensibly for other indications. The most consistently reported finding is a hyperattenuating focus of mesenteric fat, with a Hounsfield measurement of between −40 and −60 HU; normal mesenteric and retroperitoneal fat measures −100 HU to −160 HU.[4,6,10–12] The imaging appearances are very wide, ranging from a barely perceptible "haze" (Figures 1 and 2) through to those that emulate frank abdominal lymphoma and other pathologies. Some evidence of a mass effect is common, manifest by displacement of surrounding structures, normally bowel loops.[4,6,10–12] The jejunal mesentery is most frequently affected, and a leftward orientation consistent with this has been reported.[11,13] Numerous encapsulated nodes are common and more advanced cases often demonstrate a thin, hyperattenuating "pseudocapsule"[5,13] (Figures 3 and 4). The "fat halo" sign describes a rim of preserved hypodense fat surrounding encapsulated mesenteric vessels and/or nodes[3]. It has been suggested that at least three of these signs are required for definitive diagnosis.[11]

MP is not commonly identified by ultrasound but a hyperechoic, non-compressible mesenteric fatty mass, and non-deviated mesenteric vessels are reported.[12,14] The presence of focal increased fludeoxyglucose (FDG) uptake within the affected mesentery may indicate malignancy, but the majority of cases are non-avid on FDG positron emission tomography-CT (PET-CT).[6,15] It is worth noting that FDG PET-CT does not completely exclude all malignancy (*e.g.* in cases of mucinous carcinomas which may show low FDG uptake) and some non-malignant disease can show FDG uptake (*e.g.* sarcoidosis).[6,15] Therefore, in equivocal cases, a biopsy is necessary for accurate histological diagnosis.[3,15] PET-CT is also useful to identify other

Figure 3. "Severe" mesenteric panniculitis. Axial and sagittal CT slices showing markedly increased mesenteric attenuation with obvious mass effect and surrounded by a pseudocapsule (white arrows).



extra-abdominal targets for biopsy where possible.[15] Because MP describes idiopathic mesenteric inflammation, it may be necessary to consider other mesenteric pathologies, especially when the manifestation is florid.[9] Differential diagnoses range from mesenteric oedema, desmoid tumours, and retroperitoneal fibrosis, to frank malignancies such as lymphoma (Figure 5), peritoneal carcinomatosis, and well-differentiated liposarcoma[1,6] (Table 1).

Grading

Because the appearances of MP are variable, it seems sensible to consider a grading system. Coulier and co-workers applied a grading system to their prospective study evaluating the natural course of MP.[11] Table 2 describes the five CT signs they considered "typical" of MP. For each of these five signs, they applied a score of 0 to 3 points, where 0 = absent, 1 = discrete (mild) 2 = moderate, and 3 = marked.[11] Three was considered the lowest possible score to diagnose MP (*e.g.* a case where three signs are present to a mild degree) and the maximum possible score is 15 (*i.e.* a case where all five signs are "marked").[11] They then applied thresholds to categorise individual cases as "mild" (3–5 points), "moderate" (6–9 points), or "marked" (10–15 points).[11]

Figure 4. "Severe" mesenteric panniculitis. Axial CT slices showing markedly increased mesenteric attenuation with obvious mass effect, surrounded by a pseudocapsule (white arrows) and multiple discrete prominent nodes (yellow arrows).

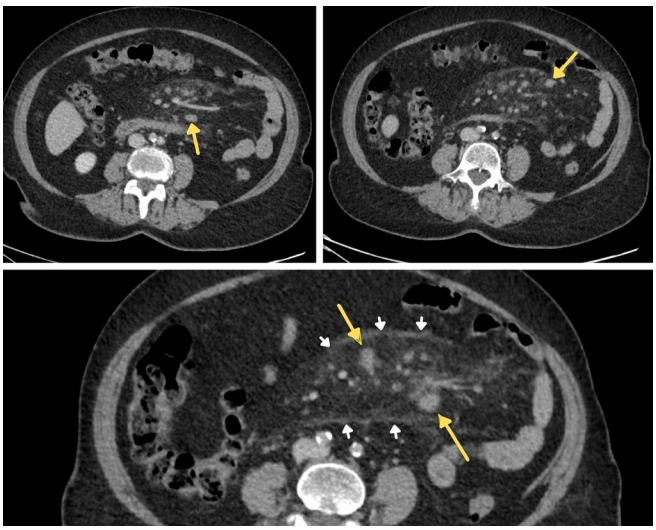
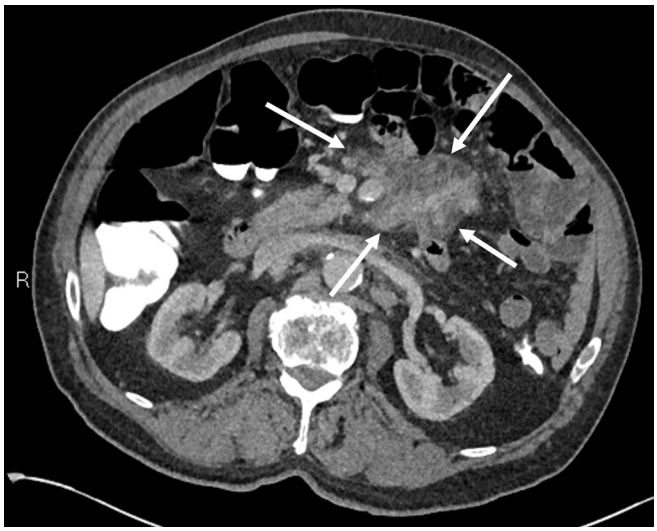


Figure 5. Lymphoma. Here, increased mesenteric attenuation is both dramatic and mass-like, and encapsulated nodes are clearly pathologically enlarged. The appearances are too advanced for this to be mesenteric panniculitis alone.



Histopathology

It has been suggested that histological evaluation provides the most reliable means of diagnosis, and it may be necessary to obtain a biopsy in equivocal cases.[3,19] However, the obvious issue is one of spectrum bias since the very large majority of MP cases will never come to biopsy and those that do will lie at the interface between MP and other pathologies such as lymphoma. In any event, it has been reported that, macroscopically, normal fatty mesenteric lobulations are lost and replaced by areas of reddish brown or pale yellow plaques representing necrosis.[10] The peritoneum is also firmly attached to, and inseparable from, the affected mesentery.[10] Of note, vessels are usually unaffected and course normally through the mesentery.[10] Microscopically, there is abundant infiltration of mesenteric fat by macrophages[10] and in cases of retractile mesenteritis, prominent fibrosis with scant inflammation and fat necrosis.[16]

Associated conditions

The literature has associated MP with several non-neoplastic and, notably, neoplastic conditions (Figure 6). However, very significant uncertainty persists regarding whether MP is genuinely associated with malignancy, and it is this uncertainty that causes clinical concern and indecision regarding how to "manage" the finding once identified on CT scanning.

Table 1. Distinguishing features of major differential diagnoses[3,6,9,12,16–18]

Features	Mesenteric panniculitis	Lymphoma	Peritoneal carcinomatosis	Mesenteric oedema	Carcinoid
Location	Most confined to the root of the mesentery	Can affect the root of the mesentery	Can affect but not confined to root of mesentery- can involve omentum, peritoneal surface of liver and spleen etc	Diffuse, involves subcutaneous fat	Can involve the root of the mesentery- desmoplastic reaction
Calcification	Presence of calcification	Absence of calcification (unless previously treated)	Can contain calcification (particularly if mucinous)	No calcification	Can contain calcification
Nodes	Lymph nodes ≤ 10 mm	Large lymph nodes ≥ 10 mm Nodes outside the mesentery		Usually, no associated lymph node involvement	
Vascular involvement	Encases vessels	Encases vessels	-	-	
Other	Fat halo sign Presence of pseudocapsule	Usually FDG-PET avid Splenomegaly	Sites of primary disease – ovarian/appendiceal/ gastric malignancy Ascites is more likely	Co-exists with other signs such as cardiomegaly, cirrhosis, ascites, pleural effusions etc.	Hyper-vascular liver lesions

FDG, fludeoxyglucose; PET, positron emission tomography.

Non-neoplastic disorders

A history of abdominal trauma and/or surgery have been linked to the development of subsequent mesenteric panniculitis.[3,9,11,16] Akram et al reported that of 92 cases of mesenteric panniculitis identified between 1982 and 2005, 40% had undergone previous abdominal surgery. They also suggested that powdered surgical gloves, used during abdominal surgery in the mid-80s, could be a possible cause of peritoneal adhesions and fibrosis,[16] a hypothesis that has long been promulgated in the surgical literature. Similar results were reported by van Putte-Katier et al, who found that 50% of 94 cases had undergone previous surgery.[9]

Fibrosclerotic disorders such as retroperitoneal fibrosis, sclerosing pancreatitis, IgG4-related disease, and Sjogren's syndrome have all been linked with MP, suggesting a common pathophysiological process of inflammation and fibrosis in multiple organs.[16] A recent retrospective study by Gunes et al reported increased rates of metabolic syndrome (45%), urolithiasis (37%), and vascular disorders (22%) in 102 patients with MP compared to 408 matched controls (32%, 27% and 15% respectively).[7]

An association has also been postulated with diabetes mellitus.[20] Development of insulin resistance in Type 2 diabetes is thought to be the result of inflammation triggered by pro-inflammatory cytokines, changes in leukocyte and macrophage populations, and increased tissue fibrosis.[20] In this inflammatory state, raised leptin facilitates macrophage accumulation within abdominal visceral adipose tissue.[20] These changes are histologically similar to those seen in MP, where foamy macrophages infiltrate adipose tissue causing necrosis, thereby suggesting an association between these two entities.[20]

Malignancy

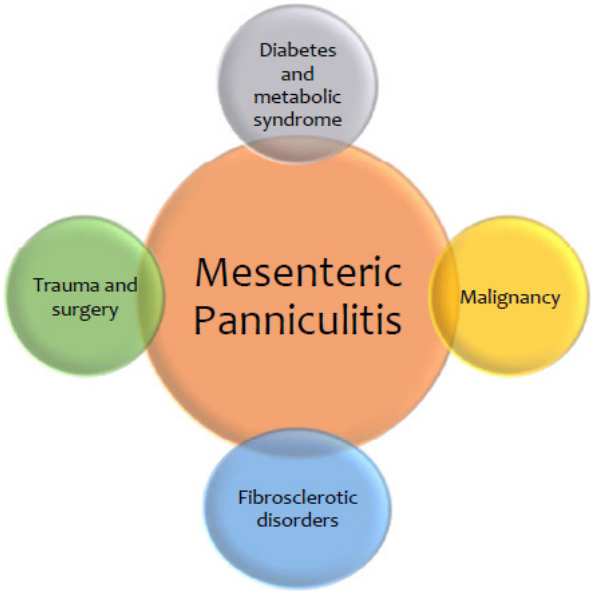
Several researchers have suggested an association between MP and malignancy, the most common association being lymphoma (usually non-Hodgkins), but gastric cancer, colonic cancer, renal cell carcinoma, melanoma, and carcinoid tumours have all been proposed.[1,6,11,18] Daskalogiannaki et al reported that 69% of their MP cases had concurrent malignancy.[13] Similar findings of a significantly higher prevalence of malignancy in patients diagnosed with MP on initial CT scan was reported in 2014 by van

Table 2. Imaging findings in cases of mesenteric panniculitis.

CT FINDINGS	
Typical*	• A well-defined mass within the root of the small bowel with mass effect on surrounding structures • Heterogenous higher attenuation than surrounding mesenteric/retroperitoneal fat • Presence of well-defined soft tissue nodules within the mass • Fat halo sign • Presence of a surrounding hyperdense pseudocapsule
Other signs	• Leftward oriented mesenteric mass • Subcentimetre lymph nodes • Congregation of mesenteric vessels within the mass

* 5* five classic diagnostic signs.[3–6,9–11,13]

Figure 6. Schematic showing the common reported associations of mesenteric panniculitis including; previous surgery (*e.g.* cholecystectomy), malignancy (lymphoma, gastrointestinal and urological malignancies), diabetes and metabolic syndrome, and fibrosclerotic conditions (retroperitoneal fibrosis, sclerosing pancreatitis, IgG4 disease).



Putte-Katier et al.[9] These researchers also reported that 14% of patients with MP went on to develop other malignancies over a 5-year follow-up period, compared with 6% of a matched control group.[9] However, Buchwald et al found no significant difference in the rates of progression of patients with MP alone, compared to those with MP and malignancy (including those whose cancer had been cured).[21] They suggested that MP is an epiphenomenon, merely existing alongside malignancy rather than a paraneoplastic process in-and-of-itself.[21]

Ultimately, it is the potential association with malignancy that causes clinical concern and results in these patients undergoing multiple subsequent examinations in an attempt to identify any worrisome progression. In an effort to clarify the issue, a 2016 systematic review identified 14 articles describing 1226 individual patients.[2] However, the authors found that the studies were too heterogenous for meta-analysis, noting especially that accrual was biased in many cases, especially by retrospective designs. They concluded that available indexed data were insufficient to determine any association between MP and subsequent malignancy.[2] Regardless, in the presence of MP, reasonable efforts should be made to exclude malignancy.

Management

Since the vast majority of cases are asymptomatic (or at least the patient's presenting symptoms are not ultimately ascribed to MP), MP requires no specific treatment. The literature on who receives treatment and for what duration is scant. There is general consensus that specific treatment should be reserved only for those with severe clinical symptoms attributable to primary MP, irrespective of the severity of CT findings. For those whose symptoms are believed to be due to primary MP, first-line treatment is with a combination of Tamoxifen and corticosteroids, usually prednisolone, with a positive response seen in about 60% of cases at 12–16 weeks.[3,16] Tamoxifen is used widely to treat breast cancer since it induces production of transforming growth factor β (TGF-β) from stromal fibroblasts. TGF-β, is thought to have a growth-modulating effect on cells and to decrease inflammation, which is the proposed mechanism that treats MP.[16] Other treatments using colchicine, azathioprine, progesterone, cyclophosphamide, and thalidomide have been reported with varying degrees of success.[3] Unless cases present with intractable bowel obstruction, surgery is not advocated.[6,16] In the study by Akram et al, medical treatment with tamoxifen was given for a median of 20 months, prednisolone for a median of 13 months, and colchicine and azathioprine for a median of 8 and 14 months respectively.[16] In their study, disease response was monitored with repeat CT scans.[16]

The natural course of MP has been described as stable or slowly progressive in the majority of cases.[9,11,22] In the authors' anecdotal experience this uncertainty regarding progression, and the putative association with malignancy, triggers long-term follow-up by CT imaging. The extent to which this happens, its duration, and outcome, is unknown currently.

CONCLUSION

MP is a non-specific inflammatory condition of the small bowel mesentery that is usually diagnosed incidentally during abdominopelvic CT scanning. MP exists either as part of a spectrum of primary disease characterised by varying degrees of inflammation, necrosis, and fibrosis, or may co-exist alongside other abdominal pathologies. The aetiology is unknown and a relationship with subsequent malignancy is not established with certainty. Accordingly, at the time of writing it remains unclear whether asymptomatic cases should be followed-up, and what the duration of any follow-up should be. Systematic review has found the primary literature around this condition inadequate to answer these questions with confidence, suggesting that methodologically robust research to clarify the issue is warranted.

KEY POINTS

- MP describes focally increased mesenteric attenuation.
- MP encapsulates a range of severities, from barely present to a florid, fibrotic, retractile mesenteritis
- MP is usually diagnosed incidentally during abdominopelvic CT scanning, which shows focal hyperattenuating mesentery, with or without mass effect, encapsulated nodes and vessels, and a pseudocapsule.
- An association with subsequent malignancy is often postulated but the primary literature is inconclusive regarding this point.
- There is no consensus regarding whether CT follow-up should be offered to patients with incidental, asymptomatic MP.

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