The Complex Relationship between Mesenteric Panniculitis and Malignancy — A Holistic Approach is Still Needed to Understand the Diagnostic Uncertainties

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Abstract

Mesenteric panniculitis is an idiopathic, localized inflammation involving the adipose tissue of the small bowel mesentery. The association of mesenteric panniculitis with malignancy, predominantly lymphomas, has been widely reported in the medical literature. In this review article, we will discuss the clinical features in the diagnosis and management of mesenteric panniculitis and the clinical association between mesenteric panniculitis and malignancies.

Introduction And Background

Mesenteric panniculitis (MP) is an idiopathic, localized inflammation involving the adipose tissue of the small bowel mesentery. The association of mesenteric panniculitis with malignancy, predominantly lymphomas, has been widely reported in the medical literature. The majority of patients with mesenteric panniculitis are asymptomatic and are picked up incidentally while performing radiological examinations, but MP patients with a high risk of malignancy warrant a thorough investigation [1]. There is a lack of clear clinical guidelines on the management and follow-up of MP.

Cardinal radiological signs of mesenteric panniculitis

Table 1 shows the five cardinal radiological signs of MP [1].

| #  | Five-cardinal radiological signs of MP on Computed Tomography (CT) Scan |
|----|---------------------------------------------------------------------|
| 1  | Fatty mass lesion in the small bowel mesentery                      |
| 2  | Hyper-attenuation of the mesenteric fat                              |
| 3  | Lymph nodes in the fatty mass                                       |
| 4  | Halo surrounding the lymph nodes or vessels                         |
| 5  | Pseudo-capsule                                                      |

TABLE 1: Five cardinal radiological signs of MP

MP: Mesenteric panniculitis

Pathology

MP is an inflammatory disorder of the mesenteric root with two distinct pathological subgroups: mesenteric panniculitis and retractile mesenteritis. The differential diagnosis of these two conditions is based on histological criteria: fat necrosis predominates in MP whereas fibrosis and retraction predominate in retractile mesenteritis [2].

The exact diagnosis is often difficult. It is usually made by finding one of these major pathological features: follicles, chronic inflammation, or fatty infiltration of the mesentery.

Clinical features

The majority of patients with mesenteric panniculitis are asymptomatic, although some may present with non-specific symptoms like abdominal pain, nausea, vomiting, fever, anorexia, and physical examination [2].

The condition occurs mostly in middle or late adulthood with a slight male predominance. Symptoms may be progressive, intermittent, or absent. Laboratory findings, including elevation in erythrocyte sedimentation rate and anaemia, are generally absent or non-specific.

Aetiology

Common causes of MP include abdominal trauma and a history of abdominal surgery. Associated inflammatory disorders, such as vasculitis or chronic rheumatic conditions, granulomatous disease, rheumatic disease, malignancies, and pancreatic fistula have also been reported.

Infectious associations with MP include mycobacterial and cryptococcal infections and cholangitis. In some patients, especially those having an acute presentation of the disease, viral mesenteritis is likely. Fever of unknown origin and chylous ascites have also been described in patients with MP [3].

Although often entirely isolated, synchronous association of MP has been observed with some neoplastic diseases, such as lymphomas, colorectal cancer, and melanomas. The possibility of MP being a paraneoplastic syndrome in the elderly should be considered [4].

When MP occurs in association with malignancy, the most common primary sites are the large bowel, the lymph nodes, and the urogenital tract. In those with MP, any cancer — with the exception of prostate cancer — can usually be seen on an index computed tomography (CT) scan. Further extensive investigation in asymptomatic patients is therefore likely to be of low yield [4].

Review

Objectives of this literature review

To discuss the clinical features and association between mesenteric panniculitis and malignancy, the diagnostic dilemmas, and their treatment plan.

Materials and methods

We conducted a literature search of articles using the US National Library of Medicine PubMed database,
PubMed, MEDLINE, Embase, Cochrane Library and Google Scholar databases, ClinicalTrials.gov for studies, and the ISI Web of Science. No date restrictions were placed on the search. A thorough search for controlled clinical trials and cohort studies was conducted. Since the rarity of condition, case reports were also included.

We used the keywords: "Mesenteric panniculitis" and "malignancy".

Included studies were those published in English that assessed the association between mesenteric panniculitis and malignancy. Reference lists were also screened. From the search results, articles with irrelevant titles were discarded, with the remaining abstracts examined for relevance.

The authors of this review independently determined the eligibility of the studies and assessed the methodology of included studies. In this review article, we will discuss the aetiology, pathogenesis, and clinical studies related to MP, as well as case studies and their management per the latest clinical guidelines.

Review of clinical studies

The findings of the literature review are summarised in Table 2, but we will discuss a few of the studies that are more relevant to the association between mesenteric panniculitis and malignancy.
Results do not suggest that patients with incidentally found MP should be followed up for early detection of a malignancy. In addition, neglect of these findings, the subsequent finding of a malignancy is less likely. In more than half of the cases, the mesenteric abnormalities did not worsen in appearance on follow-up CT scans (odds ratio, 0.03268; 95% confidence interval, 0.0028-0.3761; p = 0.0061). In the presence of an underlying disease, the prevalence of MP was 5.42% (CI 3.07-9.23). In 36 patients with MP (25.2%), malignancy was the predisposing factor in 8 of those patients.

Of the 19,869 CT scans, 36 patients had MP. Twenty-four of them were categorized as idiopathic, and malignancy was associated with these findings. The subsequent finding of malignancy is less likely. In addition, neglect of these findings, the subsequent finding of malignancy is less likely. In more than half of the cases, the mesenteric abnormalities did not worsen in appearance on follow-up CT scans (odds ratio, 0.03268; 95% confidence interval, 0.0028-0.3761; p = 0.0061). In the presence of an underlying disease, the prevalence of MP was 5.42% (CI 3.07-9.23). In 36 patients with MP (25.2%), malignancy was the predisposing factor in 8 of those patients.

### Summary of clinical studies

| Author          | Published ID | Study design | Age | M/F | Total patients (n) | Patient with malignancy | Colorectal cancer | Pancreatic cancer | Lymphoma | Cholangiocarcinoma | Prostate cancer | Breast cancer | Bladder cancer | Lung cancer | Metastases during followup | Prostate cancer surgery |
|-----------------|--------------|--------------|-----|-----|--------------------|------------------------|-------------------|-------------------|----------|---------------------|----------------|---------------|----------------|------------|-----------------------------|------------------------|
| Akren et al.    | 2270416      | Prospective  | M/F |     | 50                  | 9                      | 9                 | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Al-ronni et al. | 20199062     | Retrospective| M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Badot et al.    | 2064960      | Cross-sectional | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Belchak et al.  | 2062110      | Case-control | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Scher et al.    | 2059987      | Case-control | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Protn-Catteau et al. | 2059871   | Cross-sectional | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Smith et al.    | 2059873      | Case-control | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Wilkes et al.   | 2059874      | Cross-sectional | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |

The authors of this review gathered all the data showing the relationship between mesenteric panniculitis and malignancy. Various variables like study design, age, gender, total number of patients with malignancy, colorectal cancer, pancreatic cancer, lymphoma, cholangiocarcinoma, prostate cancer, breast cancer, bladder cancer, lung cancer, metastases during follow-up, previous abdominal surgery, inflammatory bowel disease, autoimmune disease, and death are gathered and discussed in Table 1. In particular, mesenteric panniculitis and colon cancer are also discussed.

**TABLE 2: Summary of clinical studies**

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| Akren et al.    | 2270416      | Prospective  | M/F |     | 50                  | 9                      | 9                 | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
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| Badot et al.    | 2064960      | Cross-sectional | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Belchak et al.  | 2062110      | Case-control | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
| Scher et al.    | 2059987      | Case-control | M/F |     | 50                  | 10                     | 10                | 0                  | 0        | 1                   | 0              | 0             | 0              | 0         | 0                          | 0                      |
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| Authors | Study Information | Median Age (SD) | Cases | Controls | Pathology | Results |
|---------|-------------------|----------------|-------|----------|-----------|---------|
| Gögebakan et al. [5] | Retrospective, January 2005 to April 2010, Multicenter, Chicago, USA | NR | NR | NR | NR | 61 known cases, 19 new cases |
| Mahafza et al. [13] | Retrospective, January 2012 to December 2014, Jordan University Hospital, Amman, Jordan | Male (mean age ± SD = 61.6 ± 13.0 years) | 00 | 28 | 7 | 2 | 3 | NR | 3 | 6 | 1 | 1 | NR | 44 |
| Nyborg et al. [21] | Retrospective, 2000-2013, Multicenter, Stockholm | Median age at diagnosis was 50 (24-84) years | 16/11 | 27 | NR | NR | NR | NR | NR | NR | NR | NR | NR | 3 |
| Sakin et al. [14] | Retrospective, January 2013 to December 2015, Turkey | 54 years (range 26-70) | 17/16 | 36 | 8 | 2 | 2 | NA | NR | NR | 1 | 1 | NR | 3 |
| Badet et al. [3] | Retrospective 2004-2013, France | 63 years (27-90) | 121/37 | 158 | 88 | 13 | 4 | 25 | NR | 11 | 4 | 1 | 3 | NR | 61 |
| Czyżyk et al. [22] | Retrospective, Dec 2007 to May 2016, Multicenter, Turkey | 33-78 yrs (mean (SD) = 68.2 ± 4.5 years) | NR | 2100 | 9 (of 51) | NR | NR | NR | NR | NR | NR | NR | NR | 17 |
| Kraszinsky et al. [11] | Retrospective, 2000-2013, Single center, Israel (HIL) | 19-94 yrs (mean age) | 113/53 | 153 | 64.6 yrs | 166 | NR | NR | 166 | NR | NR | NR | NR | NR |
| (Control) | 42-94 yrs (mean age) | 80/16 | 104 | 62.5 yrs | 7 out of 53 in the control had no disease | NR | NR | NR | NR | NR | NR | NR | NR |
| Buchwald et al. [7] | Retrospective, January 2002 - December 2015, Single Center, New Zealand | 63 (range 27-88) yrs | 131/42 | 173 | 75 | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| (Control) | 65.72 ± 14.35 yrs | 138/64 | 152 | 114 | 30 | NR | 14 | 6 | 2 | NR | 10 | NR | 66 |
| Gjøs et al. [5] | Retrospective, January 2010 - October 2012, Single center, New Zealand | 85 yrs (20-94) | 165/74 | 209 | 70 | 12 + 7 | 1 | 17 | 2 | 4 | 1 | 2 | 1 | NR | NR |
| (Control) | 65 ± 11.9 yrs | 55/16 | 77 | 39 | 12 | 4 | 6 | 2 | 4 | 3 | NR | 9 | NR | 10 |
TABLE 3: Demography of clinical studies

Although prior studies have described the association of MP and malignancy, a recent study shows that only 1.4% of patients with a computed tomography (CT) scan finding of MP will be found to have a previously undiagnosed or suspected cancer. The higher rate of association of MP and cancer described in prior studies likely indicates the inclusion of patients with a known history of cancer.

Additionally, this study shows that a follow-up abdominal CT in patients with cancer suggests stability and not a worsening of MP. Finally, findings indicated that positron emission tomography scans are not recommended in the evaluation of cancer patients with mesenteric panniculitis-like findings on a CT.

One retrospective study of 4,758 patients with 90 identified cases of mesenteric panniculitis found that the likelihood of associated malignancy (mostly intra-abdominal malignancy) was 2.1 times higher in patients with MP than those without it.

The crude ratio of mesenteric panniculitis patients with colon cancer is less than 10% from our studies (refer Table 4), which is worth looking into. Bigger studies with good sample size and proper research are necessary to further assess it. Even though this is simply a crude ratio, it holds promise for better understanding of the co-occurrence of MP and colon cancer.

| Author              | Total patients (n) | Colorectal cancer | Crude ratio (%) |
|---------------------|--------------------|-------------------|-----------------|
| Al-Omari et al.     | 43                 | 6                 | 13.85           |
| Ehrenpreis et al.   | 359                | 4                 | 1.67            |
| Kaye et al.         | 22                 | 1                 | 4.54            |
| Mahfza et al.       | 90                 | 7                 | 7.77            |
| Van Putte-Kats et al.| 94                | 8                 | 8.51            |
| Solin et al.        | 36                 | 2                 | 5.56            |
| Scherer et al.      | 143                | 20                | 13.96           |
| Balet et al.        | 158                | 13                | 8.02            |
| Piotin-Cailleau et al.| 288              | 38                | 13.19           |
| Cross et al.        | 259                | 19                | 7.32            |
| Googehekan et al.   | 229                | 12                | 5.24            |
| Smith et al.        | 359                | 10                | 2.78            |
| Wilkes et al.       | 118                | 14                | 11.86           |
| Daskalogiannaki et al.| 49               | 5                 | 10.20           |

TABLE 4: Mesenteric panniculitis (MP) and colon cancer

Follow-up

Computed tomography scan is optimal for accurate, non-invasive diagnosis of MP and follow-up of sclerosing mesenteritis and any complications. The presence of some radiological findings, such as lymph node size of more than 12 mm and the absence of the fat ring sign, should raise the concern of subsequent malignancy in patients with MP.

Treatment

There are no well-established treatment plans for this rare condition. Thus, any treatment prescribed is mainly for symptom relief and to address any complications. Commonly used agents include steroids and other immunosuppressants.

One study found that symptomatic patients with idiopathic mesenteric panniculitis responded to treatment with antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). Patients with obstructive or compressive symptoms may require surgery.

Strengths of the studies

This is one of the most comprehensive literature reviews discussing the association between mesenteric panniculitis and malignancy. The studies in this literature review have been done in multiple centres which will increase the generalisability of the results within a population. Studies also represent a wide range of malignancies like colorectal cancer, lymphoma, breast cancer, etc.

Limitation of clinical studies

Most clinical studies performed on MP lacked histological biopsies. Generally, a biopsy is not justified due to the incidental asymptomatic nature of the disease in most patients. For the majority of patients, the diagnosis was based on the CT appearance and on follow-up CT studies that revealed no additional findings or changes.

Most of studies are retrospective and details regarding standardisation of CT scan protocol like intravenous contrast and oral contrast were not available.

Various aspects of interest are not included such as race/ethnicity, medications, chemotherapy and are not discussed in detail.

Discussion

Mesenteric panniculitis is a rare clinical entity that can occur independently or in association with other disorders. Diagnosis of this nonspecific, benign inflammatory disease presents a challenge to gastroenterologists, radiologists, surgeons, and pathologists.

In most cases, MP is self-limiting and regression can even be observed during follow-up in the absence of medical treatment. Clinical symptoms can subside without surgery and with the use of drugs such as...
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