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Mesenteric Panniculitis in a Patient with Neuroendocrine Carcinoma: An Unresolved Association. Case Report and Literature Review

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Abstract

Mesenteric Panniculitis (MP) is an inflammatory pathology of mesentery that generally appears incidentally in typical tomographic findings and is asymptomatic in most cases. There are difficulties in the approach of symptomatic patients, mainly abdominal pain when we are in the presence of associated pathologies such as neoplasms. Multiple studies have evaluated the relationship between PM and cancer trying to identify a possible prediction of neoplasms, progression or a paraneoplastic injury with contradictory results. We present the case of a patient with an advanced neuroendocrine tumor undergoing oncological management with MP, its clinical picture, diagnosis and management, and finally, a review of the literature is carried out with an emphasis on the available evidence on the association between PM and cancer.

Keywords: Mesenteric panniculitis; Panniculitis; Peritoneal; Neoplasm; Carcinoma; Neuroendocrine; Abdominal pain

Introduction

Mesenteric Panniculitis (MP) is a rare, complex, localized fibroinflammatory pathology of unknown etiology that mainly affects the mesentery of the small intestine and occasionally the mesocolon, peripancreatic region, retroperitoneum, or pelvis [1-3]. Generally, PM is an unexpected finding found by abdominal Computed Tomography (CT), which can identify the characteristical radiological features of PM, such as the presence of a well-defined heterogeneous fat mass that emerges from the root of the mesentery of the small intestine (with increased attenuation of retroperitoneal fat), displacement of surrounding loops of intestine, sparing of adjacent fat surrounding superior mesenteric vessels and mesenteric lymph nodes ("Fat halo sign") and may coexist with presence of a peripheral band of soft tissue surrounding the inflammatory mass (tumor pseudocapsule) [4,5].

Currently, several evolutionary stages are identified according to the histologic findings, beginning with inflammation of the mesentery (Mesenteric Panniculitis), then with fat necrosis (Mesenteric Lipodystrophy) and, finally, scarring mesenteric fibrosis (Sclerosing Mesenteritis) is generated [6]. Also, is known in the literature as retractile mesenteritis, xanthogranulomatous mesenteritis, liposclerotic mesenteritis, isolated lipodystrophy, or peritoneal xanthogranulomatosis [7].

Epidemiologically, MP has a prevalence between 0.16 and 2.5% [3,5,8]. It has a higher incidence in men between 50 and 60 years old, with a 2:1 ratio [7,9]. Multiple triggering mechanisms have been described, such as infectious processes, ischemic disorders, trauma, drugs, previous abdominal surgeries, autoimmune diseases, and malignancy [10].

The evidence on the association between MP and cancer is limited, the relationship with lymphomas, colorectal and urogenital malignancy being more common, with rates between 17.6 and 69.3%. Some authors have proposed MP as a predictor of malignancy based on low-quality evidence [3,5,11,12]. Therefore, there are still doubts about the approach to these patients with PM and cancer.

We present the case of a patient with a neuroendocrine tumor undergoing cancer management who presented with persistent abdominal pain that was difficult to control and in whom were radiological signs of mesenteric panniculitis, which raised doubts about a manifestation of tumor

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progression. Finally, a discussion of the clinical case is made based on the review of the literature.

Case Presentation

Male patient, 50 years old, engineer, married, previously diagnosed with a neuroendocrine tumor of unknown primary of 6 years of evolution. Hepatic, lymph node, and bone metastases. Oncological management with Lanreotide. He consulted recurrently due to intense abdominal pain that was difficult to locate, predominantly on both flanks, without the presence of associated gastrointestinal or genitourinary symptoms, and without respiratory symptoms. On physical examination, there were no signs of systemic toxicity, no fever, tenderness on palpation in the flanks, no masses or visceromegaly, and peristalsis present, without other significant findings during the assessment. Laboratory tests did not show increased acute phase reactants, leukocytosis, no impaired renal function, and electrolytes but did show elevated phosphatase and gamma glutamyl transferase. A CT scan of the abdomen reported necrotic adenopathy's in the hepatic hilum, portocaval region, retroperitoneal, retrocrural, and the left iliac chain, unchanged from a previous study. Hepatomegaly and the progression of focal hepatic lesions remained stable in the follow-up. Also, known polyostotic involvement. Halo sign compatible with mesenteric panniculitis (Figure 1a, 1b). Also, A contrast MRI of the spine showed a diffuse heterogeneous aspect of the bone marrow without collapse or focal infiltrative lesions. It realized a contrast MRI of the spine to rule out metastases and showed a diffuse heterogeneous aspect of the bone marrow without collapse or focal infiltrative lesions. Also, is performed a gallium Positron Emission Tomography (PET) scan as a follow-up by his oncologist, which showed cervical, mediastinal, mesenteric, retroperitoneal, and retrocrural lymph node involvement. Hepatic metastasis. Bone involvement in calotte, spine, costal arches, scapulae, and clavicles. And did not report peritoneal involvement. He received multimodal analgesic management with potent opioids, morphine in escalated doses up to 4 mg intravenously QID and hyoscine 20 mg intravenously QID with partial improvement, anti-inflammatory cycle with ketorolac and steroid cycle. Intervention is carried out with a quadratus lumborum block achieving better pain control. Outpatient management continued with fentanyl 50 microgram patches every 72 h with subsequent removal of 25 micrograms and oral hyoscine 10 mg tid due to clinical improvement.

Discussion

Jura made in 1924, during abdominal surgery, the description of the first case of the disease and named sclerosing mesenteritis. Later, Kuhrmeier made the initial description of the macroscopic and histopathological typical findings. MP is a subtype of sclerosing mesenteritis, a non-specific, inflammatory, non-neoplastic condition of mesenteric adipose tissue. Histopathologically, a mixture of necrosis, chronic inflammation and fibrosis of adipose tissue is found [1,3,13]. The prevalence is variable and based on radiology databases, from 0.16% to 7.8%. Since CT is the choice study and generally incidental, it shows characteristic Coulier radiological criteria, requiring at least 3 of the 5 (Table 1) [8]. This large variability depends on the difference in terms used and radiologist operator dependency. Clinically they can be asymptomatic, but some patients present with common symptoms such as fever, malaise, weight loss, hyporexia, abdominal pain, and diarrhea. Different comorbidities were associated with MP, but a causal association has not been found [1,2]. Our patient is a man in his fifth decade, corresponding to the population with the highest prevalence reported in the literature. He had a neuroendocrine cancer and consulted due to severe abdominal pain. The CT scan showed the characteristical radiological findings of MP.

Different studies, mostly case reports and case series from radiological databases, have reported an association between MP and cancer rates of 17.6% to 38%, mainly lymphomas [12,14].

Mahafza et al. retrospectively studied the tomographic findings of 4,758 patients finding MP in 90 of them (1.9%) with a prevalence of

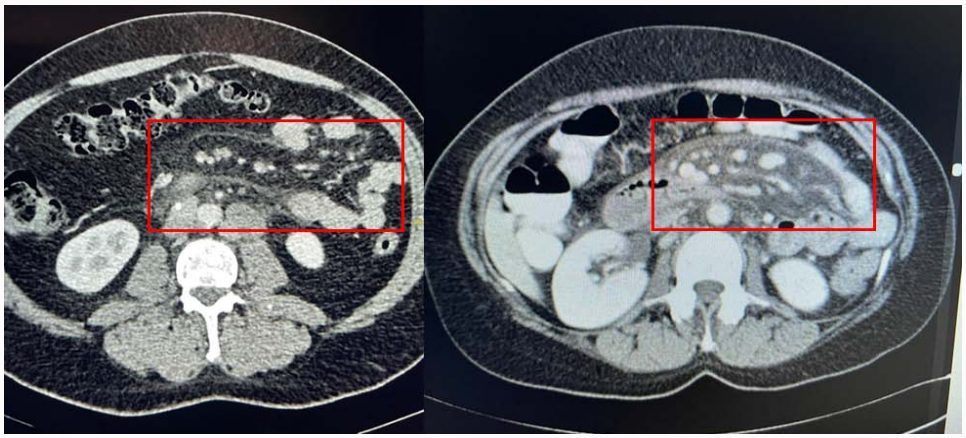

Figure 1a-1b: It observed the attenuation of the mesenteric fat and the presence of a low-density halo surrounding mesenteric vessels and ganglia.

Table 1: Signs of Coulier's PM.

1. A well-defined fatty mass at the root of the small intestinal mesentery displacing adjacent structures.
2. Sign 1 with attenuation greater than that of subcutaneous or retroperitoneal fat tissue.
3. Lymph nodes within the fat mass.
4. A hypodense halo surrounding vessels and nodules.
5. A hyperdense pseudocapsule surrounding the mesenteric fat with the lymph nodes within.

malignant disease of 28%, with two times higher probability of having it than patients without MP [15]. Gregory et al. also retrospectively evaluated tomographic signs of MP associated with malignancy in 444 patients observing that the presence of nodules >10 mm and lymphadenopathy in other abdominal areas is associated with lymphoid malignancy with high sensitivity and specificity [16].

Ehrenpreis et al. found retrospectively in 147,794 tomographic studies, 359 with findings compatible with MP, 22.6% with known cancer, and 5.3% with *de novo* cancer. Lymphomas were the most common neoplasms related to MP (follicular 47%, followed by diffuse large cell B 25%). The most frequent solid tumors were prostate 7%, lung and kidney 6%. Was performed follow-up CT in 56 patients, of which 80% had no new findings, 11% worsened, and 9% improved, and PET-CT in 44 patients showed uptake in only 5%, so it is not a recommended study [17].

In contrast, other studies have shown a poor relationship between MP and cancer. Gögebakan et al. reported a retrospective case-control study based on CT findings on the prevalence of malignancy and other diseases in patients with and without MP. 77 cases out of 13,485 were diagnosed with MP by tomographic studies (0.58%). Malignancy was present in 50.6% of the patients *vs.* 60% of the control group. They also found no correlation with chronic diseases such as hypertension, diabetes mellitus, or previous surgeries [18]. Kaminsky et al. also reported no association between non-Hodgkin's lymphoma and MP in a case-control study with retrospective CT and PET-CT findings in 166 patients with lymphoma and 332 controls with a prevalence of 1.8% *vs.* 2.1% respectively [19].

The MP also have been associated as a paraneoplastic phenomenon with contradictory results. Badet et al. a retrospective analysis of 158 patients diagnosed with MP by CT, found 56% of patients with underlying neoplastic disease, suggesting that it may be a paraneoplastic condition [20]. On the contrary, Buchwald et al. a retrospective cohort study of CT findings in 173 patients with MP over 12 years, found no difference in the remission rates of MP in patients with cancer *vs.* non-cancer, whether or not there was cancer remission, considering that it is not the behavior of a paraneoplastic phenomenon but an epiphenomenon [21]. Our patient evolved satisfactorily with multimodal and interventional analgesic management. The signs of progression documented in the CT did not influence the clinical evolution towards improvement, which supports the presence of an incidental independent condition.

Few studies have evaluated the presence of MP in patients with neuroendocrine tumors, as in this case. Patirannehalage et al. reported the late diagnosis of an ileal neuroendocrine tumor histologically diagnosed as MP [22]. There are doubts about the approach and management of these patients.

MRI and PET-CT also have been used in the diagnosis of MP. Orcajo Rincon et al. evaluated prospectively 2,666 PET-CT to determine its role in MP, 30 had signs suggestive of MP, with a positive predictive value low (49.79%). The PET-CT findings indicate intense inflammatory activity but do not allow for excluding a concurrent tumor process [23]. The patient underwent PET with gallium, which is more accurate for his type of neoplasia and did not correlate with tumor progression, leaving the diagnosis of MP based on CT findings, which, according to the literature, is still considered the method of choice [1].

Halligan et al. conducted a systematic review of imaging studies of MP to evaluate its relationship with malignancy, concluding that the studies are heterogeneous and present biases that do not allow determining this relationship [24] and recently, Hussain et al. in a meta-analysis with controlled studies with 415 patients, did not find a significant association between MP and neoplasm [3].

There are no recommendations regarding the treatment of MP. Asymptomatic cases do not require management. Multiple drugs such as steroids, tamoxifen, azathioprine, and cyclophosphamide have shown partial response in case series. In rare cases, surgery is helpful for symptomatic relief [1,14]. In our case, management was focused on symptomatic pain management and steroid cycle with clinical improvement and sustained remission.

The clinical significance of MP in patients with malignancy remains controversial, but the studies that show an association have low quality and biases. Better quality evidence available favors the presence of an epiphenomenon. Some very doubtful cases require a biopsy.

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