Mini-Review

iMedPub Journals
www.imedpub.com

Journal of Rare Disorders: Diagnosis & Therapy
ISSN 2380-7245

2018
Vol.4 No.5:22

DOI: 10.21767/2380-7245.100190

Sclerosing Mesenteritis: A Review Article

Alisha Gupta[1], Yatee A. Dave[2] and Mihir M. Shah[3*]

[1]Division of General Internal Medicine and Geriatrics, Northwestern University, 251 East Huron Street Galter Suite 3-150, Chicago, IL, 60611 USA

[2]Rutgers Robert Wood Johnson Medical School, 675 Hoes Lane West Piscataway, NJ, 08854 USA

[3]Department of Surgery, Division of Surgical Oncology, Winship Cancer Institute, Emory University School of Medicine, 5665 Peachtree Dunwoody Rd, Atlanta, GA, 30342 USA

[*]**Corresponding author:** Mihir M. Shah, Department of Surgery, Division of Surgical Oncology, Winship Cancer Institute, Emory University School of Medicine, 5665 Peachtree Dunwoody Rd, Atlanta, GA, 30342 USA, Tel: (404) 778-3307; Fax: (404) 778-1279; E-mail: mmshah7@emory.edu

Received date: July 07, 2018; **Accepted date:** October 29, 2018; **Published date:** November 5, 2018

Citation: Gupta A, Dave YA, Shah MM (2018) Sclerosing Mesenteritis: A Review Article. J Rare Disord Diagn Ther. Vol. 4 No. 5: 22.

Abstract

Sclerosing mesenteritis is a rare chronic inflammatory condition characterized by mesenteric fibrosis. There are three pathological subtypes based on level of inflammation, fat necrosis, and fibrosis: mesenteric panniculitis, mesenteric lipodystrophy, and retractile mesenteritis. The prevalence is 0.6%-1%, with the disease generally affecting middle-aged or older males. There is no known etiology, though there are a variety of potential causal factors. Clinical presentation and dual-phase abdominal CT imaging are occasionally helpful adjuncts to diagnosis, but definitive diagnosis requires surgical biopsy. Management is primarily based on anecdotal evidence, and generally consists of symptomatic treatment via surgical or medical therapy.

Keywords: Sclerosing mesenteritis; Chronic inflammatory condition; Surgical biopsy

Epidemiology and Etiology

The prevalence of this condition as reported by autopsy series and radiology series ranges from 0.6% -1% [1,2], and usually affects mid-aged or older men [3,4]. The etiology of sclerosis mesenteritis (SM) is unknown. A systematic review by Sharma et al. in 2017 reported that approximately 30% of patients had a history of prior abdominal surgery or trauma [4]. Other potential causative factors include infection, ischemia, and neoplasm [5]. Autoimmune conditions associated with SM include retroperitoneal fibrosis, sclerosing cholangitis, Riedel thyroiditis, and orbital pseudotumor [6]. The pathophysiology of SM is likewise unclear. Given the typical presence of foamy macrophages on histopathology, it has been hypothesized that molecular pathways involving foam cell formation, including upregulation of peroxisome proliferator-activated receptor-gamma (PPAR-gamma), may play a role [7]. PPAR-gamma is a transcription factor present in adipose and intestinal tissue which modulates adipocyte differentiation and glucose metabolism [8]. A recent small series of case reports further suggests a relationship between dysfunctional glucose metabolism and the molecular mechanism of SM. The authors propose that obese patients with diabetes mellitus type 2 have inflammatory changes in their abdominal visceral adipose associated with insulin resistance, which is similar to the changes in mesenteric fat in patients with SM [9]. Chronic inflammation and fat necrosis have been identified in the adipocyte tissue of both populations.

Clinical Features

Clinical presentation of patients with SM varies. Patients primarily present with abdominal pain, although patients may also present with other nonspecific symptoms such as fever, nausea, vomiting, diarrhea, constipation, abdominal distension, and weight loss [10,11]. An abdominal mass or signs of obstruction may be present [12,13]. Although very rare, there have been reported cases of patients presenting with ascites or chylous pleural effusions [11,14]. Symptoms are often related to inflammation or mass effect on adjacent structures, such as compression of the mesenteric vessels or partial intestinal obstruction. Finally, some patients may present asymptomatically, with diagnosis via incidental CT findings [1].

Diagnosis

SM is a rare, non-specific chronic inflammatory condition leading to variable amounts of mesenteric fibrosis. Although sclerosing mesenteritis has been shown in case reports to involve the pancreas [15], colon [13], and retroperitoneum [16], the pathology generally involves the fat tissue of the root of the small bowel mesentery [17]. This condition was first

described in 1924 [18], and since then numerous terms have been used to describe spectrums of the same disease based on predominant histology, such as mesenteric lipodystrophy (predominant fat necrosis) [19], mesenteric panniculitis (predominant chronic/acute inflammation and fat necrosis) [20], and retractile mesenteritis (predominant fibrosis/retraction) [21]. Other terms include mesenteric fibrosis, multifocal subperitoneal sclerosis, liposclerotic mesenteritis [22], sclerosing lipogranulomatosis, and mesenteric Weber-Christian disease [10]. To avoid confusion, SM is now considered a single disease process with three pathological subgroups, divided on the basis of their unique histopathologic differences: mesenteric panniculitis (mainly, inflammation and fat necrosis), mesenteric lipodystrophy (mainly, fat necrosis), and retractile mesenteritis (mainly, fibrosis and retraction) [12,23]. These different subgroups may be present simultaneously, making it difficult to ascertain whether these subgroups are distinct disease processes or points on a continuum of a single disease process [23]. Dual-phase abdominal computed tomography (CT) scan is the most sensitive imaging study for SM [24]. The varying histopathologic findings lead to a broad spectrum of imaging findings [17]. Kipfer et al. described three gross manifestations of SM: "Type 1" includes diffuse mesenteric thickening, "Type II" is comprised of a single mesenteric mass, and "Type III" is characterized by multiple mesenteric nodules [19]. Furthermore, similar CT findings between SM and more common diseases of gastrointestinal malignancy or inflammatory disease, such as lymphoma, carcinoid tumor, or mesenteric edema, can lower suspicion for SM [12]. One such nonspecific finding is "misty mesentery," a term coined by Mindelzun in 1996 to describe the hyperattenuation of mesenteric fat [25]. However, there are certain CT scan findings that are more unique for SM: presence of a large enhancing soft tissue mass centered in root of the mesentery, a fat ring sign (preservation of fat around mesenteric vessels without displacement of vasculature), and/or a tumor pseudocapsule (band of soft tissue attenuation separating the mass from surrounding mesentery) [12,26-28]. Moreover, mesenteric panniculitis is associated with CT findings of soft-tissue nodules of the mesenteric mass that are less than 5 mm diameter, believed to represent lymph nodes. Nodules larger than 10 mm can be suggestive of other disease processes, requiring biopsy for further identification [27]. Clinical symptoms and CT imaging are important in distinguishing SM from other diseases and suggesting the diagnosis of SM, but true diagnosis is made at the time of biopsy. Diagnosis is dependent on histology, which is demonstrative of inflammation, fat necrosis, and fibrosis, with the latter being a very regular feature [23]. Mesenteric lipodystrophy is specifically evidenced by infiltration of foamy macrophages replacing mesenteric fat, with little to no inflammation or fibrosis. Mesenteric panniculitis is characterized by fat necrosis and chronic inflammatory infiltrate of mesenteric fat by plasma cells, lymphocytes, polymorphonuclear leukocytes, and foamy macrophages [29]. The histopathology associated with retractile mesenteritis consists mainly of fibrous tissue and collagen deposits, leading to scarring and retraction [4,13,29]. There has been some recent exploration into the utilization of prostaglandin E-major urinary metabolite (PGE-MUM), a stable metabolite of prostaglandin-E2, as a potential biomarker of mesenteric panniculitis [30]. PGE-MUM was initially pursued as a noninvasive marker of intestinal mucosal inflammation and response to treatment in patients with ulcerative colitis [31]. Given the lack of diagnostic tools available for SM and the association of PGE-MUM with mucosal inflammation and fibrosis, both of which are present in SM, one case report investigated the utility of PGE-MUM as a biomarker for SM. This was done by measuring PGE-MUM levels in two patients diagnosed with mesenteric panniculitis; reduced levels were found after treatment [30]. Although more research is required, the study presents an interesting foray into the possibility of noninvasive biomarkers for a condition, which thus far can only be definitively diagnosed via biopsy.

Management

The natural progression of SM is generally localized and self-limiting, with possible occurrence of spontaneous, complete remissions [32]. Given the rarity of SM, its wide clinical spectrum, and the limited understanding of its pathophysiology, treatments are based on anectodal experience and case series. Further, their efficacy is unclear. Treatment options include surgical resection of affected tissue and medical therapy consisting of anti-inflammatory agents, antifibrotic agents, and immunosuppressive agents. Corticosteroids and colchicine have been used for their anti-inflammatory properties [33]. Combination azathioprine and corticosteroid therapy has also resulted in clinical improvement [34]. Thalidomide has anti-inflammatory, immunomodulatory, and steroid-sparing properties, which have led to its successful use as a treatment for refractory Crohn's disease, another gastrointestinal disease marked by chronic inflammation [35]. In a small study using thalidomide to treat patients with symptomatic mesenteric panniculitis, four of five patients had positive responses with no serious adverse effects [36]. Patients with more fibrotic disease have been successfully treated with tamoxifen and progesterone, agents with purportedly antifibrotic properties. Tamoxifen is an antiestrogen that has been used to treat retroperitoneal fibrosis, but has been successful in treating one case of SM in an human immunodeficiency virus-positive patient [37]. Oral progesterone has also shown positive results in treating one case of retractile mesenteritis, potentially via inhibition of fibroblast proliferation [38].

Discussion

Few studies have been published in the literature investigating SM, likely due to the rarity and nonspecific nature of the disease. Of these, even fewer have conducted outcome-based study designs. Despite the rarity, an increasing number of SM diagnoses are being reported. Van Breda Vriesman et al. conducted a review published in 2004 of the radiographic diagnosis of SM, noting the increased frequency of diagnosis in recent years due to the routine utilization of imaging modalities, such as ultrasonography and computed tomography imaging [27]. The authors reported incidental

radiographic finding of SM in a number of asymptomatic patients. A number of case reports have been published in the literature describing SM, with variable presenting symptomatology and treatment regimens [6,39,40]. In reviewing the literature, Naser et al. in 2012 reported clinical presentations which included vague abdominal pain, small-bowel masses, enteropathies, bile duct fibrosis, and pseudoneoplastic syndromes, thereby demonstrating the heterogeneity of this disease and the associated difficulty in classification and diagnosis [40]. Given this heterogeneity, Emory et al. proposed a unification of retractile mesenteritis, mesenteric panniculitis, and mesenteric lipodystrophy as a single entity based upon 84 case reports and their associated gross and microscopic histology [23]. Despite this, the literature remains inconsistent when reporting this disease entity. Unsurprisingly, treatment regimens remain as heterogeneous as clinical presentation and naming schemes, likely due to the paucity of outcomes data in the literature. Treatments range from pharmacologic management of symptoms [6] to major surgical intervention [40]. Notably, case reports of spontaneous remission have been published [39]. In 1965, Ogden et al. reviewed 27 cases of SM in a cross-sectional manner, reporting favorable symptom-free outcomes in 14 of 19 living patients [14]. Since that time, advances in medical technology have led to a large number of asymptomatic or mildly symptomatic patients being diagnosed with SM. There has also been associated advancement in treatment modalities for gastrointestinal pathologies such as SM.

In 2007 Akram et al. published a robust literature on SM. The authors conducted an ambispective cohort study of 92 cases of SM [3]. They observed an average age of 65 years with 70% male patients. Of the 48% of patients receiving treatment, 26% were treated medically alone (with tamoxifen and/or prednisone), 13% were treated surgically alone, and 9% were treated with surgery following medical therapy. Only 30% of surgically treated and 38% of medically treated patients had a favorable response. Furthermore, 18 deaths were observed during the study period, and 17% (3 patients) of these deaths were attributable to the complications or treatment of SM. Of the 18 deaths, 2 deaths were believed to be possibly treatment-related: line sepsis and thrombotic thrombocytopenic purpura. As demonstrated by this data, there exists significant heterogeneity in the treatment, response, and prognosis of patients diagnosed with SM. Authors provide a treatment algorithm at the conclusion of the article that endorses symptomatic treatment only, with surgical intervention for bowel obstruction refractory to conservative measures. Medical therapy with tamoxifen and prednisone is recommended for persistent symptoms after surgery or non-obstructive presenting symptoms.

These findings are further bolstered by a study published by Sharma et al. in 2017, who performed a systematic review of 192 cases of SM [4]. The found an average age of 61 years with 69.3% male patients, which is remarkably similar to the data above. Of the 76.6% known cases where treatment was provided, 34.9% received medical treatment (large variety of medical agents) and 41.7% underwent surgical treatment. From the 192 cases, 20.3% needed more than one treatment, and 20.5% of this population required further surgical intervention. The follow-up period was an average of 17.6 months, with 10.5% of patients unaccounted for and an overall mortality rate of 7.3% (14 patients). Of these, 85.7% were due to SM complications, including post-operative complications. A total 80% had a slow advancement of disease and positive outcomes. Interestingly, their study also supported that no imaging method (ultrasound, CT, magnetic resonance imaging or fluorodeoxyglucose-positron emission tomography) changed the development of disease altering the progression to surgical exploration. In summary, SM is a difficult to diagnose disease that has the potential to be easily misdiagnosed. Clinical presentation and imaging modalities are not sufficient for diagnosis, with biopsy required for definitive diagnosis. Although SM is a generally self-limited disease, there are reports of fatal complications related to both the disease and, as noted above, its treatment. More research is required for investigation into superior diagnostic criteria, noninvasive markers of disease, and the efficacy of medical and surgical management.

Conclusion

Sclerosing mesenteritis is a rare disease with vague clinical symptoms, which can be commonly mistaken for malignancy or inflammatory disease. This can lead to invasive testing and treatment, despite the majority of cases having a primarily slowly progressive course. Symptoms and disease complications often warrant medical or surgical intervention. Dual-phase CT imaging is a sensitive imaging technique for SM, although histopathology remains the most definitive diagnostic tool. There are no less invasive measures at this time to definitively diagnose SM. Given the mortality associated with disease complications and inability to accurately predict disease course, the risks and benefits of definitive diagnosis should certainly be considered. Management consists of empiric symptomatic treatment, beginning with conservative treatment if possible before progressing to surgical treatment. SM should remain on the differential in patients with a clinical picture or workup suggestive of gastrointestinal malignancy or inflammatory disease.

References

1. Daskalogiannaki M, Voloudaki A, Prassopoulos P, Magkanas E, Stefanaki K, et al. (2000) CT evaluation of mesenteric panniculitis: prevalence and associated diseases. AJR Am J Roentgenol 174: 427-431.
2. Kuhrmeier A (1985) Mesenteric lipodystrophy. Schweiz Med Wochenschr 115: 1218-1224.
3. Akram S, Pardi DS, Schaffner JA, Smyrk TC (2007) Sclerosing mesenteritis: clinical features, treatment, and outcome in ninety-two patients. Clin Gastroenterol Hepatol 5: 589-596.
4. Sharma P, Yadav S, Needham CM, Feuerstadt P (2017) Sclerosing mesenteritis: a systematic review of 192 cases. Clin J Gastroenterol 10: 103-111.

5. Tedeschi CG, Botta GC (1962) Retractile mesenteritis. N Engl J Med 17 266: 1035-1040.
6. Sivrioglu AK, Saglam M, Deveer M, Sonmez G (2013) Another reason for abdominal pain: mesenteric panniculitis. BMJ Case Rep bcr2013009305.
7. Schaffler A, Scholmerich J, Buchler C (2005) Mechanisms of disease: adipocytokines and visceral adipose tissue--emerging role in intestinal and mesenteric diseases. Nat Clin Pract Gastroenterol Hepatol 2: 103-111.
8. Tyagi S, Gupta P, Saini AS, Kaushal C, Sharma S, et al. (2011) The peroxisome proliferator-activated receptor: A family of nuclear receptors role in various diseases. J Adv Pharm Technol Res 2: 236-240.
9. Tavares Pereira JP, Romao V, Eulalio M, Jorge R, Breda F, et al. (2016) Sclerosing Mesenteritis and Disturbance of Glucose Metabolism: A New Relationship? A Case Series. Am J Case Rep 17: 55-59.
10. White B, Kong A, Chang AL (2005) Sclerosing mesenteritis. Australas Radiol 49: 185-188.
11. Kobayashi H, Notohara K, Otsuka T, Kobayashi Y, Ujita M, et al. (2018) An Autopsy Case of Mesenteric Panniculitis with Massive Pleural Effusions. Am J Case Rep 19: 13-20.
12. Horton KM, Lawler LP, Fishman EK (2003) CT findings in sclerosing mesenteritis (panniculitis): spectrum of disease. Radiographics 23: 1561-1567.
13. Perez-Fontan FJ, Soler R, Sanchez J, Iglesias P, Sanjurjo P, et al. (1986) Retractile mesenteritis involving the colon: barium enema, sonographic, and CT findings. AJR Am J Roentgenol 147: 937-940.
14. Ogden WW, Bradburn DM, Rives JD (1965) Mesenteric Panniculitis: Review of 27 Cases. Ann Surg 161: 864-875.
15. Scudiere JR, Shi C, Hruban RH, Herman JM, Fishman EK, et al. (2010) Sclerosing mesenteritis involving the pancreas: a mimicker of pancreatic cancer. Am J Surg Pathol 34: 447-453.
16. Ng SH, Wong HF, Ko SF, Tsai CC (1992) Retractile mesenteritis with colon and retroperitoneum involvement: CT findings. Gastrointest Radiol 17: 333-335.
17. Issa I, Baydoun H (2009) Mesenteric panniculitis: various presentations and treatment regimens. World J Gastroenterol 15: 3827-3830.
18. Hiridis S, Hadgigeorgiou R, Karakitsos D, Karabinis A (2008) Sclerosing mesenteritis affecting the small and the large intestine in a male patient with non-Hodgkin lymphoma: a case presentation and review of the literature. J Med Case Rep 2: 388.
19. Kipfer RE, Moertel CG, Dahlin DC (1974) Mesenteric lipodystrophy. Ann Intern Med 80: 582-588.
20. Durst AL, Freund H, Rosenmann E, Birnbaum D (1977) Mesenteric panniculitis: review of the literature and presentation of cases. Surgery 81: 203-211.
21. Kelly JK, Hwang WS (1989) Idiopathic retractile (sclerosing) mesenteritis and its differential diagnosis. Am J Surg Pathol 1989 13: 513-521.
22. DeCastro JA, Calem WS, Papadakis L (1967) Liposclerotic mesenteritis. Arch Surg 1967 94: 26-29.
23. Emory TS, Monihan JM, Carr NJ, Sobin LH (1997) Sclerosing mesenteritis, mesenteric panniculitis and mesenteric lipodystrophy: a single entity? Am J Surg Pathol 1997 21: 392-398.
24. Chen CC, Liao KS, Huang CJ (2018) Sclerosing mesenteritis. Tzu Chi Medical J 30: 122-123.
25. Mindelzun RE, Jeffrey RB, Lane MJ, Silverman PM (1996) The misty mesentery on CT: differential diagnosis. AJR Am J Roentgenol 167: 61-65.
26. Sabate JM, Torrubia S, Maideu J, Franquet T, Monill JM, et al. (1999) Sclerosing mesenteritis: imaging findings in 17 patients. AJR Am J Roentgenol 172: 625-629.
27. van Breda Vriesman AC, Schuttevaer HM, Coerkamp EG, Puylaert JB (2004) Mesenteric panniculitis: US and CT features. Eur Radiol 14: 2242-2248.
28. McLaughlin PD, Filippone A, Maher MM (2013) The "misty mesentery": mesenteric panniculitis and its mimics. AJR Am J Roentgenol 200: W116-W123.
29. Vlachos K, Archontovasilis F, Falidas E, Mathioulakis S, Konstandoudakis, et al. (2011) Sclerosing Mesenteritis: Diverse clinical presentations and dissimilar treatment options. A case series and review of the literature. Int Arch Med 4: 17.
30. Mizuno S, Wakui M, Machida Y, Hosoe N, Hisamatsu T, et al. (2017) Increased levels of prostaglandin E-major urinary metabolite (PGE-MUM) in active mesenteric panniculitis patients: A case report. Medicine 96: e9237.
31. Arai Y, Matsuura T, Matsuura M, Fujiwara M, Okayasu I, et al. (2016) Prostaglandin E-Major Urinary Metabolite as a Biomarker for Inflammation in Ulcerative Colitis: Prostaglandins Revisited. Digestion 93: 32-39.
32. Daumas A, Agostini S, Villeret J, Ah-Soune P, Emungania O, et al. (2012) Spontaneous resolution of severe, symptomatic mesocolic panniculitis: a case report. BMC Gastroenterol 12: 59.
33. Genereau T, Bellin MF, Wechsler B, Le TH, Bellanger J, et al. (1996) Demonstration of efficacy of combining corticosteroids and colchicine in two patients with idiopathic sclerosing mesenteritis. Dig Dis Sci 41: 684-688.
34. Bala A, Coderre SP, Johnson DR, Nayak V (2001) Treatment of sclerosing mesenteritis with corticosteroids and azathioprine. Can J Gastroenterol 15: 533-535.
35. Ginsburg PM, Dassopoulos T, Ehrenpreis ED (2001) Thalidomide treatment for refractory Crohn's disease: a review of the history, pharmacological mechanisms and clinical literature. Ann Med 33: 516-525.
36. Ginsburg PM, Ehrenpreis ED (2002) A pilot study of thalidomide for patients with symptomatic mesenteric panniculitis. Aliment Pharmacol Ther 16: 2115-2122.
37. Venkataramani A, Behling CA, Lyche KD (1997) Sclerosing mesenteritis: an unusual cause of abdominal pain in an HIV-positive patient. Am J Gastroenterol 92: 1059-1060.
38. Mazure R, Fernandez Marty P, Niveloni S, Pedreira S, Vazquez H (1998) Successful treatment of retractile mesenteritis with oral progesterone. Gastroenterology 114: 1313-1317.
39. Hasbahceci M, Basak F, Seker M, Canbak T, Kilic A, et al. (2012) Spontaneous remission of sclerosing mesenteritis. Turk J Gastroenterol 23: 378-380.
40. Naser M, Dabeh M (2012) Sclerosing mesenteritis: A rare case of large bowel and rectum involvement. Arab J Gastroenterol 13: 93-96.