Cutaneous Sclerosis

A Previously Undescribed Manifestation of Sclerosing Mesenteritis

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Background: Sclerosing mesenteritis is a rare disease of unknown etiology that is characterized by self-limited, nonspecific inflammation and fibrosis of the mesenteric adipose tissue. Histologic classification characterizes 3 main stages in the evolution of the fibroinflammatory process: mesenteric lipodystrophy (ML), mesenteric panniculitis (MP), and sclerosing (retractile) mesenteritis (SM).

Observations: A 68-year-old woman with biopsy-proven MP presented with multiple asymptomatic, indurated subcutaneous nodules on both arms, as well as 2 indurated plaques on her abdomen. The cutaneous changes preceded the diagnosis of SM by roughly 3 years. The arm lesions were centrally depressed with a prominent groove and a peau d’orange appearance. Biopsy findings revealed a subcutaneous process with almost total replacement of adipocytes by zones of woody sclerosis and fat necrosis identical to that observed in the mesentery. To our knowledge, this manifestation of sclerosing mesenteritis has not been reported previously.

Conclusions: Sclerosing mesenteritis has rarely been associated with extra-abdominal idiopathic fibrosclerotic disorders, but a cutaneous component of SM has never been characterized. The fact that the cutaneous lesions were histopathologically identical to the mesenteric changes and their presence prior to the recognition of intra-abdominal disease suggests that future patients with such lesions might be evaluated for this disorder leading to earlier recognition.

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Sclerosing mesenteritis (SM) is a rare, self-limited fibroinflammatory condition referred to by various clinical terms including retractile mesenteritis, liposclerotic mesenteritis, mesenteric Pfeifer-Weber-Christian disease (PWCD), xanthogranulomatous mesenteritis, mesenteric lipogranuloma, and systemic nodular panniculitis. The complete histologic spectrum includes 3 stages with main features of extensive fat necrosis, nonspecific chronic inflammation, and subsequent collagen deposition with florid sclerosis. The predominance of each individual histologic feature corresponds to a diagnosis of mesenteric lipodystrophy (ML), mesenteric panniculitis (MP), or SM, respectively. In 1924, Jura first described a pathologic process characterized by mesenteric fibrosis, and the requisite term sclerosing (and retractile) mesenteritis was born. Numerous presumably synonymous clinical names have been introduced subsequently. To date, neither the pathogenesis nor the etiology are well understood. Sclerosing mesenteritis seems to be most common in the fifth or sixth decade, with the reported average age of diagnosis occurring at ages 60 to 63 years. Several retrospective studies have observed the disease 2 to 3 times as frequently in men. The most common site of disease involvement is the small bowel mesentery. Rare involvement of the large bowel may occur in the area of the sigmoid mesocolon. Children are typically not affected by SM, perhaps because they have a lesser amount of mesenteric adipose tissue.

No precise causal factors have been elucidated for the possible induction of this rare inflammatory condition. Postulated etiologies are commonly based on a parallel association with mesenteric disease and include previous trauma or abdominal surgery, bacterial infection, vascular factors including ischemia, autoimmune disease, and other idiopathic inflammatory conditions. Sclerosing mesenteritis has rarely been associated with other idiopathic fibrosclerotic conditions, including idiopathic retroperitoneal fibrosis, idiopathic orbital pseudotumor, mediastinal fibrosis, Reidel’s thyroiditis, sclerosing pancreatitis, and sclerosing cholangitis. The coexistence of these observations has led to a hypothesis that SM might be a subset of idiopathic fibrosclerotic disorders. The term multifocal fibrosclerosis has typically
been reserved for instances in which 2 separate and distinct fibrosclerotic disorders were diagnosed in the same patient. Furthermore, several additional systemic diseases in association with SM were analyzed by Akram et al. Rheumatologic diseases, such as Sjogren syndrome, ankylosing spondylitis, and rheumatoid arthritis, were each concurrently observed in approximately 10% of the 92 SM cases. It is important to note that no single dermatologic disease or cutaneous manifestation has been previously reported in patients with SM. Although several malignant diseases (lymphoma, myeloma, breast cancer, lung cancer, melanoma, and colon cancer, renal cell carcinoma, Hodgkin disease, carcinoid tumor, and thoracic mesothelioma) have been reported concurrently in patients with SM, the possible mechanism, the specific type of neoplasia, and the definitive causal relationship remain to be elucidated.

REPORT OF A CASE

A 68-year-old woman presented to our clinic 4 months after exploratory laparoscopy for an incidental retroperitoneal mass visualized on abdominal computed tomographic (CT) scan. Clinical symptoms prompting the CT scan included an unintentional 9.5-kg weight loss over 6 to 8 weeks with additional symptoms of early satiety, intermittent dysphagia, and vomiting. On surgical exploration, the mass was noted to emanate in the region of the superior mesenteric artery within the root of duodenal mesentery.

Biopsy findings of the mesenteric mass revealed diffuse sclerosis of mesenteric adipose tissue with foci of fat necrosis, lipophages, and patchy chronic inflammation. Macrophage antigen CD68 was diffusely immunopositive, confirming a prominent histiocytic component. Cytokeratins AE1/AE3 and S-100 protein were essentially immunonegative for disease. A second consulting surgical pathologist concurred with the histologic features, and the subsequent diagnosis of MP was established.

The patient’s medical history was remarkable for coronary artery disease, hypertension, dyslipidemia, gastrointestinal reflux disease, osteoarthritis, and nephrolithiasis. Her surgical history included the most recent exploratory laparoscopy, 2-vessel coronary artery bypass graft surgery 15 years prior to presentation, total abdominal hysterectomy 15 years prior, and 3 separate breast biopsies in which the findings were negative for malignant disease. Her family history was negative for cutaneous familial disease or similar symptoms. The patient was a retired factory worker and denied any environmental or job-related toxin exposure. She had stopped smoking 9 years prior to presentation and denied illegal substance abuse. There was no history of L-tryptophan ingestion.

Laboratory findings included a mildly elevated erythrocyte sedimentation rate of 27 mm/h, a mild anemia with hemoglobin level of 10.5 g/dL (reference range, 12.0-16.2 g/dL [includes normal range for males, 13.2-16.2 g/dL, and females, 12.0-15.2 g/dL]), and a positive test result for antinuclear antibody with no titer provided. (To convert hemoglobin to grams per liter, multiply by 10.0.) Eosinophilia was not present. Findings for recent complete metabolic profile and liver function tests were within reference range. Her C-reactive protein level was within reference range. Serologic testing for anti-Ro (SS-A), anti-La (SS-B), anti–Scl-70, and anti–double-stranded DNA antibodies was negative for disease. Imaging findings from chest, abdomen, and pelvic CT scans and upper and lower endoscopies were unremarkable.

At the time of dermatologic evaluation, the patient reported a 3-year history of asymptomatic nodules that gradually increased in size. Two of the 4 upper extremity lesions had arisen on the right lateral upper arm approximately 3 years previously, while the remaining 2 lesions developed 1 year prior to presentation on the left lateral upper arm. In addition, 2 well-demarcated plaques that had arisen 6 months prior to presentation were identified on the lower right abdominal wall.

Physical examination revealed flesh-colored, indurated subcutaneous nodules localized to the upper arms bilaterally. The largest lesion located on the right upper lateral arm measured 2 × 3 cm (Figure 1). There was no erythema, warmth, tenderness, or fluctuance, and the skin surface was intact. The lesions were irregular in shape, with firm, bound-down borders and a central puckered fibrous depression that exhibited an edge of lateral retraction. The arm lesions also exhibited a prominent

Figure 1. A 68-year-old woman with sclerosing mesenteritis. A, Subcutaneous nodule on the right posterolateral arm exhibits a central fibrous depression with overlying peau d’orange surface changes and lateral retraction. B, Two well-circumscribed plaques on the right lower abdomen with sclerodermoid induration and hyperpigmentation along the borders.
The clinical differential diagnosis of SM is often complex, and the combined rarity and wide spectrum of disease presentation increases the propensity for its misdiagnosis. Sclerosing mesenteritis must be differentiated from inflammatory pseudotumor, mesenteric fibromatosis, idiopathic retroperitoneal fibrosis, sclerosing fibroma, sclerosing malignant lymphoma, liposarcoma, lymphosarcoma, malignant primary mesenteric tumor, sclerosing peritonitis, reactive fibrosis due to an abscess, Whipple disease, and metastatic neoplasia. In most cases, specific histopathologic features and immunohistochemical stains usually contribute to the precise pathologic diagnosis. Dual-phase CT combined with biopsy and subsequent clinicopathologic correlation aids in making the definitive clinical diagnosis.

A retrospective study performed by the Armed Forces Institute of Pathology, examined cases of SM, MP, or ML for common histologic and clinical presentations. Three separate histologic components were evaluated and confirmed with the following trends: ML characterized by fat necrosis, MP typified by chronic subcutaneous inflammation, and SM with prominent fibrotic changes. With sequential histologic progression of ML to MP, SM represents the most mature inflammatory stage with predominance of sclerotic connective tissue compressing the bowel lumen. In the surrounding background of sclerosis, there is usually extensive fat necrosis and a modest inflammatory infiltrate. However, a mixed histopathologic picture may be identified in some cases, and clear separation into distinct stages remains difficult and provides no beneficial therapeutic correlation for the patient. The relationship between the histologic stage and disease severity remains unclear. Some authors report a more severe clinical progression or duration of disease associated with a histologic predominance of marked fibrosis over chronic inflammation or panniculitis.

Although SM has rarely been reported in association with other idiopathic fibrosclerotic disorders, to our knowledge the presence of cutaneous involvement has never been previously described. In contrast, the disease entity of PWCD or idiopathic lobular panniculitis has been well described. In contrast, the disease entity of PWCD or idiopathic lobular panniculitis has been well described. In a unique review of 30 cases of PWCD by White and Winkelmann, the initial diagnosis of PWCD or idiopathic lobular panniculitis has been well characterized by both internal and cutaneous disease progression in a relapsing and remitting fashion. Like previous authors, we refer to PWCD as a part of the category of disorders erroneously considered as a specific variant of panniculitis. In a unique review of 30 cases of PWCD by White and Winkelmann, the initial diagnosis of PWCD was clinically suspected in only one-third of the patients. Further microscopic study of all cases yielded features more consistent with a specific histologic diagnosis, such as acute factitial traumatic panniculitis, erythema nodosum variant, lymphoma, or cytophagic panniculitis. Regardless of the clinicopathologic diagnosis, none of these cases showed clinical or histologic similarity to the characteristic features of SM.

Considerations in the cutaneous histopathologic differential diagnosis include fat necrosis associated with pancreatitis, lobular idiopathic panniculitis, lupus panniculitis, variants of deep morpha, postirradiation pseudosclerodermatous panniculitis, factitial panniculitis syn-
dromes (ie, factitial paraffinoma), a late-stage fibrotic variant of erythema nodosum, chronic Lyme disease, calciphylactic panniculitis, involutional lipoatrophy, traumatic panniculitis, and panniculitis due to lymphoproliferative disorders.13,10,22

The insidious onset of multiple asymptomatic, nodular skin lesions combined with distinctive histologic features of SM, favors a rare, extra-abdominal manifestation of SM. Moreover, the unique cutaneous predominance of subcutaneous woody sclerosis with fat necrosis mitigates against a diagnosis of any one of the previously recognized cutaneous panniculitides. The absence of plasma cells in the inflammatory infiltrate distinguishes this case from other sclerosing disorders in masquerade, such as post-irradiation pseudosclerodermatous panniculitis, immunoglobulin G4–related sclerosing disorders, chronic Lyme disease, and variants of deep morphoe.

Clinically, the skin lesions and the intra-abdominal process exhibited chronological and histologic overlap solidifying our diagnosis of cutaneous-sclerosing (retractile) mesenteritis. Our patient had undergone a total abdominal hysterectomy 15 years prior to presentation, which may have increased the propensity for, or triggered, the development of the fibroinflammatory process. The precise causal role of abdominal surgery and other associated factors in the pathogenesis of SM will likely require a higher volume of case observations and necessitate further research. As for reported associations of SM with malignant disease, in particular lymphoproliferative disorders, it remains unclear whether there will be a proven role for Curth’s postulates in cutaneous SM.15,23 At present, the precise relationship between the skin disease, the bowel disease, and the possible risk of internal malignant disease remains largely unknown.15,24,25

Because it is rare, therapeutic recommendations for SM are based on case reports and small case series. Medical treatment for refractory SM with tamoxifen and prednisone has been reported to have variable success.8 Alternatively, in cases with persistent obstructive symptoms or perforation, surgical correction is indicated.

In sum, we observed asymptomatic subcutaneous nodules in a patient with known fibroinflammatory mesenteric disease. The microscopic appearance was suggestive of a mature histologic stage of SM with features of prominent woody sclerosis and an associated outer-rim of histiocytes most consistent with cutaneous SM. Initially diagnosed as MP, the mesenteric biopsy was further reviewed and, because of the prominent woody sclerosis, is better classified as SM.

Our case suggests an unusual yet specific panniculitis that may be best termed cutaneous sclerosis of SM. Because our patient is asymptomatic, treatment has not been recommended. This case highlights a novel cutaneous progression of visceral disease, and dermatologists should consider cutaneous sclerosis as a marker of SM in the concurrent setting of SM and a rare cutaneous sclerosing panniculitis.

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Author Contributions: All authors had full access to all the data in this case series and take full responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Hinds, Bernardi, and Callen. Acquisition of data: Hinds, Bahrami, Bernardi, and Callen. Analysis and interpretation of data: Bahrami and Callen. Drafting of the manuscript: Hinds, Bernardi, and Callen. Critical revision of the manuscript for important intellectual content: Bahrami and Callen. Administrative, technical, and material support: Callen. Study supervision: Bahrami, Bernardi, and Callen.

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REFERENCES


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### Notable Notes

**Rin Tin Skin**

How could I NOT do this creature (Figure)? First and foremost, I am a dermatologist and in my field appearances are everything! Second, I am the son of a packaging designer, so I was raised to pay attention not just to the contents but to the container as well. Finally, the antiquarian in me loves these archaic little tins that were made for various skin creams, ointments, and powders. I like the fact that they are metal and not plastic; I like the graphics (that’s my Mom’s side—she was a graphic artist); and I particularly like the claims of which each product boasted (that’s my own humility showing). I call this creature *Rin Tin Skin,* and I think it proves the old adage, “It’s all in the packaging.”

Ears: **Wonder Salve** for burns, sores, cuts, eczema, piles, rheumatism, carbuncles, ulcers, and wounds; and **Scherzer’s Old Reliable Salve** for poisons and healing wounds.

Head: **Porter’s Liniment Salve** for bruises, rough and cracked skin due to inclement weather, insect bites, sunburn, and minor local irritations in humans, and for collar and saddle galls, bruises, and sore teats in livestock. Eyes: **Alpern Nail Crème** aids in grooming splitting and peeling nails, dry and ragged cuticles, and hangnails. Nose: **Euthymol Violet Talcum Powder.** Mouth: **Cuticura Ointment** is a mildly antiseptic emollient for skin and scalp. Neck: **Eye-Lash-Ine** is an eyelash remedy. Body: **J.C. Hutzell’s Ovelmo Treatment.** Tail: **United Supply Company’s Celebrated Foot Comfort** is a healing powder for sore and tired feet and for relieving corns, bunions, chilblains, etc; it will also relieve the soreness of corns and bunions and is a certain cure for aching, tired, and perspiring feet. Legs: **Dr Pierce’s Salve** is a cleansing dressing for superficial wounds, cuts, and scratches; and **Dill’s Healing Salve** is an antiseptic preparation for burns, cuts, sores, skin abrasions, and chapped and cracked skin as well as a local application to relieve itching piles and to allay the itching of eczema.

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