Acquired Cutaneous Pretibial Mucinosis in an Overweight Patient with Chronic Venous Insufficiency: A Case Report and Literature Review

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ABSTRACT:

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Localized acquired cutaneous pretibial mucinosis is characterized by abnormal deposition of mucin in the dermis, which can be either a primary or secondary lesion associated with systemic disease, especially hyperthyroidism in Graves' disease. Stasis mucinosis and obesity-associated lymphedematous mucinosis have been described as new and uncommon conditions. That are different entities of pretibial mucinosis without altered thyroid function. These two conditions are similar and have been described as associated with chronic venous insufficiency, increased body mass index, and chronic lymphedema. We presented a

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case of chronic erythematous and edematous plaques with vesicles on both shins in an overweight man with chronic venous insufficiency. Differential diagnosis among cellulitis-mimic conditions with associated vesiculobullous eruption was detailed. The final diagnosis was supported by clinicopathological correlation.
Key words: Stasis mucinosis, pretibial myxedema, obesity-associated lymphedematous mucinosis, cutaneous mucinosis

Introduction

Pretibial myxedema describes localized dermal mucinosis associated with Graves' disease and other thyroid abnormalities[1]. However, pretibial mucinosis may occur in patients with altered thyroid function and distinct clinical diseases. Stasis mucinosis and obesity-associated lymphedematous mucinosis contextually are described as being similar. Localized dermal mucinosis is associated with high body mass index, chronic lymphedema, and venous insufficiency[2,3].

In 1993, Somach et al. evaluated the difference in histological characteristics in twelve cases of pretibial mucinosis with Graves' disease and six cases of pretibial mucinosis without thyroid disease. Localization of mucin in the upper third of the dermis and the presence of nodular angioplasia helped distinguish pretibial mucinosis without thyroid disease from pretibial mucinosis with Graves' disease[4]. Nevertheless, the clinical difference between these two entities has not been elucidated. We report a case of uncommon manifestation of stasis mucinosis with vesiculobullous lesions in an elderly overweight patient with subtle histological evidence of stasis change on the legs.



Figure 1 Bilateral, nontender, erythematous and edematous plaques with tense vesicles and erosions on both shins

Case presentation

An 83-year-old male, displayed painless, progressive, bilateral lower extremity edema for one and a half years. Examination revealed indurated erythematous edematous plaques and a few blisters on both shins. He denied claudication, fever, or a history of trauma. His medical conditions included being overweight (body mass index (BMI) 25 kg/m^2), poorly controlled type 2 diabetes mellitus, hypertension, cerebrovascular disease, stage 4 chronic kidney disease, and colonic cancer post right hemicolectomy. A thyroid function test was performed and was within the reference range. His indirect immunofluorescent result for autoimmune vesiculobullous diseases was negative. The patient was diagnosed with diabetic bullae and treated with potent topical corticosteroid without any clinical improvement. Physical examination revealed hardened, ill-defined erythematous edematous plaques, tense vesicles, and erosion on shins (Figure 1). Pitting edema and peau d'orange appearance on the shins were observed. Peripheral pulses were symmetrically intact. A 4-mm punch biopsy was performed at the vesicle on the left shin.

Skin biopsy indicated diffuse dermal edema with increased spindled and stellate fibroblasts. A sub-epidermal vesicle with effacement of the epithelial roof and angioplasia with tortuous vertically running capillary vessels were observed. There was no inflammatory infiltrate in the vesicle or dermis (Figure 2A-2B). Colloidal iron stain showed a slightly increased dermal mucin in the papillary and upper reticular dermis (Figure 2C). The zone of normal collagen (Grenz) between the overlying epidermis and the dermal mucin deposit was not identified. A scattered hemosiderin deposit in the dermis was highlighted by Perls Prussian iron stain (Figure 2D). Direct immunofluorescence (DIF) was negative. Additionally, the venous duplex ultrasonography of both lower extremities revealed the absence of deep vein thrombosis, deep venous reflux, or reflux of sapheno-popliteal junction and sapheno-femoral junction. The patient was documented for mild peripheral arterial disease of the left leg according to the abnormal ankle-brachial index (ABI) of 0.85 (normal range between 1.0-1.4) without evidence of chronic venous insufficiency from the duplex ultrasound imaging studies.

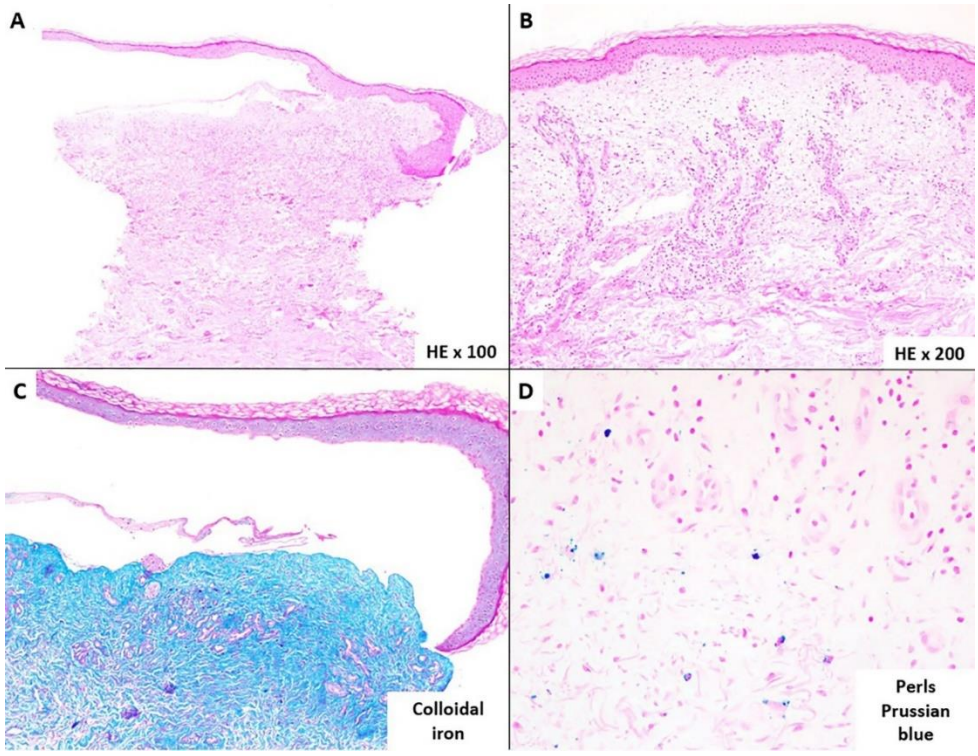


Figure2 Lesional skin biopsy for the left shin; (A and B) Effacement of the epidermis with diffuse dermal edema and vertical dermal angioplasia, (C) Mucin deposit in the papillary and upper reticular dermis (Colloidal iron stain X200), (D) Hemosiderin deposit in the dermis (Perls Prussian blue iron stain X400)

Discussion

Stasis mucinosis (SM) and obesity-associated lymphedematous mucinosis (OALM) are emerging conditions in adults with cutaneous mucinosis, including clinical mimicry of pretibial mucinosis in Graves' disease and cellulitis-like conditions[2]. These findings were established by Somach et al. in 1993, showing clinicopathological similarity. They evaluated clinicopathological features of pretibial mucin deposit in six patients with euthyroid status. The patients had previously been diagnosed with pretibial myxedema, elephantiasis verrucosa nostra, and stasis dermatitis. Interestingly, the common association documented in all six patients was obesity[4]. Thanks to research establishing more facts on clinical manifestations, histological features, and pathogenesis. More cases of euthyroid pretibial mucinosis associated with chronic venous insufficiency, lymphedema, and trauma have been increasingly determined[2-3,5-16]. We have conducted a literature review of twenty-seven cases of SM and OALM with a clinical summary in Table 1.

Table 1 A literature review of stasis mucinosis and obesity-associated lymphedematous mucinosis

Authors	Cases	Age/sex	Clinical features	Duration from the onset	Clinical diagnosis	Comorbidities	Treatment	Clinical course and follow up
Somach et al. (1993)[4]	6	38 M	Edema, flesh-colored nodules	N/A	Elephantiasis verrucosa nostra	Obesity	N/A	N/A
		77 M	Eczematous plaques and follicular papules		Stasis dermatitis	Obesity, atherosclerosis, HT		
		66 M	Waxy nodules and plaques		Not specified	Obesity, post-RT lymphedema, HT, T2DM		
		49 M	Red pretibial plaques		Pretibial myxedema	Obesity, T2DM, history of cellulitis		
		70 M	Woody nodular edema		Pretibial myxedema	Obesity, HT, CVD		
		80 M	Massive lower extremities edema		Elephantiasis verrucosa nostra	Obesity, prostate cancer, atherosclerosis		
Kim et al. (2002)[5]	1	44 F	Recurrent painful erythematous swollen patch on right shin	9 months	Pretibial mucinosis	CVI, previous trauma at the right leg	N/A	N/A
Tokuda et al. (2006)[6]	3	76 M	Swelling and erythema of both legs with vesicles	4 years	OALM	Obesity	N/A	N/A
		60 F	Pitting edema of both legs with waxy papules on shins	2 years	OALM	Obesity	Pressure bandage	Improvement of waxy papules
		36 M	Pitting edema both legs, woody plaque (scleroderma-like lesion) on shins	6 months	OALM	Obesity	Topical corticosteroids	N/A
Rongioletti et al. (2009)[7]	5	69 M	Legs edema and erythema, skin-colored papules, feet spared	4 years	OALM	Obesity, hyperglycemia, hyperuricemia	Diet control	N/A
		64 F	Pitting edema both legs with skin-colored papules and vesicles, feet spared	4 years	OALM	Obesity, hyperglycemia	Diet control	Improvement after weight reduction
		47 F	Yellow-red papules on shins	Several years	OALM	Obesity	N/A	N/A
		51 F	Papules on shins and thighs	2 years	OALM	Obesity, T2DM	N/A	N/A
		69 F	Papules, nodules and vesicles on edematous legs	3 years	OALM	Obesity	Diet control	Improvement after weight reduction
Castineiras et al. (2009)[8]	1	72 F	Erythematous swollen patches and nodules on both shins	N/A	Pretibial mucinosis	CVI, T2DM, HT, CVD	CO2 laser treatment	Elimination of nodular lesions
Pugashetti et al. (2010)[9]	2	73 M	Persistent plaque of the left lower leg	9 years	Dermal mucinosis	CVI	Intralesional and topical corticosteroids, laser therapy	No improvement
		61 M	Tender, violaceous plaque in the left leg	5 years	Dermal mucinosis	CVI, CVD	N/A	N/A
Mir et al. (2011)[10]	1	46 M	Edematous plaques on both shins, peau d'orange appearance, pruritus	6 months	Pretibial mucinosis	T2DM, psoriasis	Topical corticosteroid with occlusion	3-month follow up with improvement of pruritus and the lesion
Brauns et al. (2013)[11]	1	78 F	Slow growing painless waxy nodules on both legs	3 years	OALM	Obesity, chronic lymphedema (post-RT), HT, T2DM, CVD	Topical corticosteroid	No improvement
Woolf et al. (2014)[12]	1	71 M	Papules on shins, a plaque of right calf	3 years	OALM	Obesity, T2DM, epilepsy, COPD	Weight reduction and compressive therapy	Minimal improvement
Karadag et al. (2014)[13]	1	71 F	Swelling, erythema, and discoloration on both legs	1 year	OALM	Obesity	Pentoxyphyllin 400 mg/day, intralesional and topical potent corticosteroids, weight reduction	No improvement
Milman et al. (2016)[14]	1	70 F	Erythematous waxy papules and plaques on both shins	10 years	Pretibial mucinosis	Obesity, stroke, CVI, lymphatic insufficiency	N/A	N/A

Table 1 A literature review of stasis mucinosis and obesity-associated lymphedematous mucinosis

Authors	Cases	Age/sex	Clinical features	Duration from the onset	Clinical diagnosis	Comorbidities	Treatment	Clinical course and follow up
Ferreli et al. (2018)[15]	2	72 F	Swelling and erythema on both legs	1 year	OALM	Obesity, CVD, hypercholesterolemia, HT, T2DM	N/A	N/A
		76 F	Asymptomatic slow-growing papules on both legs with pitting edema	N/A	OALM	Obesity, T2DM, HT	Diet control, compressive therapy	Improvement of the lesion and edema
Hirt et al. (2019)[16]	1	60 M	Severe legs edema and varicosities, diffuse indurated scaly red plaques with verrucous surface	N/A	Stasis mucinosis	Obesity, CVI, HT, hyperlipidemia, cerebral palsy, lymphedema, cellulitis	Antibiotics treatment for cellulitis	Improvement of cellulitis
Tantrapornpong et al. (Present report)	1	83 M	Erythematous edematous plaques with vesicles on both shins	1.5 years	Stasis mucinosis	Overweight, T2DM, CKD, HT, colonic cancer, stroke	Topical corticosteroids and compressive therapy	Slight improvement, no new vesicles after 2-month follow up

N/A, No data available; OALM, obesity-associated lymphedematous mucinosis; CVI, chronic venous insufficiency; HT, hypertension; post-RT, post radiation; T2DM, Type 2 diabetes mellitus; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease

The pathogenesis of these conditions is associated with lymphatic and venous stasis in obesity which leads to local tissue hypoxemia and subsequent production of dermal mucin as the response of dermal fibroblasts to the hypoxic stage[2,3]. Furthermore, impaired lymphatic drainage and venous insufficiency worsen local tissue edema. The worsening effect is a result of interstitial deposits of proteinaceous plasma substances. The substances include albumin, fibrinogen, and coagulation factors. These substances may superimpose the defect of local oxygen transfer effecting, the increased production of glycosaminoglycans by fibroblasts[2,3,9].

Clinical manifestations of SM and OALM include mostly bilateral skin-colored to erythematous plaques and nodules on the pretibial area. They are typically slow-growing and asymptomatic. Leg swelling, erythema, lymphedema, and varicosities are observed with sparing of thighs, feet, and ankles[14]. Vesicles or bullae on top of the lesions concomitant with marked lymphedema are occasionally reported[9,16].

Histopathologic changes in SM and OALM provide clues to distinguish pretibial myxedema of Grave's disease. Clues can be summarized as:

(1) overlying atrophic epidermis with flattened rete ridges.

(2) zone of normal collagen (Grenz zone) separated the epidermis and dermal deposit of mucin.

(3) superficially located mucin deposits in the papillary dermis and upper reticular dermis and/or perivascular and periadnexal deposits of mucin.

(4) dermal angioplasia with vertically running vessels showing thickened vessel walls in the background of dermal edema/pallor.

(5) hemosiderin deposits in the dermis as compared to the histologic findings in pretibial

myxedema, which show epidermal hyperplasia, diffuse pandermal mucin deposits without Grenz zone, and no evidence of stasis change such as dermal angioplasia or hemosiderin deposit[2,3,6,15].

Differential diagnosis of SM and OALM is pretibial myxedema of autoimmune thyroid diseases. Diagnosis becomes critical with Graves' disease and the onset of hyperthyroidism with thyroid ophthalmopathy. However, differential diagnoses are crucial due to other causes of chronic lower leg edema and pretibial lesions. Patients may suffer from recurrent cellulitis, lymphedema, necrobiosis lipoidica, drug-induced peripheral edema, and underlying systemic diseases. Systemic diseases include congestive heart failure, cirrhosis, and nephrotic syndrome[2,3,4,6,17]. Therefore, careful history taking, complete physical examination, and investigations, especially lesional skin biopsy with histopathologic evaluation and thyroid function including tests, are favorable to confirm the diagnosis of SM and OALM. In general, SM and OALM have a gradual and benign clinical course, which leads to the disfigurement of the lower extremities and affects cosmetic concerns. Weight reduction in combination with pressure compression of the legs to improve underlying venous insufficiency and lymphostasis is the goal of management[2, 3]. Consultation with an expert in chronic venous insufficiency is beneficial for the patient with evidence of venous reflux, and patients may need to consider surgical procedures[2,9,15].

For the present case, although there was no evidence of venous reflux from the ultrasound imaging study, the presence of dispersed hemosiderin deposit in the tissue biopsy supports the evidence of stasis change in the lower extremities in this patient. Therefore, we considered stasis mucinosis a possibility and compatible diagnosis in our patient. The treatment was compression therapy with a 30-40 mmHg compression gradient. Lesions were covered with topical emollients and 0.1% triamcinolone acetonide cream. The patient was advised to elevate their legs and reduce weight. We also consulted with the geriatrician and nutritionist for continuing care of adjusting the medications for his underlying disease and nutritional guide. After treatment, the erythema and edema gradually decreased, and there was no new vesicular formation two months before the follow-up visit.

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