Macular lymphocytic arteritis: Clinical-pathologic correlation of a rare vasculitis

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INTRODUCTION

Macular lymphocytic arteritis (MLA) and *lymphocytic thrombophilic arteritis* (LTA) are terms used to describe an indolent, cutaneous medium-vessel vasculitis that has been suggested to follow a benign but persistent disease course.[1] Pathologically, this condition is characterized by medium-vessel vasculitis composed primarily of lymphocytes and notably lacking neutrophils, thus distinguishing it from cutaneous polyarteritis nodosa.[2,3] Clinically, published cases have typically presented with macules, papules, livedoid patches, and ulcerations on the lower extremities, and to date, no cases have described progression to systemic vasculitis.[4,5]

Our understanding of the clinical presentation, pathophysiology, and treatment of MLA/LTA is lacking, which is largely attributable to the rarity of the condition and the unfamiliarity of providers. When performed, histology alone may result in a diagnosis of polyarteritis nodosa or other medium-vessel vasculitis. The pathology likely causes confusion, as the benign clinical presentation appears incongruent with the largely obliterative vasculitis seen under the microscope.[3] In this vein, treatments have ranged from systemic immunosuppression to supportive care mirroring the dichotomous clinical and pathologic findings. Herein, we describe 4 additional cases of this rare vasculitis (Table I) and discuss the clinical-pathologic correlation. We also present the second known case of MLA/LTA treated with dapsone and the first case, to our knowledge, treated with narrow-band ultraviolet B light.

Abbreviations used:

LTA:	lymphocytic thrombophilic arteritis
MLA:	macular lymphocytic arteritis
NBUVB:	narrow-band ultraviolet B

CASE REPORTS

Case 1

A 34-year-old African-American woman presented for asymptomatic, hyperpigmented, reticulated patches on the lower extremities for 1 years' duration (Fig 1, *A*). Punch biopsy found perivascular lymphocytic infiltrate of medium-sized vessels at the dermal-subcuticular junction with luminal narrowing (Fig 2, *A*). Laboratory evaluation was negative or unremarkable (Table I). The diagnosis of MLA/LTA was made, and the patient was started on doxycycline, 100 mg twice daily for 1 month, and triamcinolone cream, twice daily for 5 months, without improvement. The patient was transitioned to narrow-band ultraviolet B (NBUVB) light with improvement in pigmentation noted at 3-month follow-up.

Case 2

A 60-year-old healthy white woman presented for evaluation of asymptomatic, pink, macules and

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Table I. Summary of newly described patients with MLA/LTA

Case	Age (y)	Sex	Ethnicity	Symptoms	Duration (y)	Distribution	Morphology	Laboratory evaluation	Treatments	Clinical course
1	34	F	African-American	None	1	LE	Hyperpigmented, reticulated macules and patches	CBC, CMP, UA, ANA, Anti-Ro/La, cryoglobulins, lupus anti-coagulants, protein C/S, Factor V—all negative or normal	NBUVB	Modest improvement in pigmentation
2	60	F	White	None	1	LE, UE	Predominantly pink macules and thin papules	CBC, CMP, ESR, CRP—all normal	None	Waxes and wanes, but persistent
3	44	F	Nigerian	Minor pruritis	4	LE	Hyperpigmented macules and patches	CBC, CMP, ESR, SPEP, ANA, RF, cryoglobulins, hepatitis panel, HIV—all negative or normal	None	Persistent
4	60	F	White	None	4	LE, UE	Pink to purple reticulated macules and patches	CBC, CMP, UA, ESR, lupus anticoagulants, ANA, anti-Ro/La, RF, anti-ccp, anti-RNP, anti-Sm, SPEP/UPEP, hepatitis panel—all negative or normal	Dapsone, 50 mg daily	Improved overall

ANA, Antinuclear antibody; *CBC*, complete blood count; *ccp*, cyclic citrullinated peptide; *CMP*, complete metabolic panel; *CRP*, C-reactive protein; *ESR*, erythrocyte sedimentation rate; *LE*, lower extremity; *NBUVB*, narrow-band ultraviolet B; *RF*, rheuatoid factor; *RNP*, ribonucleoprotein; *Sm*, Smith; *SPEP*, serum protein electrophoresis; *UA*, urinalysis; *UE*, upper extremity; *UPEP*, urine protein electropheresis.

papules on the lower extremities that spread cephalad (Fig 1, *B*). Punch biopsies initially read as polyarteritis nodosa. Repeat biopsies found a medium vessel vasculitis of mostly lymphocytes (Fig 2, *B*). The patient denied any systemic symptoms, and systemic evaluation was unremarkable or negative (Table I). Subsequent re-evaluation of the patient's clinical and pathologic data led to a revised diagnosis of MLA. The patient noted no changes in her symptoms on 6-month follow-up.

Case 3

A 44-year-old Nigerian woman with a history of type II diabetes mellitus presented with asymptomatic, brown macules and small patches on the lower extremities (Fig 1, *C*). The lesions were initially pruritic but became asymptomatic. Initial treatment with clobetasol 0.05% ointment was ineffective and stopped because of hypopigmentation. Pathologic testing found a medium vessel lymphocytic vasculitis (Fig 2, *C*). Laboratory evaluation was unremarkable (Table I). MLA/LTA was diagnosed, and the patient was treated conservatively. After 4 months of follow-up, the patient's condition remains unchanged.

Case 4

A 60-year-old white woman with a history of coronary vasospasm presented with asymptomatic, erythematous reticulated macules and patches on the lower extremities of several years' duration (Fig 1, *D*). Histology testing found a medium vessel vasculitis with a diagnosis of polyarteritis nodosa. Serologic evaluation was unremarkable or negative (Table I). Treatment with oral steroids was ineffective. Results of a subsequent biopsy suggested thrombophlebitis. She was treated with clopidogrel 75 mg daily without effect, and the lesions progressed to her upper extremities. A repeat biopsy found evidence of a small- to medium-vessel vasculitis consistent with MLA/LTA (Fig 2, *D*). The patient was started on dapsone, 100 mg daily, with improvement in the appearance of her skin lesions, and she was titrated to a maintenance dose of 50 mg daily. The patient has been followed up for 2 years, and her disease is improved on her current treatment with an occasional new lesion.

DISCUSSION

MLA/LTA is a rare lymphocytic vasculitis that affects the skin. We describe 4 additional cases, which are clinically and histologically consistent with prior reports of MLA/LTA. Because the patients in all 4 of our cases were women, our series supports previous reports showing that women are primarily affected.[6] Other vasculitides have been reported to

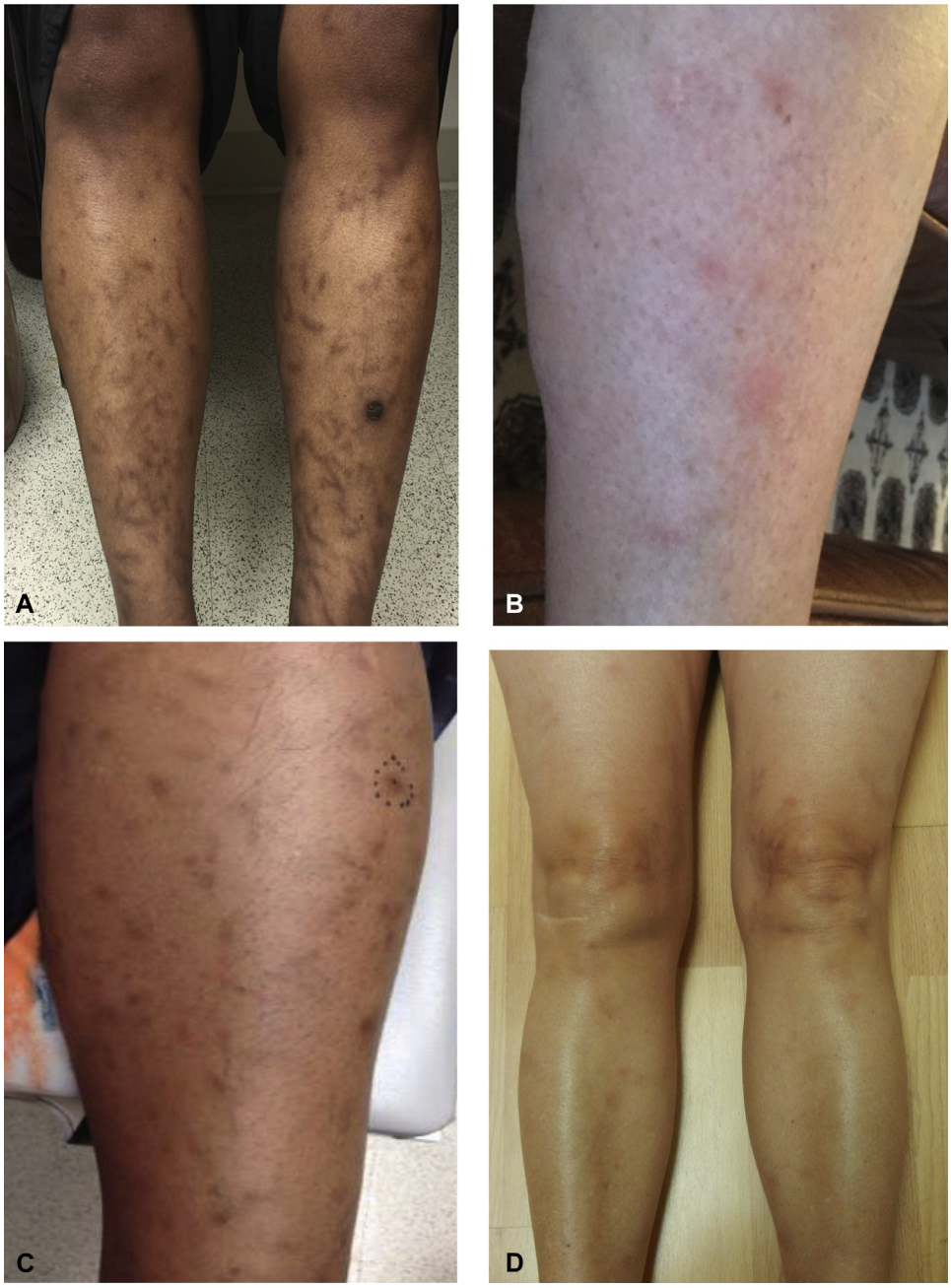

Fig 1. Macular lymphocytic arteritis. Case clinical presentation. **A**, Coalescing macules into patches in black skin take on a purple-brown color. **B**, Ill-defined, erythematous, blanchable macules on the legs, extending to the thigh. **C**, Discrete lesions may be slightly indurated and papular. **D**, Macules can be subtle and almost imperceptible.

have a 1:1 male/female ratio, suggesting that MLA/LTA may have a gender predilection.[7,8] Similarly, prior cases have described a preponderance of North African women. Our cases support this finding with 2 of 4 cases representing white patients along with 1 Nigerian woman and another of African-American decent.[6] Interestingly, other vasculitides are reported to have a higher incidence among white patients.[7,8] Speculation on racial disparities or differences in disease presentation requires further investigation.

Our cases presented with asymptomatic macules, papules, and larger hyperpigmented patches. Previous reports suggest that livedoid patches are common.[9] One of our patients has been followed up with for at least 2 years, and there has been no reported progression to systemic disease. The restriction of MLA/LTA to the skin is a defining

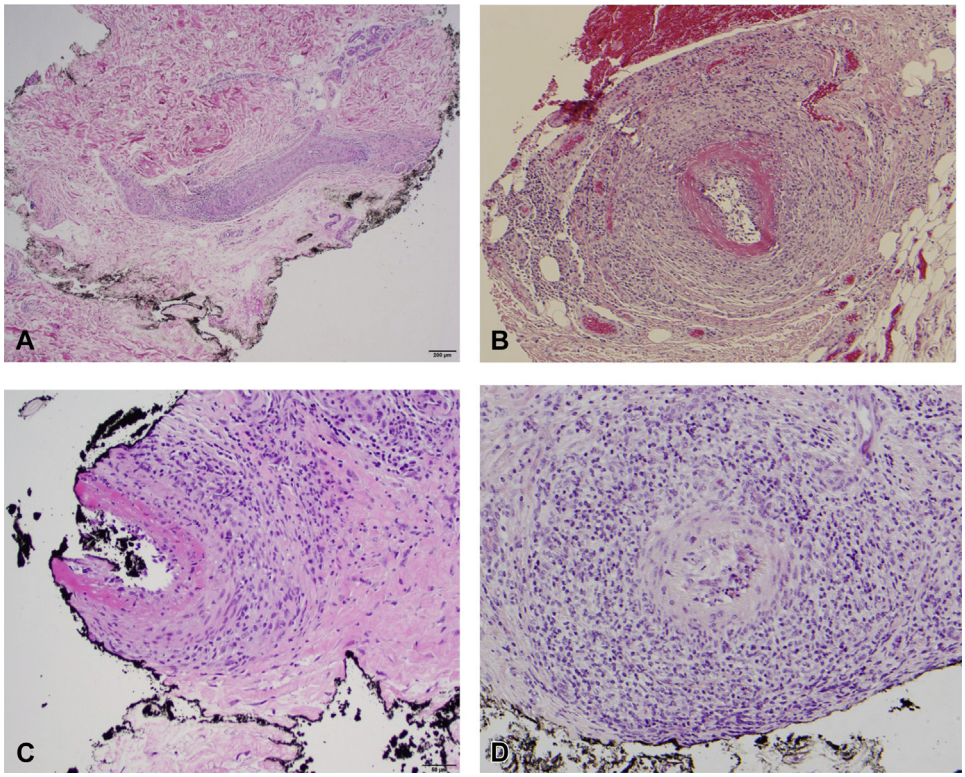

Fig 2. Macular lymphocytic arteritis (MLA). Pathologic correlation from case presentations. **A**, Evaluation of a vessel in longitudinal cross section shows the primarily lymphocytic inflammatory infiltrate extending along the length of the vessel with focal areas of nuclear debris. **B**, Histologic evaluation finds a medium-vessel vasculitis with a primarily lymphocytic inflammatory infiltrate, fibrin deposition, and degeneration of the vessel wall. **C**, Both small and medium-sized vessels can be affected in MLA/LTA (lymphocytic thrombophilic arteritis). **D**, Partial vessel occlusion can be seen in this thick-walled vessel.

feature, and if other organs are involved, the diagnosis of MLA/LTA should be questioned. There are rare cases associating the condition with infections such as HIV, hepatitis B, or medication such as minocycline.[10,11] However, these isolated reports make these associations only speculative.

The correlation of the clinical picture to the underlying pathologic condition has been the primary motivator in the description of this disease entity. Indeed, the relatively underwhelming clinical presentation seems discordant with the lymphocytic medium-vessel vasculitis seen on histology.[12] Luminal occlusion and vessel obliteration are common features but do not result in the painful nodules, ulcerations, and stellate scarring seen in other vasculitides, such as polyarteritis nodosa. In this setting, it is likely that MLA/LTA is underdiagnosed. Being innocuous in appearance and largely asymptomatic, lesions may never prompt biopsy by the provider. Alternatively, if tissue is evaluated, providers may rely too heavily on pathology findings and patients may be misdiagnosed as having polyarteritis nodosa. Misdiagnosis may result in unnecessary and harmful treatments such as immunosuppressive therapy.

Treatment of this condition has largely been supportive, as no cases of this vasculitis have been reported to progress to systemic involvement. Treatments such as topical steroids, oral steroids, anticoagulants, and oral antibiotics have yielded disappointing results in the past. In our series, we attempted NBUVB for 1 African-American patient who reported modest improvements in skin pigmentation; however, new lesions continued to develop, suggesting persistent disease activity. To our knowledge, this is the first reported case of NBUVB being used to treat MLA/LTA. The inflammation seen in MLA/LTA is primarily in the deep dermal vessels. As NBUVB penetrates to the papillary dermis it is unlikely to exert an effect on the source of the inflammation. For our patient, dyschromia was her primary concern, and the benefit she noted was likely the result of more even pigmentation. Psoralen with ultraviolet A has

not yet been attempted and may offer a better option for treating the underlying inflammation given its ability to penetrate deeper into the skin. Another woman in this series was treated with dapsone and reported significant improvement after several months. A previously reported case also suggested that dapsone was beneficial.[13] Although dapsone is thought to inhibit neutrophils via myeloperoxidase inhibition, other anti-inflammatory effects have been reported with dapsone and may be beneficial in treating MLA/LTA.[14]

These cases show the clinical-pathologic correlation in this rare vasculitis. The discordant clinical and pathologic findings highlight the current dilemma in the literature, which primarily surrounds the nosology and classification of MLA/LTA. The question of whether this entity reflects a form of cutaneous polyarteritis nodosa or a separate disease entity has not been fully elucidated. Our cases of MLA/LTA add to the current body of literature and may help clarify the natural history of this condition. Knowledge of this entity will help providers in both assessment and treatment. We present the first, to our knowledge, known use of NBUVB for treatment of MLA/LTA and provide an additional case showing improvement with dapsone.

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