Lymphocytic Thrombophilic Arteritis
A Newly Described Medium-Sized Vessel Arteritis of the Skin
Joyce Siong-See Lee, MMED(UK), FAMS; Steven Kossard, FACP; Michael A. McGrath, MD, FRACP

Background: We encountered a distinct arteriolar histopathologic finding of lymphocytic vasculitis associated with a hyalinized fibrin ring in vessel lumina. Identical histologic findings have previously been described as macular arteritis.

Observations: We describe 5 women (mean age, 25 years; age range, 20-34 years) with persistent, slowly progressive, patchy and reticular hyperpigmentation associated with livedo racemosa affecting predominantly the lower limbs. In the biopsy samples, infiltration of muscular vessel wall by inflammatory cells, affecting small arteries of the dermosubcutaneous junction or superficial subcutis, was present. Of the infiltrate, 90% or more consisted of mononuclear cells, mainly lymphocytes with an admixture of histiocytes. Neutrophils and eosinophils were absent or scant. Inflammation was confined to the vicinity of the vessel and the immediate surrounding panniculus. A concentric fibrin ring involving the entire periphery of the lumina of affected vessels was present in all the patients. Laboratory investigation results revealed that 4 patients had antiphospholipid antibodies in their serum. One of these patients had a heterozygous mutation of the factor V Leiden gene.

Conclusion: We term this arteritis lymphocytic thrombophilic arteritis to reflect the histologic features that combine lymphocytic vascular inflammation with changes representing a thrombophilic endovasculitis.

Arch Dermatol. 2008;144(9):1175-1182

We describe a series of 5 patients presenting clinically with livedo racemosa and subtle subcutaneous indurations predominantly over the lower limbs. Histologic examination findings revealed lymphocytic vasculitis of the small arteries in the deep dermis and superficial subcutis associated with a hyalinized fibrin ring in the vessel lumina. The distinct clinical and histologic findings set this condition apart from other cutaneous vasculitides and may represent a distinct variant of lymphocytic vasculitis that results in the endovasculopathy usually seen in thrombophilic states.

For editorial comment see page 1215

REPORT OF CASES

All 5 patients were young women (mean age, 25 years; age range, 20-34 years) (Table 1). There was 1 Chinese patient, 1 patient of mixed Japanese and English descent, 1 Indian patient, and 2 patients of Middle Eastern origin. The mean duration of disease before presentation was 2.4 years (range, 1-4 years) (Table 1). Patient 1 had similar lesions appearing 11 years earlier that resolved after 2 months. In all the patients, the main complaint was persistent, slowly progressive, patchy discoloration over the limbs. Pain was not a frequent finding, being present in only 1 patient. Physical examination findings revealed patchy and reticulonodular hyperpigmentation associated with livedo racemosa over the lower limbs in all the patients and to a lesser extent over the upper limbs in 4 patients (Figures 1A, 2A, 3A, and 4A). This netlike pigmentation was fixed and did not resolve on warming. Subtle indurations of the subcutis were better felt than seen in focal areas clinically in association with livedo. In 1 patient, palpable small erythematous to hyperpigmented nodules were observed (Figure 1A). There were no ulcers or signs of cutaneous infarction, gross scarring, atrophie blanche, or purpura. The distal foot pulses of all the patients were felt, and blood pressure recordings were normal. One patient had Raynaud phenomenon and numbness of the lower limbs, which was worsened in cold weather.

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There were no cases of fixed digital ischemia. One patient felt muscle weakness, and another complained of severe headaches for 1 year. No patients experienced arthralgia or other systemic involvement. There were no cases of deep vein thrombosis or superficial thrombophlebitis.

**LABORATORY INVESTIGATIONS**

Four patients had antiphospholipid antibodies detected in their serum (Table 2). Patient 3 had a high positive titer of anticardiolipin IgM antibodies (51 U/mL), which returned to the baseline level 1 month later. She also had a heterozygous mutation of the factor V Leiden gene (Figure 2A). Patient 5 had a moderately positive level of anticardiolipin IgG (24 U/mL) and a significant level of anti–β2-glycoprotein 1 IgG antibody (37 U/mL). Patients 1 and 2 tested negatively for antiphospholipid antibodies initially but on repeated testing developed borderline to low positive titers.

The erythrocyte sedimentation rate was increased in 3 patients. Antinuclear antibodies were detected in 3 patients, 2 of whom showed negative levels on repeated testing. There was a polyclonal increase in serum γ-globulins in 2 patients.

Findings from other investigations were essentially normal or negative, including complete blood cell count, serum urea and electrolyte levels, renal and liver function test results, rheumatoid factor, antibody levels to soluble extractable nuclear antigens, antineutrophil cytoplasmatic antibody levels, C-reactive protein level, hepatitis B and C serologic results, anti–β2-glycoprotein 1 IgM antibody level, lupus anticoagulant level, prothrombin gene mutation, antithrombin III level, and protein C and S levels. Patient 1 had borderline low functional activity of protein S but normal enzyme levels. Muscle enzyme levels were normal in the patient who had muscle weakness.

### Table 1. Demographic and Clinical Characteristics of 5 Female Patients With Lymphocytic Thrombophilic Arteritis

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>27</td>
<td>23</td>
<td>21</td>
<td>20</td>
<td>34</td>
</tr>
<tr>
<td>Race</td>
<td>Chinese</td>
<td>Middle Eastern</td>
<td>Iraqi</td>
<td>Mixed Japanese and English</td>
<td>Indian</td>
</tr>
<tr>
<td>Smoker</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Duration of disease, y</td>
<td>2a</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Livedo racemosa</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Subtle subcutaneous indurations</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Palpable nodules</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Purpura</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ulcers</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Atrophic blanche</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lower limb involvement</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Upper limb involvement</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pain or tenderness</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Peripheral numbness</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other complaints</td>
<td>-</td>
<td>Raynaud phenomenon</td>
<td>Headache</td>
<td>-</td>
<td>Muscle weakness</td>
</tr>
</tbody>
</table>

Abbreviations: +, present; −, absent.
a Had similar lesions 11 years earlier that lasted 2 months.

### HISTOPATHOLOGIC FINDINGS

In the patient biopsy samples, infiltration of muscular vessel wall by inflammatory cells, affecting the small arteries of the dermosubcutaneous junction or superficial subcutis, was present (Table 3 and Figure 1B). Of the infiltrate, 90% or more consisted of mononuclear cells, mainly lymphocytes with an admixture of histiocytes (Figures 1C, 2B, 3B, and 4B). Neutrophils and eosinophils were absent or scant. Multinucleate histiocytes and granulomas were not present. The prominent lymphocytic infiltrate was confined to the vicinity of the vessel and the immediate surrounding panniculus. A concentric fibrin ring involving the entire periphery of the lumen of affected vessels was present in all 5 patients (Figures 1C, 2B, 3B, and 4B). Nuclear dust was present in the lumen and fibrin ring and in the vessel wall (Figures 1C, 2B, and 3B).

Deep vessels with features of endarteritis obliterans were present in 2 biopsy samples. Intersitial mucin was present to a mild degree in 3 of 5 biopsy samples, and focal epidermal basal vacuolar change was seen in 1 case. There was a mild lymphocytic infiltrate around superficial dermal blood vessels that was not associated with other features of vasculitis. No extravascular dermal granulomas were seen.

Immunohistochemical stains were performed on the biopsy samples from patients 1 and 2. The infiltrate in and around the inflamed deep dermal vessels showed a predominance of T lymphocytes comprising fairly similar proportions of CD4 and CD8 cells. A few B lymphocytes were also detected on CD20 staining. In patient 1, the results of staining for CD56 to detect natural killer cells, Epstein-Barr virus latent membrane protein 1 encoded small RNA 1 in situ hybridization were all negative. In addition, strong positivity for the macrophage...
marker CD68 was seen, but no granulomas were evident. Myeloperoxidase staining performed on 3 of the 5 biopsy samples did not show any significant staining.

**TREATMENT AND PROGRESS**

Patient 1 responded to oral prednisolone therapy, but the lesions recurred when the dosage was tapered after a month. She has not taken any medications for 6 months, and the lesions have not progressed. Patient 2 did not respond to 8 months of low-dose aspirin and clopidogrel bisulfate therapy and was given warfarin sodium, pending response. Patient 3 did not improve after 6 months of low-dose aspirin and nifedipine therapy, and her lesions progressed. She is currently taking warfarin. Patient 4 took low-dose aspirin for 3 months, with no improvement. She discontinued oral medication use for 7 months, with no change in her condition. Patient 5 defaulted follow-up after skin biopsy.

We describe a series of patients with distinct clinical and histologic findings. These patients were young women with slowly progressive patchy hyperpigmentation associated with fixed livedo racemosa affecting predominantly the lower limbs and to a lesser extent the upper limbs. Most patients had only subtle palpable subcutaneous indurations, with 1 patient having more prominent nodularity and papules. There was neither ulceration nor purpura. These lesions were relatively asymptomatic, and there was no associated systemic involvement. Histologic findings were distinctive. An intense infiltrate that was predominantly lymphocytic surrounded and invaded the walls of arterioles in the dermosubcutaneous junction, associated with nuclear dust. Neutrophils were scarce or absent. A hyalinized fibrin ring encircling the entire periphery of the lumina.
of affected vessels was visible on scanning magnification. Four patients were positive for antiphospholipid antibodies on serologic analysis. One patient with a heterozygous mutation of the factor V Leiden gene had the most extensive disease clinically.

Infiltration of the muscular vessel wall of dermosubcutaneous arterioles by lymphocytes and histiocytes associated with intraluminal fibrin deposition is, by definition, a medium-sized vessel lymphocytic vasculitis. However, based on the Chapel Hill Consensus Conference criteria and the American College of Rheumatology criteria for the classification of systemic vasculitides, we could not classify this vasculitis into any of the known categories for vasculitides. We introduce the term lymphocytic thrombophilic arteritis to describe this distinctive histopathologic combination.

Although certain forms of vasculitis and vasculopathies shared similarities with the present cases, there were sufficient differing points to warrant separating the present cases from these differential diagnoses (Table 4 and Table 5). Polyarteritis nodosa is a vasculitis that affects medium-sized and small arteries. The classic form is associated with systemic symptoms and multiorgan involvement, and the cutaneous form is limited to the arterioles of the skin, generally without systemic involvement. Common cutaneous manifestations of polyarteritis nodosa include palpable purpura, painful nodules, ulceration, livedo racemosa, and severe digital ischemia (Table 4). The present patients differed from those with polyarteritis nodosa in clinical presentation because they did not have purpura or ulceration. Pain was an infrequent complaint. The histologic feature characteristic of the early stage of polyarteritis nodosa is neutrophilic infiltration with fibrinoid necrosis involving the muscle coat of medium-sized or small arteries, with more mononuclear cell involvement and fibrosis in the later stage (Table 5). In the biopsy specimens of the present patients with lymphocytic thrombophilic arteritis, arterioles in the deep dermis and superficial subcutis showed intense infiltration of lymphocytes and histiocytes in their muscular walls. Neutrophils were scarce or absent. The changes seen were active, as evidenced by the dense infiltrate, nuclear dust, and luminal fibrin deposition. Unlike polyarteritis nodosa, the hyalinized fibrin ring in the lumina of affected vessels was a consistent feature in these patients, attesting to the thrombophilic nature of the condition. Biopsy samples of cutaneous polyarteritis no-
dosa need to be obtained from new and active lesions, and because of the presence of skip lesions, negative biopsy results are not unusual and multiple biopsies may be required to capture the pathologic condition. In contrast, biopsy samples showing the diagnostic features of the present patients were easily obtained, with all 5 patients requiring a single biopsy of sufficient depth that included the panniculus.

Livedoid vasculitis presents in the early stages as purpura and painful ulceration mainly affecting the lower limbs (Table 4).10 In the later or healed stages, there is porcelain white scarring, or atrophie blanche. Histologically, lesions show luminal fibrin deposition and fibrin thrombi mainly affecting small dermal vessels, producing a segmental hyalinizing vasculopathy (Table 5).8,9,11 Inflammatory infiltrate is often scant and consists mainly of lymphocytes perivascularly. Disturbances in coagulation or fibrinolysis have been found with increasing frequency in livedoid vasculitis, suggesting a prothrombotic state as the etiology.10,12-14 The patients described herein did not present with purpura, ulceration, atrophie blanche, or scarring. Histologically, the hyalinized fibrin ring of livedoid vasculopathy seems to be similar to that seen in the present patients but was localized to deep dermal and subcutaneous arterioles rather than to the small vessels in livedoid vasculopathy, and the lymphocytic inflammation is dense in lymphocytic thrombophilic arteritis.

The antiphospholipid syndrome is an autoimmune and multisystem disorder of recurrent thrombosis, pregnancy loss, and thrombocytopenia associated with the presence of antiphospholipid antibodies, persistently positive antiphospholipid antibodies, anti-β2-glycoprotein I antibodies, or antilupus anticoagulant (Table 4).15,16 Of 5 patients in the present case series, 4 had positive antiphospholipid antibodies. Based on the latest revised classification criteria for antiphospholipid syndrome, none of these patients fulfilled the clinical or laboratory criteria for definite antiphospholipid syndrome.16 Histologic findings in antiphospholipid syndrome are those of thrombosis without significant evidence of inflammation in the vessel wall (Table 5).16,17 In the biopsy specimens of all the present patients, there was a dense mononuclear infiltrate in the deep dermal arterioles, a feature not consistent with vasculopathy primarily due to the antiphospholipid syndrome. Antiphospholipid antibodies have also been positive for disease in a variety of primary systemic vasculitides, including

**Table 2. Significant Laboratory Findings in 5 Female Patients With Lymphocytic Thrombophilic Arteritis**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Patient No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR, mm/h (N &lt; 20 mm/h in females)</td>
<td></td>
<td>34</td>
<td>24</td>
<td>N</td>
<td>N</td>
<td>70</td>
</tr>
<tr>
<td>ANA</td>
<td></td>
<td>Neg</td>
<td>1/80; Neg on repeated testing</td>
<td>1/80; Neg on repeated testing</td>
<td>N</td>
<td>Neg</td>
</tr>
<tr>
<td>ACL IgG, U/mL</td>
<td></td>
<td>N</td>
<td>N initially; became 11 (borderline positive) 4 mo later and was persistent on repeated testing 6 wk later</td>
<td>N initially; became 11 (borderline positive) 4 mo later and was persistent on repeated testing</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>ACL IgM, U/mL</td>
<td></td>
<td>N initially; became 16 (low positive) 1 y later</td>
<td>N</td>
<td>51 (High positive; became N 4 wk later)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Anti-β2-glycoprotein I IgG, U/mL</td>
<td></td>
<td>N</td>
<td>N initially; became 13 (low positive) 4 mo later</td>
<td>N</td>
<td>N</td>
<td>37</td>
</tr>
<tr>
<td>Factor V Leiden gene R506Q mutation</td>
<td></td>
<td>Neg</td>
<td>Neg</td>
<td>Heterozygous mutation</td>
<td>Neg</td>
<td>ND</td>
</tr>
<tr>
<td>D-dimers, mg/L (N &lt; 0.50)</td>
<td></td>
<td>0.89</td>
<td>N</td>
<td>0.89</td>
<td>N</td>
<td>ND</td>
</tr>
</tbody>
</table>

Abbreviations: ACL IgG, antiphospholipid antibody of the IgG subclass; ACL IgM, antiphospholipid antibody of the IgM subclass; ANA, antinuclear antibodies; ESR, erythrocyte sedimentation rate; N, normal; Neg, negative; ND, not done.
Wegener granulomatosis, giant cell arteritis, polyarteritis nodosa, and Churg-Strauss syndrome. In a recent study, 17% of patients with primary systemic vasculitis had positive antinuclear antibodies or lupus anticoagulant on at least 1 occasion. It has been suggested that antinuclear antibodies present in these situations were an epiphenomenon of exposed endothelial cells and did not have prothrombotic properties. This could explain why 2 of the present patients who initially tested negative for antiphospholipids had low positive titers on repeated testing months later. The pathogenicity of the antibodies may also be affected by host genetic factors, antibody isotype, and antigenicity. The presence of antiphospholipid antibodies in 1 patient, and the presence of a prominent lymphocytic component are points against antiphospholipid syndrome. It is unclear what role antiphospholipid antibodies play in the pathogenesis of lymphocytic thrombophilic arteritis. However, the low levels of antiphospholipid antibodies, the lack of significant systemic involvement, the absence of evidence of macrovascular thrombosis, the absence of antiphospholipid antibodies in 1 patient, and the presence of a prominent lymphocytic component are points against antiphospholipid antibodies contributing significantly to the pathogenicity of this condition.

Recently, a cutaneous arteritis presenting with hyperpigmented macules, termed macular arteritis, has been described. Clinically, hyperpigmented, reticulated patches and macules were present mainly over the extremities. Histologically, there were dense infiltrates of lymphocytes in the muscular wall of small arteries of the antiphospholipid syndrome. It is not clear what role antiphospholipid antibodies play in the pathogenesis of lymphocytic thrombophilic arteritis. However, the low levels of antiphospholipid antibodies, the lack of significant systemic involvement, the absence of evidence of macrovascular thrombosis, the absence of antiphospholipid antibodies in 1 patient, and the presence of a prominent lymphocytic component are points against antiphospholipid antibodies contributing significantly to the pathogenicity of this condition.

Table 3. Histologic Findings in 5 Female Patients With Lymphocytic Thrombophilic Arteritis

<table>
<thead>
<tr>
<th>Finding</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation of arterioles in the DSJ</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>or superficial cutis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mononuclear cells, %</td>
<td>&gt;90</td>
<td>&gt;90</td>
<td>&gt;90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;3</td>
<td>5</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Eosinophils, %</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>3-5</td>
<td>5-8</td>
</tr>
<tr>
<td>Concentric fibrin ring around the lumina of the inflamed arteriole</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nuclear dust</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Endarteritis obliterans</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Interstitial dermal mucin</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Epidermal involvement</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Abbreviations: DSJ, dermosubcutaneous junction; +, present; −, absent.

a Mild basal vacular change.

Table 4. Clinical Characteristics of Patients With Cutaneous Polyarteritis Nodosa, Lymphocytic Thrombophilic Arteritis, Livedoid Vasculitis, and APS

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Patients With Cutaneous Polyarteritis Nodosa</th>
<th>Patients With Lymphocytic Thrombophilic Arteritis</th>
<th>Patients With Livedoid Vasculitis</th>
<th>Patients With APS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>F &gt; M*</td>
<td>F &gt; M</td>
<td>F &gt; M</td>
<td>F &gt; M</td>
</tr>
<tr>
<td>Livedo racemosa</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
</tr>
<tr>
<td>Nodules</td>
<td>+ +</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Purpura</td>
<td>+ +</td>
<td>−</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Ulceration</td>
<td>+ +</td>
<td>−</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Atrophie blanche</td>
<td>+/-</td>
<td>–</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Pain</td>
<td>+ +</td>
<td>+</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Site of involvement</td>
<td>LL &gt; UL b</td>
<td>LL &gt; UL</td>
<td>LL</td>
<td>Any site</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>+/-</td>
<td>–</td>
<td>– c</td>
<td>+</td>
</tr>
<tr>
<td>Systemic involvement</td>
<td>−</td>
<td>−</td>
<td>– c</td>
<td>+</td>
</tr>
<tr>
<td>Associated systemic diseases</td>
<td>Inflammatory bowel disease in 6%</td>
<td>−</td>
<td>Often associated with chronic venous insufficiency and less commonly with SLE, APS, scleroderma</td>
<td>Secondary APS associated with SLE, other autoimmune diseases, malignancy, infections, and drugs</td>
</tr>
<tr>
<td>Disease course</td>
<td>Chronic, relapsing, and benign</td>
<td>Chronic and persistent</td>
<td>Variable</td>
<td>(eg, catastrophic APS)</td>
</tr>
</tbody>
</table>

Abbreviations: APS, antiphospholipid syndrome; LL, lower limbs; SLE, systemic lupus erythematosus; UL, upper limbs; −, usually not present; +/−, infrequently or rarely present; +, sometimes present; + +, often present.

* Indicates females affected more often than males.

b Indicates LL affected more commonly than UL, or predominantly LL involvement.

c Generally nil, unless associated with secondary causes, such as SLE or APS.
subcutis. In the photomicrographs, a hyalinized ring of fibrin could be seen in the vessel lumina.23,24 In the study by Fein et al,25 2 of the 3 patients described had positive titers of antiphospholipid IgG antibodies. We believe that the vasculitic process in these patients is identical to that in the present patients. We termed this vasculitis lymphocytic thrombophilic arteritis to emphasize the likely pathogenic role of lymphocytes and to highlight the thrombophilic state of this condition, as evidenced histologically as a localized phenomenon and to a variable degree on laboratory evaluation.

Angiocentric lymphoma may also be considered in the histopathologic differential diagnosis owing to the prominence of the lymphoid infiltrate, the angiocentricity, and the vessel wall changes. However, clinically, angiocentric lymphoma is a progressive disease with noduloulcerative lesions that are not usually confined to the lower limbs. The lymphoid infiltrate is usually atypical, and vessel wall destruction is more profound and is not confined to the lower dermis and subcutis.

Churg-Strauss syndrome may rarely present with granulomatous arteritis involving cutaneous vessels.27 In this condition, patients present clinically with asthma and eosinophilia, features not present in this cohort of patients. Histologically, there is marked infiltration of histiocytes and multinucleated giant cells in and around arterial walls associated with lymphocytes and increased eosinophils in the infiltrate. Multiple serial sections performed on the biopsy specimens of the present patients did not reveal any giant cells, whereas the eosinophils in the infiltrate ranged from nil to occasional.

Lymphocytic vasculitis is not a widely accepted pathologic mechanism, although more attempts to delineate its process have been made in recent years.2,3,28 The distinct histopathologic findings in the present patients may represent a variant of lymphocytic endovasculitis.2 Other examples of lymphocytic endovasculitis, such as Sneddon syndrome and Degos disease, had lymphocytic arteriolitis and arteritis preceding vascular thrombocclusion.29-31 This raises the issue of whether localized thrombotic states can be induced by lymphocytes that target the endothelium of arterioles. Nonspecific prodromal symptoms, such as headache, may precede graver consequences of Sneddon syndrome by many years. As such, vigil has to be kept for these patients for possible signs and symptoms of systemic involvement.

In summary, we described 5 patients with lymphocytic vasculitis of the small arteries of the skin. These patients presented with livedo racemosa of the extremities, and the condition is generally asymptomatic. Histologically, a dense infiltrate of mononuclear cells in the muscular wall of small arteries in the deep dermis or subcutis associated with a ring of hyalinized fibrin in the affected vessel lumina is characteristic. Laboratory findings may reveal abnormalities in thrombophilia screening and, particularly, increased antiphospholipid antibody levels. The pathogenic significance of these antibodies remains unclear. Although the patients observed so far have followed an indolent course and have not had systemic vasculitis, longer follow-up is required. The possibility that a systemic counterpart to this distinctive form of lymphocytic endovasculitis may exist, similar to the situation in polyarteritis nodosa, cannot be excluded. However, we have not, as yet, identified such cases. We termed this arteritis lymphocytic thrombophilic arteritis to highlight the unusual histopathologic features seen in the context of a recognizable subset of patients with livedo racemosa.

Accepted for Publication: October 29, 2007.

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Author Contributions: Drs Lee and Kossard had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Lee and Kossard. Acquisition of data: Lee, Kossard, and McGrath. Analysis and interpretation of data: Lee and Kossard. Drafting of the manuscript: Lee. Critical revision of the manuscript for im-

Table 5. Histologic Characteristics of Patients With Cutaneous PAN, Lymphocytic Thrombophilic Arteritis, Livedoid Vasculitis, and Antiphospholipid Syndrome

<table>
<thead>
<tr>
<th>Histologic Characteristic</th>
<th>Patients With Cutaneous PAN</th>
<th>Patients With Lymphocytic Thrombophilic Arteritis</th>
<th>Patients With Livedoid Vasculitis</th>
<th>Patients With Antiphospholipid Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involvement of small dermal blood vessels</td>
<td>−</td>
<td>−</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Involvement of medium-sized arterioles</td>
<td>+ +</td>
<td>+</td>
<td>+/−</td>
<td>+</td>
</tr>
<tr>
<td>Presence of a fibrin ring around the vessel lumina</td>
<td>−</td>
<td>−</td>
<td>+ +</td>
<td>−</td>
</tr>
<tr>
<td>Presence of thrombi</td>
<td>+/−</td>
<td>+</td>
<td>+ +</td>
<td>+ +</td>
</tr>
<tr>
<td>Degree of inflammation in vessel wall</td>
<td>+ +</td>
<td>+ +</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Neutrophils in vessel wall</td>
<td>+ (Less with older lesions)</td>
<td>+/− (Few even in active lesions)</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Mononuclear cells in vessel wall</td>
<td>+ (More with older lesions)</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Eosinophils in vessel wall</td>
<td>−</td>
<td>+/−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Nuclear dust</td>
<td>+</td>
<td>++</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

Abbreviations: PAN, polyarteritis nodosa; −, usually not present; +/−, infrequently or rarely present; +, sometimes present; ++, often present.


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portant intellectual content: Lee, Kossard, and McGrath. Administrative, technical, or material support: Lee. Study supervision: Kossard and McGrath. Financial Disclosure: None reported. Funding/Support: Dr Lee received a Health Manpower Development Programme grant from the National Healthcare Group and Ministry of Health, Singapore, for her fellowship in dermatopathology at the Skin and Cancer Foundation Australia.

Role of the Sponsor: The sponsor had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

REFERENCES


Correction

In the Observation by Farmerter et al titled “Value of a Novel Neisseria meningitidis-Specific Polymerase Chain Reaction Assay in Skin Biopsy Specimens as a Diagnostic Tool in Chronic Meningococcemia,” published in the June issue of the Archives (2008;144(6):770-773), the Author Contributions paragraph should have included the sentence, “Drs Parmentier and Garzoni equally contributed to the work.”