Small Vessel Vasculitis, an Uncommon Presentation of Systemic Lupus Erythematosus

Madhumita Priyadarshini Das¹, Purabi Borah², Bhaskar Thakuria³, Sahidul Islam⁴, Ankit Patawari⁴

Abstract
We report a nineteen year old female with gangrene of toes as the only clinical feature of systemic lupus erythematosus. She was treated successfully with pulse cyclophosphamide and steroid.

Introduction
Systemic lupus erythematosus (SLE) is characterized by protean manifestations.

SLE is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue binding autoantibodies and immune complexes. Clinical manifestations are heterogenous, and ninety percent of patients at diagnosis are women of child bearing age.¹ It is characterized by the production of antibodies against a variety of nuclear antigens.

A web search on small vessel vasculitis as the sole presentation of SLE yielded scant reports.² We report a case presenting with gangrene of the toes due to small vessel vasculitis.

Case Report
A 19-year-old unmarried female was admitted to the hospital in November 2014 with history of pain of both limbs since 4 months, and blackening of 2nd and 3rd toes of right foot since 2 months (Figure 1). The pain was gradual in onset, progressively increasing in intensity, excruciating in nature, with no aggravating factors. On the next day of admission, she developed pain and blackening of right middle finger. This was associated with oral ulcers twice within the last 6 months, healing spontaneously. There was history of insignificant hair loss and photosensitivity of the same duration, for which medical consultation was never sought.

She denied any systemic symptoms like fever, joint pain, skin rash or fatigue. Neither was there any history of medications taken in the past. Nor any history of smoking, illicit drug consumption or high risk behaviour.

Bilateral dorsalis pedis, posterior tibialis and popliteal artery pulsations were not felt; bilateral brachial, radial and ulnar artery pulsations were well felt. Sharply demarcated dry gangrene was noted involving tip of 2nd and 3rd toes, and the tip of right middle finger. (Figure 2).

Laboratory investigations are as tabulated (Table 1).

Vascular Doppler of right lower limb showed monophasic high resistance flow pattern in distal anterior tibial artery with no power Doppler detectable flow in distal anterior tibial and dorsalis pedis arteries - features suggestive of small vessel disease. Similarly, Doppler of right upper limb showed monophasic high resistance flow pattern in distal ulnar artery.

Patient did not consent for biopsy

Fig. 1: Disappearance of gangrene in the right leg 2nd and 3rd toes following treatment. A: Pretreatment and B: After treatment

Fig. 2: Disappearance of gangrene in the right hand middle finger following treatment. A: Pretreatment and B: After treatment

¹Professor of Medicine, ²Registrar of Medicine, ³Assistant Professor of Medicine, ⁴Post Graduate Trainee, Gauhati Medical College and Hospital (GMCH), Guwahati, Assam
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of the affected tissue. Immunological reports are listed in Table 2.

Table 1: Investigations on presentation

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>10.3 gm/dl</td>
</tr>
<tr>
<td>Platelet count</td>
<td>1,30,000/cumm</td>
</tr>
<tr>
<td>ESR</td>
<td>75 mm at the end of 1st hour</td>
</tr>
<tr>
<td>CRP</td>
<td>50 mg/L</td>
</tr>
<tr>
<td>PT(INR), APTT</td>
<td>16.6 (1.34), 31.9</td>
</tr>
<tr>
<td>HBsAg, anti-HCV, HIV-1 &amp; 2</td>
<td>Non Reactive</td>
</tr>
<tr>
<td>Chest X-Ray (PA-view), ECG</td>
<td>Normal</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Normal</td>
</tr>
<tr>
<td>24 hr urinary protein</td>
<td>124 mg/dl</td>
</tr>
</tbody>
</table>

On the basis of clinical and laboratory findings she was diagnosed as small vessel vasculitis with SLE as she satisfied 4 out of 11 criteria as per ACR guidelines (1-oral ulcer, 2-photosensitivity, 3-ANA positivity, 4-dsDNA positivity). She was treated with steroid-pulse dose (methylprednisolone 1 gm/day intravenous infusion on three consecutive days) and injectable cyclophosphamide (10 mg/kg/month for six doses) as per the NIH guidelines.

During first follow up i.e. four weeks after the 1st dose of cyclophosphamide, there was a dramatic response with halit in the progression of gangrene, overall well-being and reappearance of the peripheral pulses in lower limbs. ESR was 30 mm at the end of first hour, CRP-20 mg/L. These values came down significantly compared to the baseline as shown in Table 1. CT angiography of both lower limbs reported sluggish flow in the distal branches with irregular outlines could be due to small vessel vasculitis. The medium and large arteries appear normal (Figure 3).

At 20 weeks follow up (before 6th dose of cyclophosphamide), she showed no signs of disease activity. Complete haemogram, blood biochemistry and urinalysis were normal. All along she was placed on oral low dose steroid (prednisolone-10 mg/day), aspirin 75 mg od, pentoxyfylline 400mg tid, iron-500mg and folic acid-5mg od, calcium-carbonate 500 mg od, nifedipine 20 mg od, as maintenance therapy.

Fig. 3: CT – Angiography of lower limbs of the patient. Red arrows shows the sluggish flow in the distal branches with irregular outlines

Discussion

We report a patient with digital gangrene as the primary presenting symptom of SLE with vasculitis. Gangrene and ischemia in the extremities have diverse causes. Small vessel vasculitis may be primary or secondary to diseases such as SLE, rheumatoid arthritis, Sjogren’s syndrome and systemic sclerosis. Small vessel vasculitis presenting as gangrene of digits in SLE is rare. This may be ANCA or immune complex associated. ANCA positivity has been reported in 3-69% in SLE.3,4 However p-ANCA can be false positive in SLE with anti-ds DNA antibodies. To differentiate this one needs to look into the subspecificities of p-ANCA mainly myeloperoxidase subspecificities which if positive rules out ds-DNA mediated false positivity of p-ANCA.

In a series of 6 patients of gangrene of the extremities in lupus, the diagnosis was suggested by a good response to immunosuppression.5 The manifestations included fingertip, toe or gangrene of the foot. The prevalence of digital or distal limb gangrene was reported to be 1.3% from a large series of 520 lupus cases.6

Lupus vasculitis requires an exclusion of antiphospholipid associated vascular occlusion or embolic vascular occlusion. Differentiation is often difficult as both can occur simultaneously. Our patient tested positive for lupus anticoagulant and was negative for anticardiolipin antibodies. However, in view of immediate arrest of progressive gangrene with pulse methylprednisolone, without any anticoagulation, we feel that the pathogenesis of her digital gangrene is due to SLE vasculitis. This is further supported by the CT angiography findings (Figure 3).

Conclusion

From this case report we can conclude that when a young female comes with gangrene of the digits as the principal presenting feature, we should keep in mind the possibility of vasculitis and work up for a connective tissue disease. It is important to remember that ANCA positivity has been reported in various studies, however p-ANCA can be falsely positive due to anti-ds DNA antibodies.

References