Superficial Migratory Thrombophlebitis: A Clinical and Histologic Review of 8 Cases

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Abstract. Introduction. Superficial migratory thrombophlebitis (SMT) or thrombophlebitis migrans is characterized by recurrent episodes of localized thrombosis of the superficial veins in the limbs and trunk. It has been associated with various systemic diseases that should be taken into consideration when assessing the patient.

Material and methods. Between 1997 and 2007, 8 patients with SMT were seen at Hospital General Universitario de Valencia in Valencia, Spain. We review the clinical features and histopathology, along with the associated diseases.

Results. The most common clinical presentation was with painful nodules mimicking erythema nodosum on the lower extremities. Other sites were on the abdomen and trunk. Only in 1 case was SMT diagnosed clinically. In other cases, the clinical diagnoses were cellulitis, lymphangitis, nodular vasculitis, and panarteritis nodosa. The histologic characteristics were compatible with superficial thrombophlebitis, and orcein staining revealed the internal elastic lamina to be absent in all cases. No evidence of an occult tumor was found in any of the cases. Two cases had a history of Buerger disease and in another the condition presented in association with a fever of unknown origin.

Conclusion. The possible association of SMT with systemic diseases, including cancer, makes its diagnosis important. In our case series we did not find evidence of associated disease in the majority of cases. However, since cancer can manifest months and even years after the appearance of SMT, follow-up is necessary in these patients.

Key words: superficial migratory thrombophlebitis, thrombophlebitis migrans, Mondor disease, Trousseau sign.
Introduction

Superficial migratory thrombophlebitis (SMT) or thrombophlebitis migrans is characterized by recurrent episodes of localized thrombosis of the superficial veins in the limbs and trunk. It has been associated with various systemic diseases that should be considered when examining the patient.

Here we describe a series of 8 patients seen by the Dermatology Department of Hospital General Universitario de Valencia, in Valencia, Spain, between 1997 and 2007.

Materials and Methods

A search was undertaken to identify patients diagnosed with SMT in the Dermatology Department of Hospital General Universitario de Valencia between January 1997 and April 2007.

The following data were routinely collected from the patient’s medical history: age, sex, clinical presentation, clinical diagnosis, additional tests, and associated diseases. All biopsies were reassessed to analyze the characteristics of the epidermis, papillary dermis, type of infiltrate in the vascular wall, existence of organized thrombus, hemorrhage, and conditions of surrounding fat. Orcein staining was performed in all cases.

Results

Tables 1 and 2 describe the results obtained from the search. Eight patients (5 men, 3 women) with a mean age of 52 years (range, 39-60) were identified. The most common clinical

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/Age, y</th>
<th>Clinical Presentation</th>
<th>Clinical Diagnosis</th>
<th>Associated Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/60</td>
<td>Painful erythematous plaques on the legs</td>
<td>Periarteritis nodosa</td>
<td>Thromboangiitis obliterans</td>
</tr>
<tr>
<td>2</td>
<td>F/45</td>
<td>Recurrent infraumbilical erythematous nodules with a linear distribution</td>
<td>Superficial migratory thrombophlebitis</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>M/57</td>
<td>Hot erythematous plaques on right foot</td>
<td>Cellulitis</td>
<td>Peripheral venous insufficiency</td>
</tr>
<tr>
<td>4</td>
<td>M/47</td>
<td>Linear erythematous lesion on the chest wall</td>
<td>Lymphangitis</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>M/52</td>
<td>Painful recurrent nodules on the legs</td>
<td>Nodular vasculitis</td>
<td>Peripheral venous insufficiency</td>
</tr>
<tr>
<td>6</td>
<td>F/60</td>
<td>Painful pretibial plaque</td>
<td>Erythema nodosum</td>
<td>Fever of unknown origin Viral hepatitis C treated with interferon and ribavirin</td>
</tr>
<tr>
<td>7</td>
<td>F/39</td>
<td>Painful erythematous nodules with a linear distribution on the right leg</td>
<td>Erythema nodosum</td>
<td>No associated diseases</td>
</tr>
<tr>
<td>8</td>
<td>M/58</td>
<td>Painful erythematous nodules with a linear distribution on the right leg</td>
<td>Erythema nodosum</td>
<td>Thromboangiitis obliterans</td>
</tr>
</tbody>
</table>

Abbreviations: F, female; M, male.
presentation was painful nodules in the legs (n = 6). Other
sites were the abdominal region (n = 1) and trunk (n = 1).
The various clinical diagnoses (Figures 1 and 2) were erythema
nodosum (n = 3), nodular vasculitis (n = 1), periarteritis
nodosa (n = 1), lymphangitis (n = 1), and cellulitis (n = 1).
SMT was diagnosed clinically in only 1 case.

A total of 9 biopsies were carried out. In most, pathology
showed epidermal atrophy (n = 7) and proliferation of the
capillary vessels along with a thickened basement membrane
that stained positive with periodic acid Schiff stain in the
papillary dermis (n = 6). Ulceration was not observed in
any patient.

<table>
<thead>
<tr>
<th>Epidermis</th>
<th>Papillary Dermis</th>
<th>Infiltration of Vascular Wall</th>
<th>Organized Thrombus</th>
<th>Hemorrhage</th>
<th>Perivascular Infiltrate</th>
<th>Surrounding Fat</th>
<th>Orcein</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Atrophy</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Histiocytes Giant cells</td>
<td>–</td>
<td>–</td>
<td>Histiocytes Giant cells</td>
<td>Septal fibrosis</td>
<td>Absence of internal elastic lamina</td>
</tr>
<tr>
<td>2 Normal</td>
<td>Normal</td>
<td>Neutrophils Eosinophils Histiocytes</td>
<td>–</td>
<td>+</td>
<td>Histiocytes Eosiophils Endarteritis obliterans Septal fibrosis</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>3 Atrophy</td>
<td>Normal</td>
<td>Neutrophils Eosinophils Histiocytes</td>
<td>–</td>
<td>–</td>
<td>Histiocytes Eosiophils Endarteritis obliterans Lipophagy</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>4 Atrophy</td>
<td>Normal</td>
<td>Histiocytes Fibrosis</td>
<td>+ Minimal recanalization</td>
<td>–</td>
<td>Histiocytes Fibrosis</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>5 Normal</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Lymphocytes Histiocytes</td>
<td>+</td>
<td>+</td>
<td>Lymphocytes Histiocytes Septal fibrosis</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>6 Atrophy</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Lymphocytes Histiocytes Neutrophils</td>
<td>+</td>
<td>–</td>
<td>Lymphocytes Histiocytes Endarteritis obliterans Septal fibrosis</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>7a Atrophy</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Neutrophils Eosinophils Histiocytes</td>
<td>–</td>
<td>–</td>
<td>Neutrophils Eosiophils Histiocytes Endarteritis obliterans Mucin</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>7b Atrophy</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Eosinophils Histiocytes</td>
<td>+</td>
<td>–</td>
<td>Lymphocytes Histiocytes Eosiophils Endarteritis obliterans Mucin</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
<tr>
<td>8 Atrophy</td>
<td>Proliferation of capillary vessels with thickened PAS+ basement membrane</td>
<td>Histiocytes Lymphocytes Giant cells</td>
<td>+</td>
<td>–</td>
<td>Histiocytes Lymphocytes Giant cells Endarteritis obliterans</td>
<td>Absence of internal elastic lamina</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: PAS, periodic acid Schiff.
All cases showed involvement of a large vein in the superficial subcutaneous tissue with occlusion of the vascular lumen (Figures 3 and 4). The inflammatory infiltrates in the vessel wall were composed of neutrophils (n = 4), eosinophils (n = 4), histiocytes (n = 9), lymphocytes (n = 3), and giant cells (n = 2). In addition, 5 biopsies showed an organized thrombus and 1 case had minimal recanalization of the vascular lumen. Hemorrhaging was observed in 2 patients. The surrounding fatty tissue showed lipophagy (n = 1), proliferation of the capillary vessels and
endarteritis obliterans (n = 6), septal fibrosis (n = 5), and mucin (n = 2). In all cases, orcein staining confirmed the absence of the internal elastic lamina.

The mean time from the onset of symptoms until SMT diagnosis was 10 months (range, 1–24 months).

The extended study for each patient included a complete laboratory workup consisting of blood counts, biochemistry, autoimmunity, tumor markers, and a coagulation and thrombosis study, along with chest x-ray, and abdominal ultrasound. The patients were also assessed by a vascular surgeon. No evidence of an occult tumor (Trousseau sign) was seen in any patient. Patients 1 and 8 had a history of Buerger disease (thromboangiitis obliterans). Another case presented with a fever of unknown origin in a patient with viral hepatitis C treated with interferon and ribavirin. In patient 5, the initial thrombosis study showed a partial deficiency of protein C that was not confirmed in subsequent tests. Case 7 was initially associated with lupus anticoagulant, although the patient did not report a history of spontaneous abortions or other thrombotic phenomena. A repeat laboratory workup at 6 weeks showed no abnormalities and, therefore, the patient was referred to the hematology department where repeated studies ruled out this initial association.

Patient 3 developed a depressive syndrome, leading to suspicion of a possible associated pancreatic tumor. Computed tomography scans of the chest and abdomen were therefore performed, showing thickening of the gastric wall; however, malignancy was ruled out by gastroscopy.

Deep vein thrombosis was not observed in any patient. Two patients showed signs of chronic venous insufficiency in the legs. No patient was found to have inflammatory bowel disease or Behçet disease.

All patients (except patient 4) had recurrences. The therapeutic options employed included conservative measures such as rest and elastic compression stockings, as well as systemic treatment with nonsteroidal anti-inflammatory drugs, pentoxyphylline, corticosteroids, and anticoagulants (thromboangiitis obliterans). Another case of Mondor disease, the lesions tend to resolve within a few days, with a low frequency of recurrence. Most clinicians use anticoagulants only for patients with deep vein disease. In cases of associated tumors, adjuvant anticoagulants (particularly heparin) are used in addition to treatment of the tumor.
Conclusion

The possible association of SMT with various systemic diseases, including occult tumors, makes its diagnosis important. Our case series shows, however, that the condition is not always easily recognized because it can be confused with other, more common, entities such as cellulitis or erythema nodosum. In fact, the mean time to definitive diagnosis was 10 months. SMT was diagnosed clinically in only 1 patient. Therefore, SMT should be included in the differential diagnosis whenever the patient has recurrent cutaneous nodules with a linear distribution. In our case series, we were unable to find an associated disease in most cases. However, because cancer can present months or years after SMT is diagnosed, follow-up is necessary in these patients.

Conflicts of Interest
The authors declare no conflicts of interest.

References