Multiple Dermatofibromas in a woman with Systemic Lupus Erythematosus

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Multiple dermatofibromas have been reported in patients with various autoimmune disorders such as systemic lupus erythematosus in receiving immunosuppressive therapy. We report a case of systemic lupus erythematosus in a 30-year-old woman who developed 23 dermatofibromas while she was treated with systemic corticosteroid. The mechanism for the development of multiple dermatofibromas in the setting of immune disturbance remains unclear. The altered immune system may play a role in the pathogenesis of this cutaneous condition. (Ann Dermatol 13(2) 106-109, 2001).

Key Words: Multiple dermatofibromas, Systemic lupus erythematosus

Dermatofibroma is a common, benign hyperpigmented intradermal nodule that is commonly found on the lower extremities in middle-aged women. It usually occurs as a solitary lesion or in some cases as a few lesions. However, the occurrence of multiple dermatofibromas (15 or more in number) is rare, and many reported cases have been associated with autoimmune disorders. In Korean literature, only one case of multiple dermatofibromas has been reported in association with systemic lupus erythematosus.

We describe here a woman with systemic lupus erythematosus who developed multiple dermatofibromas during corticosteroid treatment. This case is supposed to be the second report on multiple dermatofibromas in association with systemic lupus erythematosus in Korea.

CASE REPORT

A 30-year-old woman presented with multiple pigmented pea-sized papules or nodules in both upper and lower extremities, trunk and buttocks. The lesions, ranging from 5 to 10 mm in diameter, were round, firm, slightly raised, erythematous to brownish lesions (Fig. 1). They were 23 in number and grew rapidly within a year. She had a 2 year history of systemic lupus erythematosus (SLE) and lupus nephritis, which had been treated with oral prednisone, 5 to 10 mg daily. Laboratory examinations showed elevated erythrocyte sedimentation rate (81 mm/hr; normal rate is 0 to 20 mm/hr), strong positive ANA test (homogenous pattern), positive LE cell test, elevated anti-double-stranded DNA (>100 IU/ml; normal level is 0-7 IU/ml), positive antinuclear ribonucleic acid protein (anti-rRNP), decreased serum complements level, and decreased level of CD4/CD8 ratio (0.43; normal value is 2:1).

One year ago, she experienced intermittent headaches, dizziness, nausea, vomiting and double vision, and was admitted to the department of neurology due to seizure attack and mental confusion. She was diagnosed as cryptococcal meningitis and received intravenous amphotericin B for 6 weeks with concomitant oral prednisone, increased to 20 mg daily, to control exacerbated symptoms of SLE. After 8 weeks of hospitalization, symptoms of cryptococcal meningitis and SLE were improved but still oral prednisone, 10 mg daily, was maintained due to SLE. At that time she found several nodules on the leg, which did not change in size but new lesions had been developing until this visit.

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Table 1. Multiple dermatofibromas in patients with autoimmune disorders or immunosuppressive therapy appeared in the previous literatures

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Autoimmune disorder</th>
<th>Dermatofibromas</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Onset age (yr)</td>
<td>Disease</td>
<td>SIT</td>
</tr>
<tr>
<td>1</td>
<td>53</td>
<td>M</td>
<td>53</td>
<td>MG, T</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>M</td>
<td>since childhood</td>
<td>AD</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>26-27</td>
<td>UC, PV</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>F</td>
<td>31</td>
<td>SLE</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>F</td>
<td>19</td>
<td>SLE</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
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<td>1</td>
<td>SLE</td>
<td>+</td>
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<tr>
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<td>F</td>
<td>23</td>
<td>SLE</td>
<td>+</td>
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<tr>
<td>8</td>
<td>49</td>
<td>F</td>
<td>29</td>
<td>SLE</td>
<td>-</td>
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<tr>
<td>9</td>
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<td>F</td>
<td>35</td>
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<td>+</td>
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<tr>
<td>10</td>
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<td>F</td>
<td>33</td>
<td>SLE, SS</td>
<td>+</td>
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<tr>
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<td>F</td>
<td>35</td>
<td>SLE</td>
<td>-</td>
</tr>
<tr>
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<td>21</td>
<td>SLE</td>
<td>-</td>
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<td>F</td>
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<td>SLE</td>
<td>+</td>
</tr>
<tr>
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<tr>
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<td>38</td>
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<td>22</td>
<td>SLE</td>
<td>+</td>
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<tr>
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<td>SLE</td>
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<td>22</td>
<td>SLE, HIV</td>
<td>+</td>
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<td>42</td>
<td>SLE</td>
<td>+</td>
</tr>
<tr>
<td>20</td>
<td>46</td>
<td>F</td>
<td>?</td>
<td>SLE, SS</td>
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</tr>
<tr>
<td>21</td>
<td>39</td>
<td>F</td>
<td>27</td>
<td>SLE</td>
<td>+</td>
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<tr>
<td>22</td>
<td>30</td>
<td>F</td>
<td>28</td>
<td>SLE</td>
<td>+</td>
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</table>

SIT, systemic immunosuppressive therapy; MG, myasthenia gravis; T, thymoma; AD, atopic dermatitis; UC, ulcerative colitis; PV, pemphigus vulgaris; SLE, systemic lupus erythematosus; SS, Sjögren's syndrome; ?, description not reported; CR, current report.

* Number of months that the initial appearance of the dermatofibromas followed the start of systemic immunosuppressive therapy.

The histopathological examination of a pigmented nodule on the leg revealed increased spindle-shaped or stellate cells arranging in the storiform patterns, infiltrating between thickened collagen bundles in the dermis and mild hyperplasia of the overlying epidermis, consistent with a diagnosis of dermatofibroma (Fig. 2).

DISCUSSION

Dermatofibroma was first described by Unna in 1894, and was regarded as a fibrohistiocytic lesion. It usually manifests as a firm papule or nodule on the lower extremities of middle-aged women. The tumor is a red, brown, or blue, dome-shaped mass of a few millimeters to a centimeter in diameter. One or several dermatofibromas less than 5 lesions are common, but multiple dermatofibromas more than 15 are extremely rare.

Multiple dermatofibromas have been reported to develop in patients with abnormalities in cell-mediated immunity by immunosuppressive therapy and various autoimmune disorders such as SLE. Among reported
multiple dermatofibromas cases, 22 cases have been associated with autoimmune disorders in which 16 cases had received immunosuppressive therapy (Table 1). Most of them were found in women, and all of the women's cases had been associated with SLE. In our case she had been treated with oral prednisone for 2 years and was revealed to be inverted CD4/CD8 ratio at her 1st visit to our clinic. Several authors have documented multiple dermatofibromas in HIV infection\(^5\)\(^\text{10}\). Multiple dermatofibromas have also been reported in otherwise healthy individuals\(^5\)\(^\text{11}\) or in association with other medical conditions, such as hydronephrosis\(^5\), glycosuria and/or diabetes\(^5\)\(^\text{12}\)\(^\text{15}\), hypercholesterolemia or hyperlipidemia\(^4\)\(^\text{14}\)\(^\text{16}\), hypertension\(^6\), obesity\(^5\)\(^\text{15}\)\(^\text{16}\) and pregnancy\(^7\).

The pathogenesis of dermatofibroma is unknown. Dermatofibroma has been considered as the reactive hyperproliferation of either histiocytes\(^8\), fibroblasts\(^9\) or dermal dendritic cells\(^10\), rather than a true neoplasm\(^11\). The antigenic stimulation for this proliferation has been proposed to be caused by insect saliva, trauma or a virus\(^2\), but the presence of such predisposing factors was not essential for the development of dermatofibroma\(^2\)\(^3\)\(^\text{12}\)\(^\text{14}\).

It is assumed that dermatofibromas are caused by an abortive immunoreactive process, based on the fact that they frequently occur in the condition of defective cell-mediated immunity. Recently an abortive immune response mediated by dermal dendritic cells has been reported as the pathogenesis of dermatofibromas\(^15\). In contrast, Yamamoto et al.\(^2\)\(^6\)\(^\text{37}\) suggested that various fibroblast growth factors derived from mast cells may play a role in induction and exacerbation of the fibrous process of multiple dermatofibromas, from their immunohistochemical study showing the increased number of mast cells in the lesions of multiple dermatofibromas. But in this case, there is no increase in mast cells number by toluidine blue stain (figure not shown).

We report a 63-year-old woman of systemic lupus erythematosus receiving immunosuppressive therapy, who developed multiple dermatofibromas. Further studies are warranted to understand pathogenic relationship between multiple dermatofibromas and autoimmune disease or immunosuppressive treatment.

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