Angiolupoid Sarcoidosis: 
A Clinicopathological Study of a Distinct Variant of Cutaneous Sarcoidosis

Hsiang-Ju Tsai Yue-Zon Kuan Wen-Rou Wong Yea-Huey Chuang Wei-Ming Wu

Sarcoidosis is a multisystem granulomatous disorder with protean manifestations ranging from self-limited skin lesions to intractable organ failure. Angiolupoid sarcoidosis is a rarely reported variant of cutaneous sarcoidosis characterized by erythematous plaques with superficial telangiectasia on the face. Such disfiguring manifestation can cause profound social embarrassment. We reviewed the dermatological files in Chang Gung Memorial Hospital from 1985 to 2001. Eight cases with consistent features of angiolupoid sarcoidosis were identified. The clinical and pathological features, systemic associations, response of treatments, and course of the disease were reviewed retrospectively. The result of our study suggested that angiolupoid sarcoidosis is a distinct and significant subgroup of cutaneous sarcoidosis in Taiwan. (Dermatol Sinica 21: 113-118, 2003)

Key words: Angiolupoid, Granuloma, Sarcoidosis

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INTRODUCTION

Sarcoidosis, a granulomatous disorder with unknown etiology, has been known to have prominent cutaneous involvements.1-3 A diagnosis of sarcoidosis is based on the combinations of clinical, laboratory, and histopathologic findings. Classically, the cutaneous presentations of sarcoidosis are classified as nonspecific (when noncaseating granuloma is not present in microscopic examinations) and specific findings.1-3

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/ Sex</th>
<th>Location and size (mm)</th>
<th>No.</th>
<th>CXR</th>
<th>Duration before first visit</th>
<th>Treatment</th>
<th>Clinical course</th>
<th>Other systemic disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54/F</td>
<td>left, 10x15</td>
<td>10</td>
<td>normal</td>
<td>8 months</td>
<td>prednisolone, hydroxychloroquine, isoniazid, rifampin for 3 months</td>
<td>No response during the treatment. Resolved 2 years later.</td>
<td>hemolytic anemia</td>
</tr>
<tr>
<td>2</td>
<td>53/M</td>
<td>left, 10x12</td>
<td>1</td>
<td>enlarged hilum</td>
<td>1 year</td>
<td>hydroxychloroquine, KI, dapsone, excision with CO₂ laser</td>
<td>No response to hydroxychloroquine, KI, dapsone. Lesions recurred after CO₂ laser but resolved 3 years later.</td>
<td>chronic cough; chest pain</td>
</tr>
<tr>
<td>3</td>
<td>66/F</td>
<td>left, 8x12</td>
<td>4</td>
<td>normal</td>
<td>2 months</td>
<td>doxycycline, excision</td>
<td>No response to doxycycline, resolved after excision.</td>
<td>chronic cough, diabetes</td>
</tr>
<tr>
<td>4</td>
<td>43/F</td>
<td>bilateral: left, 10x12 right, 10x20</td>
<td>2</td>
<td>normal</td>
<td>2 months</td>
<td>intraltesional triamcinolone acetonide</td>
<td>Resolved 3 months after two injection of steroid. Recurrence (+)</td>
<td>transient arthralgia 1 month after skin lesions</td>
</tr>
<tr>
<td>5</td>
<td>54/F</td>
<td>left, 5x4</td>
<td>2</td>
<td>normal</td>
<td>1 month</td>
<td>excision</td>
<td>Recurrence after excision. Persist to date (6 months)</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>35/F</td>
<td>right, 5x5</td>
<td>4</td>
<td>normal</td>
<td>3-4 months</td>
<td>doxycycline, topical steroid</td>
<td>No response during the treatment. Persist to date (2 years)</td>
<td>HTN</td>
</tr>
<tr>
<td>7</td>
<td>58/F</td>
<td>right, 10x10</td>
<td>3</td>
<td>NA</td>
<td>NA</td>
<td>excision</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>50/F</td>
<td>right, 10x10</td>
<td>2</td>
<td>calcified 6 months with fibrotic changes</td>
<td>doxycycline</td>
<td>NA</td>
<td>NA</td>
<td>diabetes</td>
</tr>
</tbody>
</table>

No.: number of lesions, CXR: chest roentgenography, F: female, M: male, NA: not available, KI: potassium iodide, HTN: hypertension
Erythema nodosum is a well-known nonspecific presentation of acute sarcoidosis. Specific cutaneous lesions including lupus pernio, maculopapular eruptions, angiolupoid lesions, and subcutaneous nodules are accompanied with diverse clinical course and prognosis respectively. An angiolupoid variant of cutaneous sarcoidosis was first reported in 1913. It is characterized by erythematous plaques with superficial telangiectasia and typically appear on the characteristic paranasal areas. From then on, only a few cases had been reported in the English language literature. The purpose of the study is to clarify the clinical and pathological manifestations and determine whether angiolupoid sarcoidosis represents a distinctive subgroup of cutaneous sarcoidosis.

PATIENTS AND METHODS

We retrospectively reviewed the medical records of Chang Gung Memorial Hospital between January 1985 and January 2001. A total of 32 cases of sarcoidosis with cutaneous manifestations were found. After reviewing the clinical presentations, microscopic features and medical records, 4 cases were excluded because of possible etiologies other than sarcoidosis. Diagnostic criteria of cutaneous sarcoidosis proposed by Niels, et al. are adopted and include (1) compatible clinical features, (2) noncaseating granuloma in microscopic examination, (3) no growth of cultures of fungi and bacteria including mycobacteria. The 28 cases of cutaneous sarcoidosis can be further classified as maculopapular eruptions (11 cases), subcutaneous nodules (3 cases), scar sarcoidosis (2 cases), and infiltrated plaques (localized or disseminated, 12 cases). In cases presenting infiltrated plaques, we identified 9 cases of facial involvement and 3 cases of disseminated lesions on the trunk. Interestingly, 8 out of the 9 cases with facial involvements developed erythematous plaques on the almost identical locations (the lower aspect of inner canthi), compatible with the diagnosis of angiolupoid variant of sarcoidosis. We investigated the clinical and pathological features, systemic associations, the methods of treatments and the outcome of the 8 cases. In addition, laboratory examinations including chest roentgenography, electrocardiography and pulmonary function test were also obtained. All cases had also received ocular examinations when the diagnosis was made.

RESULTS

This subgroup of cutaneous sarcoidosis comprised seven females and one male. The clinical data were summarized in Table I. The average age of onset is 51.6 years (ranges from 35 to 66). The average duration before the first visit is 5 months. All cases presented asymptomatic erythematous plaques measuring 0.4-1.5 cm in diameter on the area between nasal root and inner canthi. Superficial telangiectasia was evident in 6 cases (Fig. 1). Bilateral involvement was seen in a case. Mild atrophic change can be observed in one of the lesions. In addition to the paranasal main lesions, which were the heralding and the largest in size in all cases, small papules on the forehead, nose, chin and the cheek can also be observed in 6 cases (Fig. 2). Seven cases had received chest roentgenography and abnormalities can be found in two of them. One case showed perihilar lymphadenopathy in chest roentgenography and computed tomography, and the specimen of
transbronchial lung biopsy showed well-defined granuloma without caseation. Another case showed mild pulmonary fibrosis and calcification. Pulmonary function tests in the two cases with abnormal chest roentgenography showed mild restriction pattern. Electrocardiography and ocular examinations were normal in the 8 cases.

Under the microscopic examinations, all of the 8 cases showed noncaseating granuloma composed of well-defined nodules of epithelioid histiocytes in the dermis (Fig. 3). Hair follicles and sweat glands were absent in the granulomatous areas. Lymphocytic infiltrates surrounding the granuloma can be graded as rare in 4 cases, moderate and dense in 2 cases respectively. No remarkable changes were seen in the epidermis and the subcutis. No microorganisms were detected with Ziehl-Neelsen, periodic acid-Schiff, or Fite stains of biopsy specimens of the 8 cases.

The methods of treatments among the 8 cases included systemic, topical and intralesional glucocorticoids, hydroxychloroquine, antituberculosis agents (isoniazid and rifampin), doxycycline, surgical excision, and laser vaporization. Follow-up data were available in 6 cases. The response is variable. Most lesions resolved in 2-3 years though with frequent recurrences. Systemic disorders of the 8 cases included chronic cough (2 cases), hemolytic anemia, arthralgia, diabetes mellitus and hypertension (1 case respectively), but their relationship with the cutaneous sarcoidosis is not clear.

DISCUSSION

Sarcoidosis is a disorder of unknown origin and characterized by the accumulation of lymphocytes and mononuclear phagocytes forming noncaseating epithelioid granuloma.\textsuperscript{1-3, 10} The worldwide incidence of sarcoidosis ranges from 1.2 to 81 per million people but is lower in Asian.\textsuperscript{11} Classically, the diagnosis of sarcoidosis is made when noncaseating granulomas are identified in more than one organ system with exclusions of other possibilities.\textsuperscript{12, 13} It is still debated that whether isolated sarcoidosis of the skin is a variant of chronic sarcoidosis or a sarcoid reaction. There is no easy answer because no diagnostic test exists for sarcoidosis.
Among the protean manifestations of cutaneous sarcoidosis including maculopapules, nodules, plaques, subcutaneous nodules, infiltrative scars and lupus pernio, an angiolupoid variant is rarely reported. Only two reports were found in our searching PubMed database with the keyword "angiolupoid". In this study, eight cases, consisting of seven females and only one male, with the identical clinical features of angiolupoid sarcoidosis described in reference 17 can be identified. The result is surprising because 28.5% (8/28) of cutaneous sarcoidosis cases collected can be entered in the variant. To our knowledge, this is the largest series to date with a first male case.

Although the skin lesions were asymptomatic, the prolonged course and severe disfigurement disturbed the patients very much. Most of our cases (6/8) showed the characteristic telangiectasia of angiolupoid sarcoidosis. Moreover, bilateral symmetric involvement was seen in one case and the presentation had not been reported. All lesions appeared first on the paranasal area but subsequent smaller scattered papules were noted on the faces of 6 cases. It is also a unique feature of our patients.

Specific cutaneous sarcoidosis were reported to carry 41-86.5% risk of abnormal chest radiography. However, the low incidence of pulmonary involvement (25%, 2/8) in our patients is consistent with previous reports of angiolupoid sarcoidosis and considered to be a specific finding. The male patient developed perihilar lymphadenopathy with noncaseating granuloma in the transbronchial biopsy specimens. The case may support that angiolupoid sarcoidosis is a real variant of sarcoidosis with the low incidence of pulmonary involvement rather than a local skin reaction. A case of angiolupoid sarcoidosis associated with bilateral posterior uveitis had been reported in German, but there is no ocular abnormality in our cases.

Pathologically, all of the 8 cases showed well-defined noncaseating granuloma in the dermis. Four cases showed classical "naked tubercles" with rare mononuclear cells surrounding the granuloma. The other 4 cases showed mild to dense lymphocytic infiltrates. However, the two groups cannot be differentiated by the clinical and other pathological features and the "naked" is not an absolute criteria in the diagnosis of sarcoidosis.

Though asymptomatic, treatment of angiolupoid sarcoidosis is mandatory because of the prolonged course and severe disfigurement disturbing the patients. However, no definite management is available for the disorder. The methods of treatments performed in our cases are diverse and include the systemic, topical and intralesional glucocorticoids, doxycycline, hydroxychloroquine and anti-tuberculosis agents. A case received anti-tuberculosis agents for 3 months without significant response, supporting that the angiolupoid is a real variant of sarcoidosis rather than tuberculosis. Intraliteral injection of glucocorticoids was reported effective in palpebral sarcoidosis. Rapid response was also observed in one of our cases treated with intralesional injections of triamcinolone. Interestingly, two of our cases showed spontaneous resolution in 2 to 3 years without any treatment. The benign course is different from the usual plaque variant of cutaneous sarcoidosis in which a persistent course was shown in 93% cases. However, more cases are needed to confirm the optimistic conclusions.

The differential diagnosis of angiolupoid sarcoidosis includes lupus pernio, mycobacterial and fungal infections, rosacea, lupus miliaris disseminatus faciei and leprosy. However, the clinical and pathological features of angiolupoid sarcoidosis are distinctive to differentiate it from other granulomatous diseases. A persistent and destructive course, frequent systemic association, and clinical features of infiltrated plaques and nodules characterize lupus pernio, a variant of sarcoidosis. Although eyelid mass is reported as a feature of sarcoidosis, the character of skin-colored papules or nodules and absence of superficial telangiectasia is obviously different.

In conclusion, we report 8 cases of angio-
olupoid sarcoidosis herein. Intralesional corticosteroid injection may be an effective treatment for this disfiguring variant. The clinical features are distinctive to be isolated as a variant of sarcoidosis. We believe it may be a major variant of cutaneous sarcoidosis in Taiwan because of the surprisingly high incidence in our survey.

REFERENCES