Disseminated Lupus Vulgaris with Clinical Manifestations of Classical plaque, Cicatricial Alopecia and Chronic Ulcer

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Lupus vulgaris (LV) is a chronic and progressive form of cutaneous tuberculosis occurring in individual with a moderate to high degree of immunity. It generally arises from endogenous spread of tuberculosis of other organs. The lesions are usually solitary and affect the head and neck. We report a 65-year-old woman with a history of metastatic breast cancer who showed multiple lesions on different skin areas. There was an ulcerated lesion on the right thigh for about two years. Two large dusky red plaques on the scalp with scarring alopecia and another plaque on the left jaw were noted for about one year. The report of histopathology showed non-caseating tuberculoid granuloma composed of Langhans giant cells and epithelioid histiocytes. Tissue culture from the scalp lesion grew *Mycobacteria tuberculosis*. Under the impression of disseminated LV, an antituberculous therapy comprising isoniazid and ethambutol was prescribed. All the skin lesions healed gradually with residual scarring in 2 months. The patient continued the antituberculous therapy for 7 months until she died of the complications of breast cancer metastasis.

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Key words: Disseminated lupus vulgaris, Cicatricial alopecia, Chronic ulcer

以典型斑塊、疤痕性禿髮及慢性潰瘍為表現的播散性尋常性狼瘡

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尋常性狼瘡是一種緩慢進展的皮膚結核病，多發生在具有中度至高度免疫力的個體。通常是由內部器官的結核感染蔓延而來。其中尋常性狼瘡病灶並非發生於頭頸部。我們在此報告一例罹患轉移性乳癌的六十五歲女性病患，身上多處的皮膚病灶。其右大腿有一持續兩年的潰瘍性病灶。頭皮有兩塊暗紅色的板塊樣病灶伴隨疤痕性禿髮的表現，在左側下顎則有一板塊樣病灶，這些都已有一年的時間。組織病理下可見由胚幹巨細胞及上皮樣組織細胞所構成的結核性肉芽腫。頭皮病灶處的組織培養證實是結核菌感染。在符合尋常性狼瘡的診斷之下，給予抗結核藥物isoniazid及ethambutol，其病灶在兩個月內逐漸纖合。治療持續了七個月，直至病人死於乳癌轉移後的併發症。(中華皮誌 24: 32-37, 2006)
INTRODUCTION

Lupus vulgaris (LV) is the most common form of cutaneous tuberculosis in many series. It classically considered as the resurgence of an endogenous focus. The most usual clinical picture is a solitary, sharply marginated, red-brown papule of gelatinous consistency slowly evolving by peripheral extension and central atrophy into a large plaque. We report a 65-year-old woman of LV with several scattering lesions and rare clinical manifestation. About 2 years ago, an ulcer gradually developed on the right thigh, which was followed by several dusky red plaques on the face and the scalp. The infiltrated plaques of the scalp even resulted in cicatricial alopecia. There was a dramatic response with healing of the ulcer and marked resolution of the plaque lesions within two months of antituberculous therapy.

CASE REPORT

A 65-year-old woman with a 2-year history of breast cancer with multiple bone metastases (including the skull, the rib cage, the lumbar spines, the pelvis and long bones) was treated with palliative radiotherapy and tamoxifen in the past two years. She visited our clinic in April, 2004 with the complaint of a huge ulcerated wound over the upper part of the right thigh for two years. There were also asymptomatic red-brown plaques on the left temporoparietal and the right temporal scalp with scarring alopecia and another asymptomatic red plaque on the left jaw, which were noted for about one year. All the lesions mentioned above began as small brownish to red discoloration and gradually changes to infiltrated plaques in months. The plaque over the right thigh grew outward and evolved into an ulcerative wound insidiously. She was treated with multiple courses of topical and oral antibiotics without any effect. No previous medical history of primary tuberculous infection was noted. There was no history of evening fever, cough or expectoration.

On examination, the patient was undernourished with ill looking. Two dusky red alopecic plaques were present on the right temporal and left temporoparietal regions, respectively (Fig. 1A, 1B). Another dusky red smooth-surfaced plaque on the left jaw was noted (Fig. 1C). Diascopic examination showed an ed with palliative radiotherapy and tamoxifen in the past two years. She visited our clinic in April, 2004 with the complaint of a huge ulcerated wound over the upper part of the right thigh for two years. There were also asymptomatic red-brown plaques on the left temporoparietal and the right temporal scalp with scarring alopecia and another asymptomatic red plaque on the left jaw, which were noted for about one year. All the lesions mentioned above began as small brownish to red discoloration and gradually changes to infiltrated plaques in months. The plaque over the right thigh grew outward and evolved into an ulcerative wound insidiously. She was treated with multiple courses of topical and oral antibiotics without any effect. No previous medical history of primary tuberculous infection was noted. There was no history of evening fever, cough or expectoration.

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**Fig. 1**

Tan, infiltrated plaques located on (A) the right temporal scalp, (B) the left temporoparietal scalp, (C) the left jaw, and another 15 x 10 cm ulcer over the upper part of the right thigh (D).

**Fig. 2**

Histopathology of the lesional skin from (A) the margin of the ulcer on the right thigh and (B) the right temporal scalp showed epithelioid cell tubercules with some Langhans giant cells and a mononuclear cell infiltrate. No caseous necrosis was found. Pseudop epitheliomatous hyperplasia of the epidermis was also noted in the margin of the ulcer (A). (H&E, magnification x 40)
"apple jelly" appearance in these plaques. Moreover, a huge ulcer, about 10 x 15 cm, with rolled edge and satellite infiltrating nodules was present on the upper part of the right thigh (Fig. 1D). No presence of regional lymphadenopathy was noted. A 3 x 3 cm contracture scar over the left breast was noted. The remainder of the physical examination was normal. Laboratory studies of blood showed: CEA 38.0 ng/mL (0-2.5), CA 15-3 149.7 U/mL (0-30) and alkaline phosphatase 409 IU/L (60-205). Complete blood count with differential analysis, liver function tests, BUN, creatinine, erythrocyte sedimentation rate and urinalysis were all within normal limits. X-ray examination of the chest revealed no pathological findings. Sputum examination did not show acid-fast bacilli.

A skin biopsy from the spreading margin of the huge ulcer on the right thigh was done in April 2004, which showed non-caseating tuberculoid granulomas composed of epithelioid histiocytes, lymphocytes and multinucleated giant cells of Langhans or foreign-body types in the dermis (Fig. 2A, 3). The overlying epidermis reveals focal pseudoepitheliomatous hyperplasia and focal ulceration. Stains and tissue cultures for common bacteria and fungi were negative. No acid-fast bacillus was showed in pathology, and the mycobacterial culture was contaminated. A presumptive diagnosis of atypical mycobacterial infection was made. The patient was treated with oral minocycline 100 mg twice a day with little improvement of the skin lesions.

Another biopsy from the plaque of the right temporal scalp was done in June 2004, which also disclosed a granulomatous infiltrate in the dermis (Fig. 2B). Acid-fast, PAS and GMS stains showed no evidence of specific microorganisms, but the tissue culture grew Mycobacteria tuberculosis with fully susceptibility. Under the diagnosis of disseminated LV, the patient was treated with antituberculous therapy comprising isoniazid 300mg, rifampin 450mg, ethambutol 800mg, and pyrazinamide 1000mg daily. However, deterioration of the liver function tests was noted one week later (GOT 86 IU/L, GPT 42 IU/L). Then, she was continuing with isoniazid 300mg and ethambutol 800mg daily in the following months. The ulcerative wound on the right thigh had shown a remarkable amelioration and all other plaques had regressed considerably in the first month. All lesions healed with scarring in two months (Fig. 4). The patient died of multiple-organ failure secondary to metastatic breast cancer seven months later.

**DISCUSSION**

Tuberculosis is remaining a dominant pub-
lic health problem in Taiwan. It prevails as pandemic to our country with an incidence estimated to 66.67/100,000 in 2003. Extrapulmonary tuberculosis accounts for about 20% of all tuberculosis infection in Taiwan, and cutaneous tuberculosis constitutes less than 2% of the extrapulmonary types of the disease and shows considerable morphologic variability. LV is the most common type of cutaneous tuberculosis in U.S., Europe, Middle East, India and Hong Kong. It may result from hematogenous, lymphatic or contiguous spreading of a tuberculous lesion or a clinically inapparent tuberculous focus localized elsewhere. Rarely, LV occurs within three years after bacille Calmette-Guérin vaccination. It has also been reported to be acquired exogenously following primary inoculation. The typical initial lesion is single reddish-brown papule or plaque with a smooth surface that by diascopy has an apple-jelly appearance. It grows extremely chronic, and without therapy its course usually extends over many years. The disease is progressive and may lead to impairment of function or disfiguration.

In addition to the classical plaque type lesions, the hypertrophic, ulcerative and vegetative forms are other less common types of LV lesions. In very rare instances, LV may present with multiple lesions, especially in patient with active pulmonary tuberculosis or impairment of immunity. The current patient developed disseminated lupus vulgaris with classical plaque type lesions and ulcerative variant simultaneously. The underlying metastatic breast cancer and malnutrition could contribute to the impairment of the immunity. That might explain why our patient tended to develop disseminated LV. However, no evidence of visceral involvement was noted. We supposed that the disease of our patient was caused either by hematogenous spread of an old, quiescent primary complex locating elsewhere or by direct exogenous inoculation at the skin. In fact, only 14.3% (22/154) of patient with LV had a concurrent systemic organ involvement in a large series of study in India. The current patient got multiple bone lesions for 2 years, and the problem was attributed to bone metastasis of breast cancer by the oncologist. Without tissue proof we could not exclude the possibility of bone tuberculosis, which might be the source of LV. Since the problem of multiple bone lesions kept persistent during the course of the antituberculous therapy, we favored that the bony destruction was a separate event from mycobacterial infection.

The typically affected areas of LV are the face and the neck, and less commonly, the arm and the leg. The involvement of the trunk and the scalp is rare. Our patient had LV affecting the scalp and resulting in scarring alopecia, a very uncommon presentation of LV, which is due to the extension of the granulomatous infiltrate deeply around the follicles. This condition should be differentiated from metastasis of the breast cancer, discoid lupus erythematosus, sarcoidosis, morphea, necrobiosis lipoidica and other destructive or infectious cutaneous disease.

Histopathologic evaluation of LV usually reveals a tuberculoid-type granulomatous reaction composed of epithelioid cells and Langhans giant cells with no or minimal caseation in the dermis. There is also an associated infiltrate of lymphocytes. Tubercle bacilli are sparse and therefore not frequently seen by staining methods. Secondary changes in the epidermis are common. The overlying epidermis may become atrophic, ulcerative, hyperplastic or papillomatous. At the margin of the ulcers, pseudoepliheplomatous hyperplasia often exists.

Isolation of M. tuberculosis by culture is the single most important procedure for the diagnosis of cutaneous tuberculosis, and it is required to determine antibiotic susceptibility. However, detection of microorganisms by conventional methods, such as special stains and mycobacterial culture, is often difficult in paucibacillary cutaneous tuberculosis such as LV. Microscopic pathology, therefore, is the mainstay. The introduction of polymerase chain reaction (PCR) for the detection of M. tuberculosis DNA in paraffin embedded tissue has greatly improved the diagnosis of different type of tuberculosis. Since the first mycobacterial
culture of our patient was contaminated and PCR of M. tuberculosis DNA was not available, it was very difficult to determine a proper plan of treatment at first. However, the histopathology of the ulcer on the right thigh revealed tuberculoid granuloma in the dermis. Besides, the plaque lesions over the scalp and the jaw showed apple-jelly nodules on diascopy. Hence, the diagnosis of lupus vulgaris was still highly suspected. We performed another biopsy of the plaque on the right temporal scalp two months later, and this time the tissue culture grew M. tuberculosis. It taught us a lesson that we should keep on performing tissue culture until yielding a positive result when we were confronted with skin lesions highly suspected as cutaneous tuberculosis.

Although typical LV plaques may not present diagnostic problems, they have to be distinguished from many other lesions which have similar clinical and histological appearances. Sarcoidosis, lymphocytoma cutis, lymphoma, discoid lupus erythematosus, tertiary syphilis, leprosy, deep mycotic infections, non-tuberculous mycobacterioses, chronic vegetating pyoderma, Wegener's granulomatosis, rosacea and cutaneous leishmaniasis should be included in the differential diagnosis of LV. The huge ulcerated lesion in our patient was hardly differentiated from metastasis of breast cancer clinically, and it called for histopathology to make a correct diagnosis. Furthermore, multiple lesions are rarely reported in lupus vulgaris and may be confusing especially with sarcoidosis and atypical mycobacterial infection when confronted with non-specific granulomatous histology like our patient. Culture and/or PCR of cutaneous samples are required in case of doubt.

Patients should have a baseline laboratory evaluation at the start of therapy that includes hepatic enzymes, bilirubin, CBC, and serum creatinine level. Monthly evaluations with specific inquiries about symptoms of drug toxicity are essential. Regimens used for pulmonary tuberculosis are adequate for treating cutaneous tuberculosis because there is much lower bacillary load in cutaneous tuberculosis.17 However, because of the relatively high frequency of clinically inapparent simultaneous visceral involvement, treatment should consist of standard multiple drug antituberculous medications in order to prevent recurrence of tuberculosis.12 In most circumstances, the treatment regimen consists of a 2-month initial phase of isoniazid, rifampin, pyrazinamide, and ethambutol.16 Since deterioration of liver function tests in our patient was noted in the first week, rifampin and pyrazinamide were discontinued immediately. In patients whose initial phase of treatment did not include PZA, a further 7-month continuous phase is recommended.19 Hence, our treatment plan was to fulfill a 9-month course of antituberculous therapy comprising isoniazid and ethambutol. Unfortunately, the patient died of breast cancer seven months later. In fact, all the cutaneous lesions started to heal with scarring in the second month of the treatment course.

In summary, this case showed disseminated skin lesions with chronic ulcer and scarring alopecia, which were rare manifestations of LV. Cutaneous tuberculosis is an important diagnostic possibility in immunocompromised patients with chronic cutaneous granulomatous disease. In highly suspected cases, it deserves more times of performing mycobacterial culture to make the exact diagnosis and determine antibiotic susceptibility.

REFERENCES