Dear Editor,

A 69-year-old woman with underlying diabetes mellitus and chronic hepatitis B suffered from multiple indurated erythematous plaques on the trunk and extremities for 3 years (Figure 1A and B). The plaques, initially noted on the bilateral thigh with progression to trunk and upper arms, were asymptomatic. She had also lost weight during the past year. Physical examination revealed enlarged lymph nodes at the bilateral axillae. We obtained a skin biopsy from the thigh. The histopathological examination showed mild atrophic epidermis with focal epidermotropism and dense infiltrate of small- to medium-sized atypical lymphocytes in the dermis (Figure 2A–D). Nodular pattern infiltration with granulomatous reaction and multinucleated giant cells were found in the granuloma area. Acid-fast stain, periodic acid–Schiff stain, and Grocott–Gomori methenamine silver stain showed negative findings. Immunohistochemical studies revealed that atypical small- to medium-sized lymphocytes expressed CD3+ and CD4+ (Figure 2E) with CD7 loss. The atypical lymphocytes did not express CD8, CD20, or CD30. The diagnosis of CD4-positive granulomatous mycosis fungoides (GMF) was made on the basis of clinical and histological findings.

Laboratory examination revealed anemia (hemoglobin, 10.6 g/dL), thrombocytopenia (platelets, 120 × 10^12/L), and normal white blood cell counts (4.7 × 10^9/L). Elevated blood lactate dehydrogenase level (303 U/L) was also noted. Human T-lymphotrophic virus-1 antibody was negative. The peripheral smear reported normochytic erythrocytes, normochromic white blood cells, and adequate platelets. Bone marrow study reported no abnormal lymphoid cell infiltration. The whole-body computed tomography showed multiple enlarged axillary, mediastinal, and inguinal lymph nodes without extralymphatic organ involvement. Positron emission scanning also showed hypermetabolic nodes in bilateral thighs, bilateral inguinal, bilateral iliac, and bilateral axillary areas. Ill-defined areas with increased fluorodeoxyglucose uptake in the soft tissue of bilateral lower legs and left upper arm were also seen. The final diagnosis was MF T2N1M0 Stage IIA. Although no tumor was found clinically, because the histopathology revealed tumor-like deeper infiltration rather than plaque-type MF, the oncologist suggested treating this case aggressively as stage IIB (T3N1M0) disease.

She was diagnosed in August 2011 and received one course of chemotherapy with the ProMACE regimen. She next received oral psoralen plus ultraviolet A therapy at the outpatient department with improvement (Figure 1C). However, chest computed tomography revealed newly found multiple nodules of lung involvement in July 2013. Chemotherapy (ProMACE–CytoBOM) was resumed in August 2013.

GMF is a rare histological variant of mycosis fungoides (MF), characterized by a granulomatous infiltrate pattern. The first description of this variant was reported by Ackerman and Flaxman in 1970. However, the clinical features of GMF have no distinct difference from classic MF. Patients often present with typical stepped

Figure 1 Multiple asymptomatic erythematous indurated plaques over (A) trunk and (B) proximal limbs with fine scales. (C) After chemotherapy and PUVA therapy, the 1-year follow-up photograph showed improvement of leg lesions.
patch, plaque, or tumor stages. Poikiloderma as a clinical presentation has also been reported.1

The diagnosis of GMF can be challenging, because its granulomatous inflammation pattern can be mistaken for other types of granulomatous dermatitis. Sarcoid granuloma patterns are most often found, and granuloma annulare patterns and tuberculoid-like granuloma have also been reported.2,3 Other causes of infectious and noninfectious granulomatous disease must be ruled out. CD4-positive GMF is most common, although rare cases of CD8-positive GMF have been reported.4 Atypical lymphocytes, epidermotropism, Pautrier microabscesses, and dural fibrosis are common histological findings of classic MF.5 These findings are also typical features for GMF, but epidermotropism has been found in approximately half of reported GMF cases.6 Atypical lymphocyte infiltration and clinical correlation are important for differential diagnosis. T-cell receptor gene clonal rearrangement detection may be helpful for diagnosis. However, MF in its granulomatous form can still be difficult to diagnose. A previous study found that the average duration before diagnosis of GMF was longer than for classic MF (8.4 years vs. 4.3 years, respectively).7

The granulomatous infiltrate pattern has not been found to be a conclusive positive prognostic marker. Initially, a granulomatous reaction was thought to be an immune response reaction and a sign of a better prognosis. However, a case-control study1 reported more frequent disease progression in granulomatous MF than in classic MF (46% and 30%, respectively). Compared with classic MF, the progression-free rate of GMF was significantly lower at 5-year (84% of classic MF vs. 56% of GMF) and 10-year follow-up (59% of classic MF vs. 33% of GMF).8 However, no significant difference was found in overall survival. Poorer response to skin-directed therapy was observed in GMF patients versus classic MF patients, and more aggressive treatment may be required for the former.9

Our patient received one cycle of PromACE chemotherapy, followed by PUVA therapy. Disease progression with multiple lung nodules involving was noted 23 months later.

In summary, we present a case of GMF, which is rarely reported in Taiwan. Dermatologists should be alert to the possibility of mistaking GMF for other types of granulomatous inflammation infiltrate disease. The prognosis of GMF is controversial, and more study is needed.

Wen-Chien Tsai
Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Fu-Chen Chuang
Department of Cosmetic Applications & Management, Yuh-Ing Junior College of Health Care & Management, Kaohsiung, Taiwan

Shang-Hung Lin, Ji-Chen Ho*
Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

* Corresponding author. Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Ta-Pei Road 123, Niao-Sung district, 83301 Kaohsiung, Taiwan.
E-mail address: jichenho@cgmh.org.tw (J.-C. Ho).

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