A 56-year-old Thai woman progressively developed multiple asymptomatic ulcerated nodules on her trunk and extremities for 5 months. The patient was otherwise healthy and had no past history of any medical conditions. Physical examination revealed multiple discrete ulcerated nodules with central keratinous plugs at the trunk, upper and lower extremities (Fig 1). The lesions varied in size from 1×1 cm. to 3×3 cm. There was no superficial lymphadenopathy. Other physical examinations were unremarkable. Skin biopsy revealed pseudoepitheliomatous hyperplasia with central ulceration of the tumor. These findings could lead to misdiagnosis of squamous cell carcinoma or keratoacanthoma. The expression of CD30 antigen can be found in both anaplastic large cell lymphoma and lymphomatoid papulosis. Histopathology alone is insufficient to differentiate between these 2 conditions. The definite diagnosis should always be based on the clinical course and the histological finding. Our patient did not have a clinical history, but there was clinical evidence of lymphomatoid papulosis and more than 75% of the tumor cells in the dermis to subcutaneous fat expressed CD30 antigen. Therefore, the definite diagnosis in this patient was CD30+ anaplastic large cell lymphoma (ALCL). Further investigations were done to exclude other conditions such as B-cell lymphomas and NK-cell lymphomas by using CD20 (B cell), CD56 and EBER (NK-cell) respectively. They were negative for CD20, CD56 and EBER in this patient.

The distinction between primary cutaneous CD30 positive ALCL and systemic ALCL that involves the
skin secondarily is necessary because primary cutaneous CD30 positive ALCL is a more favorable prognosis. Using the immunophenotype, primary. ALCL differs from the systemic form because it is always Anaplastic Lymphoma Kinase (ALK) –negative whereas the systemic form can be positive or negative. Immunostaining also demonstrated ALK-negative in this patient. Additional investigations were done to exclude extracutaneous involvement and to determine staging of the disease. Complete blood count and lactate dehydrogenase were within normal limits. Both abdominal and chest sonography revealed no abnormal findings. Bone marrow biopsy showed hypercellularity with normal maturation and no CD30+ large cell staining by immunohistochemistry. All of the evidences confirmed the diagnosis of primary cutaneous CD30+ ALCL.

The patient was initially treated with a systemic chemotherapy, CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) regimen, with a total of 3 consecutive cycles administered at 4-week intervals. However, she continued to develop new lesions with partial regression of the old lesions. Another regimen, fludarabine and mitoxanthone, was tried with no improvement. Finally, the drastic etoposide, methylprednisolone, cisplatin, cytosar (ESHAP) regimen was considered. The ESHAP regimen was administered continuously at 4-week intervals. Her lesions showed complete regression after the third cycle. The regimen was completed through 6 cycles because of renal insufficiency deriving from the treatment. The patient comes to check-up at hospital monthly after stopping ESHAP regimen. She now is well and has not developed any new lesion. The second bone marrow biopsy was done and showed no evidence of lymphoma. The patient has been in remission since the last ESHAP regimen until now (3 years).

DISCUSSION

According to the WHO-EORTC classification for cutaneous lymphomas, primary cutaneous CD30+ lymphoproliferative disorders include primary C-ALCL, lymphomatoid papulosis and borderline cases. Primary cutaneous CD30+ anaplastic large cell lymphoma typically affects adult males more than females (2-3:1) and has insidious clinical courses. Most patients present with single or localized tumors with ulceration. Multifocal tumors, as in our case, are seen in only 20% of reported cases. C-ALCL with a keratoacanthoma (KA)-like tumor is unusual but it has been reported. We searched the MEDLINE database for reports of representative cases of primary cutaneous CD30+ ALCL presenting as keratoacanthoma. We found five reported cases. The similarity and difference between former reported cases and our case were demonstrated as Table 1. The clinical differentiation includes squamous cell carcinomas, multiple eruptive keratoacanthomas and cutaneous lymphomas. C-ALCL is composed of large cells with kidney-shaped nuclei and abundant cytoplasm and expression of the CD30 antigen in more than 75% of the infiltrated tumor cells.

Ulcerating lesions may show abundant inflammatory infiltrate of reactive T cells, histiocytes, eosinophils and/or neutrophils with prominent epidermal hyperplasia. Most of the former reported cases demonstrated pseudoepitheliomatous hyperplasia and contained numerous neutrophils and eosinophils. The skin biopsy from our patient also revealed pseudoepitheliomatous hyperplasia but neither eosinophils nor neutrophils were detected. The epithelial proliferation in C-ALCL is not well understood. The presence of pseudoepitheliomatous hyperplasia usually associates with CD30+ lymphop-
proliferative disorder more than other types of cutaneous T-cell lymphomas. Various mechanisms have been postulated for developing through CD30+ lymphoid cells, such as when the cell indirectly inhibits an apoptotic homeostatic mechanism, the cell directly induces proliferation of keratinocytes similar to the proliferation of “T-cell-like” Hodgkin-derived lymphoblastoid cells and, finally, that the cell produces epidermal growth factor-like molecules causing epithelial proliferation. T-cell lymphomas may have eosinophils as a reactive component, but the presence of neutrophils in the absence of necrosis is uncommon in malignant lymphoma.

Takimoto et al. reported the case of ALCL with expression of interleukin-5 (IL-5) mRNA and eosinophilic invasion in 1996. The authors speculated that production of IL-5 by tumor cells recruited eosinophils into the tissue. Eosinophilopoiesis is associated with IL-5, IL-3 and granulocyte-macrophage colony-stimulating factor (GM-CSF) and the production of these cytokines by tumor cells may be responsible for eosinophilic and neutrophilic infiltration in tissue.

Extracutaneous involvement, mainly regional lymph nodes, occurs in about 10% of all cases. The choice of treatment is based on size, extent, and clinical behavior of the disease. The standard treatment for either solitary or localized disease employs local radiotherapy, excision or combination. In contrast to therapy for multifocal lesions, such as ours, there is no available standard regimen. The combination chemotherapy is considered the most appropriate first-line treatment of multifocal primary cutaneous disease. No specific chemotherapy regimen shows superiority, but doxorubicin-based combinations such as CHOP are generally used. The Dutch Cutaneous Lymphoma Group found that patients with skin-limited CD30+ lymphomas who were treated with CHOP regimen, which is the traditional combination chemotherapy, usually experienced one or more relapses in the skin lesions as did our patient. In recalcitrant multifocal C-ALCL cases, etoposide is shown to produce convincing result. The prognosis of C-ALCL is usually favorable with a 10-year disease-related survival rate exceeding 90%.

The number of lesions and the involvement of lymph nodes have no significant correlation with the survival rate.

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**REFERENCES**