A Case of Primary Cutaneous CD30(Ki-1)-positive Large Cell Lymphoma Showing Repetitive Spontaneous Regression and Recurrences

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Primary cutaneous CD30+ large cell lymphoma(LCL) is a rare cutaneous peripheral T cell lymphoma with a favorable prognosis. This lymphoma characteristically presents itself as a solitary or localized skin tumor with frequent cutaneous relapses and partial or complete spontaneous remission. Recently we saw a sixty-three year old male who had developed primary cutaneous CD30+ large cell lymphoma that waxed and waned. He presented with localized multiple nodules that had shown repetitive spontaneous regression and recurrences with the same morphology in the same area for several years. There was no evidence of nodal and visceral involvement. The immunohistochemical studies demonstrated that most neoplastic cells in the tumor were positive for CD30 and pan-T cells and negative for pan-B cells, S-100 proteins, EMA and monocyte-macrophage related antigen(CD68).

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Key Words : CD30(Ki-1)+ LCL, Spontaneous regression and recurrence

CD30+ lymphoma is a distinct type of non-Hodgkin's lymphoma that generally originates in lymph nodes. CD30+ lymphoma generally presents itself with nodal disease, but extranodal CD30+ lymphoma is common. Skin is the most common site of extranodal CD30+ lymphoma[1-2]. CD30+ lymphoma occurring in the skin is observed according to the following three groups: first, origin in the skin(primary cutaneous CD30+ LCL). second, secondary cutaneous involvement of a primary non-cutaneous CD30+ LCL or of Hodgkin's disease(primary non-cutaneous CD30+ LCL). third, resulting from another type of cutaneous lymphoma like mycosis fungoides(MF), lymphomatoid papulosis(LyP)[3-6].

Primary cutaneous CD30+ LCL represents the recently recognized group of cutaneous T-cell lymphoma with a favorable prognosis. This lymphoma generally occurs in adults, usually shows T-cell lineage and expresses the CD30 antigen. Characteristically it also presents itself as a solitary or localized skin tumor with frequent cutaneous relapses and, in rare cases, partial or complete spontaneous remission[7-9].

We report a case of primary cutaneous CD30+ LCL showing repetitive spontaneous regression and recurrences with the same morphology in the same area.

CASE REPORT

A 63-year-old man visited our department with well circumscribed, discrete, brown colored, multiple nodules on the right outer thigh of two months duration(Fig. 1). He had had a 3-year history of recurrent cutaneous nodules on the same area. The lesions had enlarged over several weeks and usually ulcerated before spontaneous resolving. Resolution had taken 2-4months depending on the size of the lesion. Firstly a single nodule developed on the same site 3 years ago and spontaneously resolved in several months. Secondly 3 nodules developed on the same area 2 years ago

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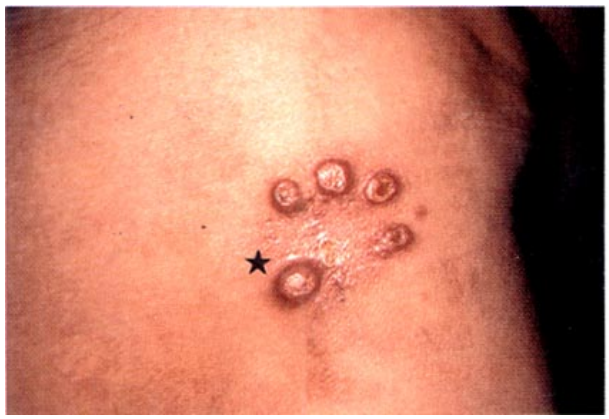

Fig. 1. Well circumscribed, discrete, brown colored, multiple nodules on the right thigh(* : biopsy site).

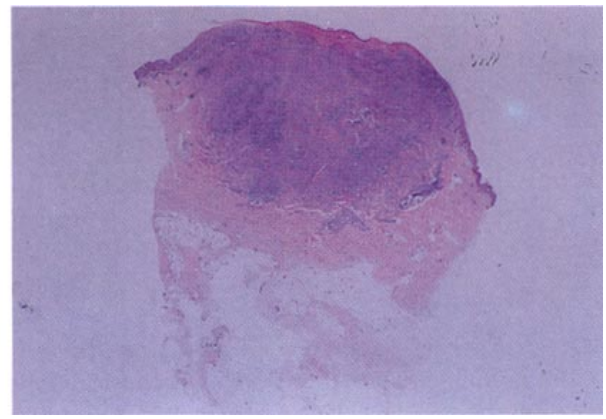

Fig. 2. Elevated and well circumscribed dermal tumor(H & E, ×10).

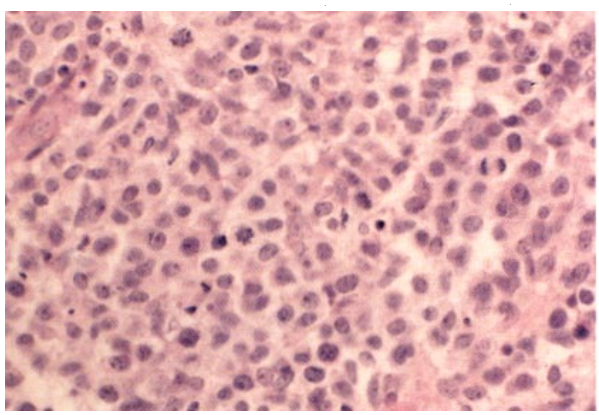

Fig. 3. Biopsy specimen shows cohesive sheets of large lymphomoid cells with round, oval, irregular-shaped nuclei, prominent nucleoli, and abundant cytoplasm(H&E, ×400).

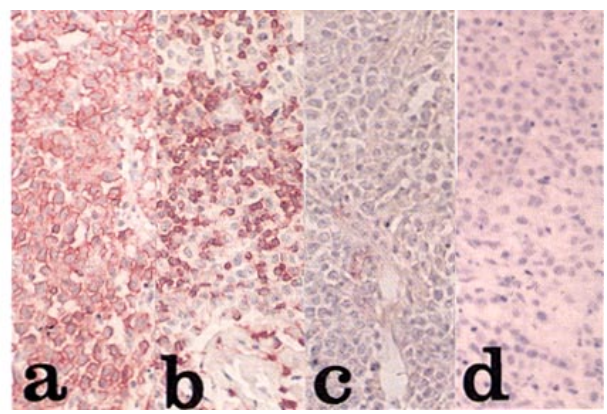

Fig. 4. Immunohistochemical stainings show positive reactions to CD30(A), UCHL-1(B), and negative reactions to MB2(C), EMA(D)(×100, ×200).

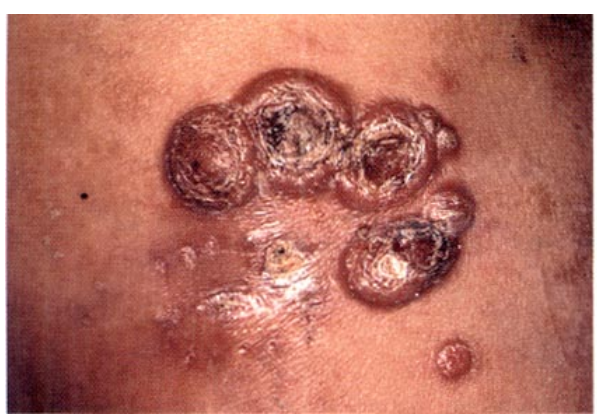

Fig. 5. The nodules became coalescing and multiple ulcerating nodules can be seen. A new single nodule developed, one month later.

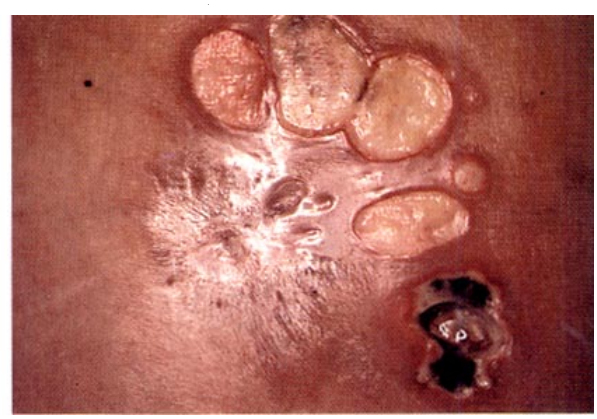

Fig. 6. Spontaneous regression with ulceration and necrosis occurred, 2 months later.

and also spontaneously resolved in 2 months. Thirdly a single nodule developed on the same site 1 year ago. This single nodule was removed by excision at a local clinic. After that, new 5 nodules developed on the same area. The family and past medical histories were not significant. Palpable lymph nodes were not detectable. Results of a complete blood count, urinary analysis, and blood chemistry analysis were either within normal limits or negative except a white blood cell count that was 11.000/mm^3 with 42% lymphocytes.

A skin biopsy specimen revealed an elevated and well-circumscribed dermal tumor(Fig. 2). Tumor cells showed a cohesive growth pattern forming large clusters. The tumor showed dense non-epidermotrophic infiltrates of atypical tumor cells with round, oval, irregularly shaped nuclei with abundant cytoplasm(Fig. 3). There were variable accompanying infiltrates of lymphocytes, eosinophils, and histiocytes at the periphery of these clusters. The immunohistochemical studies demonstrated that most proliferating lymphoid cells in the dermis were positive for CD30, pan-T cells(UCHL1, MT1), and LCA, negative for pan-B cells(MB2, L26), S-100 protein, monocyte-macrophage-related antigen(CD68), CEA, cytokeratin, and EMA(Fig. 4). Staging tests including chest roentgenography, UGI, a Barium enema, bone scan and brain computer tomography did not reveal any extracutaneous involvement. A peripheral blood smear finding revealed no evidence of circulating atypical lymphocytes. Bone marrow aspiration showed granulocytic hyperplasia with eosinophilia.

One month later, the nodules became coalescing and ulcerating, and a new single nodule developed nearby(Fig. 5). Two months later, spontaneous regression with ulceration and necrosis occurred(Fig. 6). Four months later, a new papulonodules appeared on the same area. The patient did not receive any specific treatment.

DISCUSSION

Cutaneous CD30+ lymphoma composed of sheets of atypical lymphoid cells with pleomorphic or anaplastic nuclei arise in the skin, either primarily or following involvement of other sites.[1-2,10].

According to Willemze and Beljaards[4], CD30 expression is exhibited in various cutaneous CD30+ lymphoproliferative disorders; firstly, primary cutaneous CD30+ lymphoproliferative disorders including primary cutaneous anaplastic or non-anaplastic CD30+ large cell lymphoma, LyP, primary cutaneous Hodgkin's disease, and boderline cases. secondly, cutaneous CD30+ lymphoma resulting from another type of cutaneous lymphoma such as MF and LyP. thirdly, secondary cutaneous involvement of a primary non-cutaneous CD30+ large cell lymphoma or of Hodgkin's disease. Our patient belonged to the first group, because there were no other types of cutaneous lymphoma and primary non-cutaneous CD30+ LCL or of Hodgkin's disease. Also our patient showed characteristics of primary cutaneous CD30+ LCL of the first group. Willemze and Beljaards[4] defined primary cutaneous CD30+ LCL, including the anaplastic or non-anaplastic types, by the following criteria: 1) predominance (>75%) or large clusters of CD30+ blast cells in the initial skin biopsy specimen 2) no evidence of LyP 3) no prior or concurrent LyP and MF of other types of cutaneous lymphoma 4) no extracutaneous localization at presentation. Our case satisfied the above criteria. Recent studies have demonstrated many differences between primary cutaneous and primary non-cutaneous CD30+ LCL clinically and histologically[3]. Primary cutaneous CD30+ LCL is characterized by being confined to the skin with solitary or localized skin lesions, frequent cutaneous relapses, a peculiar tendency to spontaneous regression(about 25%), and a favorable prognosis. However, primary non-cutaneous CD30+ LCL usually shows a rapid spread into the other lymph node regions and non-lymph organs including the skin, and has an unfavorable prognosis[4,7]. Primary cutaneous CD30+ lymphoma generally occurs in adults and, in contrast to primary non-cutaneous CD30+ LCL, is rarely seen in children and adolescents. The neoplastic cells are often positive for the cutaneous lymphocyte-associated antigen HECA-452 and do not generally express the epithelial membrane antigen(EMA), in contrast to primary non-cutaneous CD30+ LCL[9-12].

Our patient had typical features of primary cutaneous CD30+ LCL that: 1) satisfied the criteria by Willemze and Beljaards, 2) showed typical clinical findings including being confined to the skin with localized skin lesions, frequent relapses, and spontaneous regressions, 3) were old in age, 4) were of T-cell origin(positive for UCHL1, MT1), and negative for EMA.

Primary cutaneous CD30+ LCL must be differentiated from other cutaneous CD30+ lymphoproliferative disorders, especially LyP. The spontaneous regression and recurrences in our patient are similiar to the clinical course of Lyp[13]. However the clinical presentation was clearly different: there are multiple disseminated papules in LyP, but several localized nodules were present in our case. Histologically, both diseases have common large, atypical cells expressing the CD30 antigen. However, our case differed from LyP in several aspects. Our case showed the cohesive growth pattern of CD30+, atypical and inflammatory cells, and mainly eosinophils and lymphocytes were located at the periphery of the clusters. In LyP it does not show cohesive sheets of CD30+ cells and CD30+ atypical cells often show considerable admixture with inflammatory cells, in particular neutrophils and/or eosinophils. In primary cutaneous Hodgkin's disease, histological features useful for differentiating CD30+ LCL from Hodgkin's disease are dense concentration of neoplastic cells, their cohesive nature and sparsity of typical Reed-Sternberg cells[14]. There are reports about borderline cases of LyP or CD30+ LCL, that are LyP with the histological features of a CD30+ LCL and CD30+ LCL with histological features of LyP type A[4].

The atypical cells of LyP and cutaneous CD30+ lymphoma can share aberrant T-cell phenotypes and clonal rearrangement of the T-cell receptor α and ß genes in most cases. CD30 expression by lymphocytes was thought to be stimulated by infection with viruses such as EBV and HTLV-1[15-17]. In immunosuppressed patients, CD30+ LCL are apt to harbor the EBV, possibly clonally intergrated into the genomes of the neoplastic cells. The increased frequency of CD30+ LCL in patients with HIV disease suggests that HIV itself could upregulate CD30+[18]. Chromosomal abnormalities were observed in CD30+ LCL, such as a reciprocal translocation involving the short arm of chromosome 2 (band p23) and the long arm of chromosome 5 (band q35), t(2;5)(p23;q35)[19], and abnormality of chromosomal 7, which encodees the γ and ß chain of the T cell receptor. Our patient did not have the serologic tests for HTLV-1 and HIV, in situ hybridization for EBV, TCR gene rearrangement, and chromosomal study.

The treatment of primary cutaneous CD30+ LCL varies depending on the initial clinicopathological diagnosis and extent of the disease, but treatment of these localized cutaneous forms seems to be local radiation therapy or surgical resection. Only in patients with more generalized skin lesions, who seem to have an increased risk of systemic disease, and in patiens in whom systemic disease develops, systemic chemotherapy should be administrated[3,4]. In European multicenter study of 47 patients[3], only four patients showed repetitive spontaneous regression of cutaneous relapses. 38 patients had a relapse after non-treatment or treatment. These relapsing lesions often had the same morphology and were generally located in the same anatomic area as the initial skin lesions. Twelve patients developed extracutaneous disease. The follow-up data showed that 36 of 47 patients are alive without disease; four patients have died of systemic lymphoma, and seven have died of unrelated causes.

Although both primary cutaneous CD30+ LCL and LyP share some features of a benign and protracted course of disease, both diseases should be closely followed-up, because primary cutaneous CD30+ LCL can have extracutaneous spreading and LyP can progress to secondary cutanoeus CD30+ lymphomas.

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