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Coexisting Mycosis Fungoides and Hodgkin's Disease as a Composite Lymphoma: A Case Report

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Within the past few years, an increasing number of reports of Hodgkin's disease following the diagnosis of, and frequently coexisting with, mycosis fungoides have appeared. Previously, Hodgkin's disease found in the lymph nodes of the patient diagnosed as mycosis fungoides was considered as a transformed form of the mycosis fungoides. But, now it has been proven that Hodgkin's disease and mycosis fungoides are histologically and immunohistochemically distinct disease entities. We report a well-documented case of a man who developed Hodgkin's disease and mycosis fungoides simultaneously as a composite lymphoma. Our case emphasizes the importance of considering the diagnosis of another lymphoma in patients with mycosis fungoides who have lymphadenopathy. The cutaneous mycosis fungoides and the Hodgkin's disease should be treated as an independent disease.

Key Words: Mycosis fungoides, Hodgkin's disease, composite lymphoma

Hodgkin's disease and mycosis fungoides have been reported in the same patient (Chan *et al.* 1979; Donald *et al.* 1980; Powell *et al.* 1980; Lipa *et al.* 1982; Hawkins *et al.* 1983; Caya *et al.* 1984; Scheen *et al.* 1984; Simrell *et al.* 1986). This coexistence has been debated in the medical literature. The earlier medical literatures described the coexistence of mycosis fungoides and Hodgkin's disease in the same patient as a single disease entity (Block *et al.* 1963; Cyr *et al.* 1966). At this time, it is accepted that mycosis fungoides transforms to reticulum cell sarcoma, lymphosarcoma, leukemia, Hodgkin's disease, or other lymphomas in its terminal stage (Hamington 1976; Lofgren *et al.* 1978). But Rappaport and Thomas (1974), and Long and Mihm (1974) had challenged this concept. In their autopsy series, neither group found out any evidence of evolution, or transformation of mycosis fungoides to any other lymphoma. Rappaport pointed out that, because of the frequent presence of a pleomorphic cellular infiltrate, often with eosinophils and bizarre mononuclear giant cells that resemble Reed-Sternberg cells, the erroneous diagnosis of transformation to Hodgkin's disease could have been made.

Furthermore, recent studies have reported that, in patients with longstanding cutaneous mycosis fungoides, nodal lymphomas with different morphologic pictures from cutaneous T-cell lymphoma may also develop-for example, Hodgkin's disease and other forms of T-cell lymphomas, or B-cell type lymphomas (Scheen *et al.* 1984). And immunohistochemically, the coexistence of Hodgkin's disease and mycosis fungoides has been also proven (Simrell *et al.* 1986). In the present article, we report a case in which mycosis fungoides and Hodgkin's disease had coexisted in the same patient as a composite lymphoma.

CASE REVIEW

A 37-year old male was admitted to Severance

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Hospital in March 1985 for the evaluation of multiple erythematous scaly patches and nodules on the neck, both shoulders, and the interscapular area that he had first noticed in 1975. He had been treated for rheumatoid arthritis with nonsteroidal anti-inflamatory drugs during the past ten years. Except for the rheumatoid arthritis, he had been relatively in good health. On physical examination, erythematous scaly patches and nontender nodules were found on the neck, both shoulders and the interscapular area (Fig. 1). And a lx1 cm sized movable mass was palpated on the right axillary lymph node area. The hemoglobin was 13.3 g/dl. The white blood cell count was 6,800/mm^3 with lymphocyte 56%, segmental neutrophil 28% and eosinophil 16%. The total eosinophil count was 555/mm^3. The platelet count was 411,000/mm^3. The ESR by the Wintrobe method was 47 mm/hr. An ultrasonogram of the abdomen showed no abnormality. Biopsy specimens of skin from the back and shoulder revealed mycosis fungoides extending into the dermis (Fig. 2, 3). Biopsy specimens of lymph nodes from the axilla revealed a lymphoma which was diagnosed as Hodgkin's disease with mixed cellularity (Fig. 4, 5). The bone marrow finding was normal without any evidence of involvement of mycosis fungoides or Hodgkin's disease. We considered the axillary lymph node as the nodal involvement of mycosis fungoides and it's tranformation, because at that time, we did not have the concept of the coexisting mycosis fungoides and Hodgkin's lymphoma. So, we diagnosed the diasese as a stage IVA (T3N3MO) of mycosis fungoides. The patient received photochemical therapy with oral methoxalen followed by ultraviolet A light irradiation to the entire skin surface (PUVA: 8-MOP was given per os, and 2 hour after 8-MOP, 3 J/cm^2 of UVA was administered with an increasing step dosage of 0.5 J/cm^2, for a total of 6 cycles). Radiotherapy was given with 6 MeV electron beam to the interscapular area and both arms, respectively, and 15 MeV electron beam to the right axilla. Finishing the radiotherapy of 3450 cGy, the skin lesions and the axillary lymphadenopathy were completely controlled; a clinical complete remission was induced. After the following 4 years of complete remission, the patient was readmitted due to fever, night sweating, and weight loss of 8 kg during the past 4 months. On physical examination, multiple neck nodes and axillary nodes were palpated on both sides. A biopsy was done in the neck and axillary nodes, which showed histological features of Hodgkin's disease of mixed cellularity as previously diagnosed. The chest X-ray, abdominal ultrasonogram

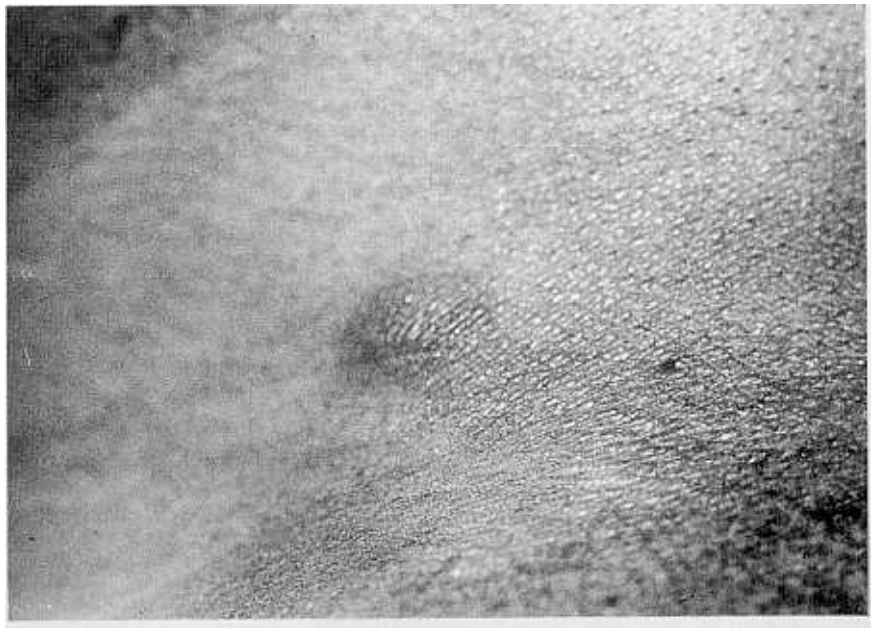

Fig. 1. Well defined, pea-sized, erythematous papule on the shoulder.

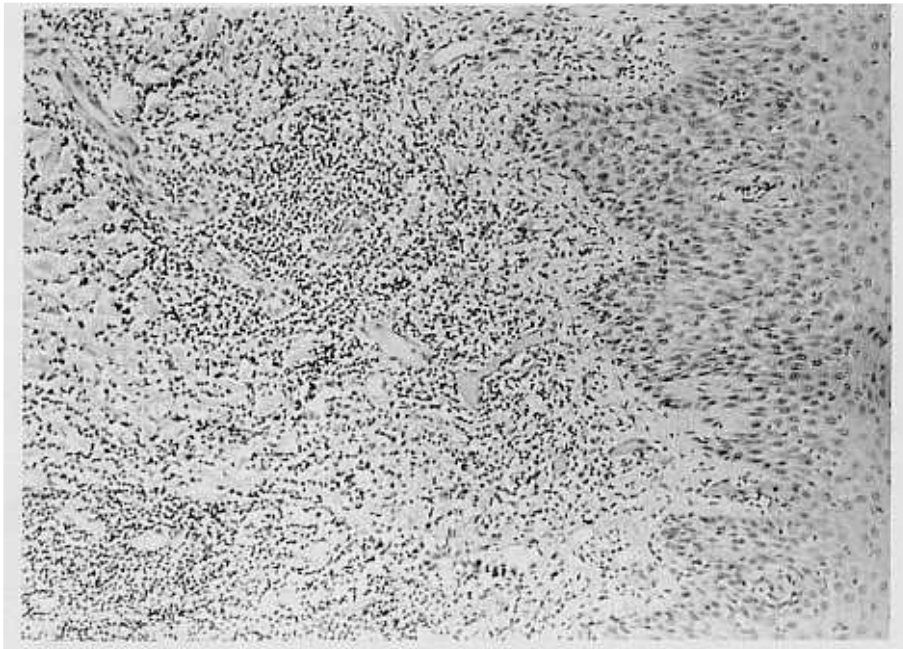

Fig. 2. Skin biopsy: diffuse dermal infiltration of lymphocytes with epidermotropism (H & E, × 100).

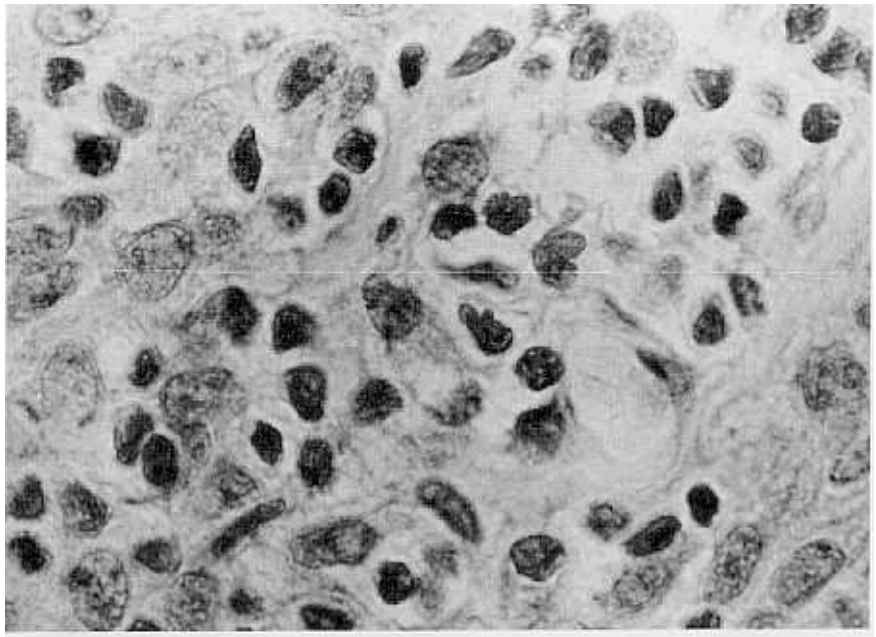

***Fig. 3.** Skin biopsy: Epidermal infiltration of atypical lymphocytes showing nuclear convolution (H & E, × 1000).*

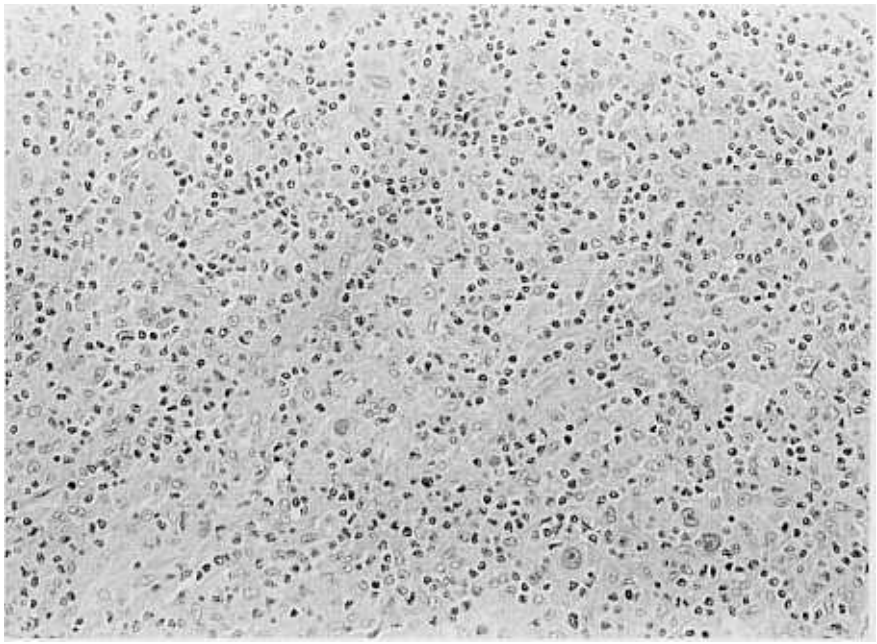

Fig. 4. Axillary lymph node biopsy: diffuse effacement of nodal structure (H & E, × 100).

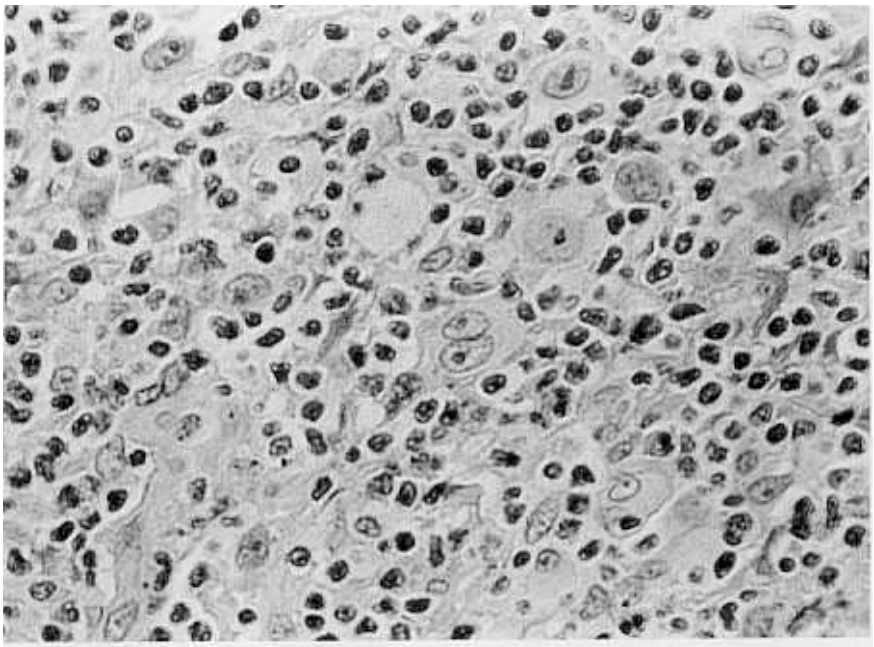

Fig. 5. Axillary lymph node biopsy: backgroud infiltration of mature lymphocytes and eosinophils with scattered Reed-Sternberg and Hodgkin's cells (H & E, × 400).

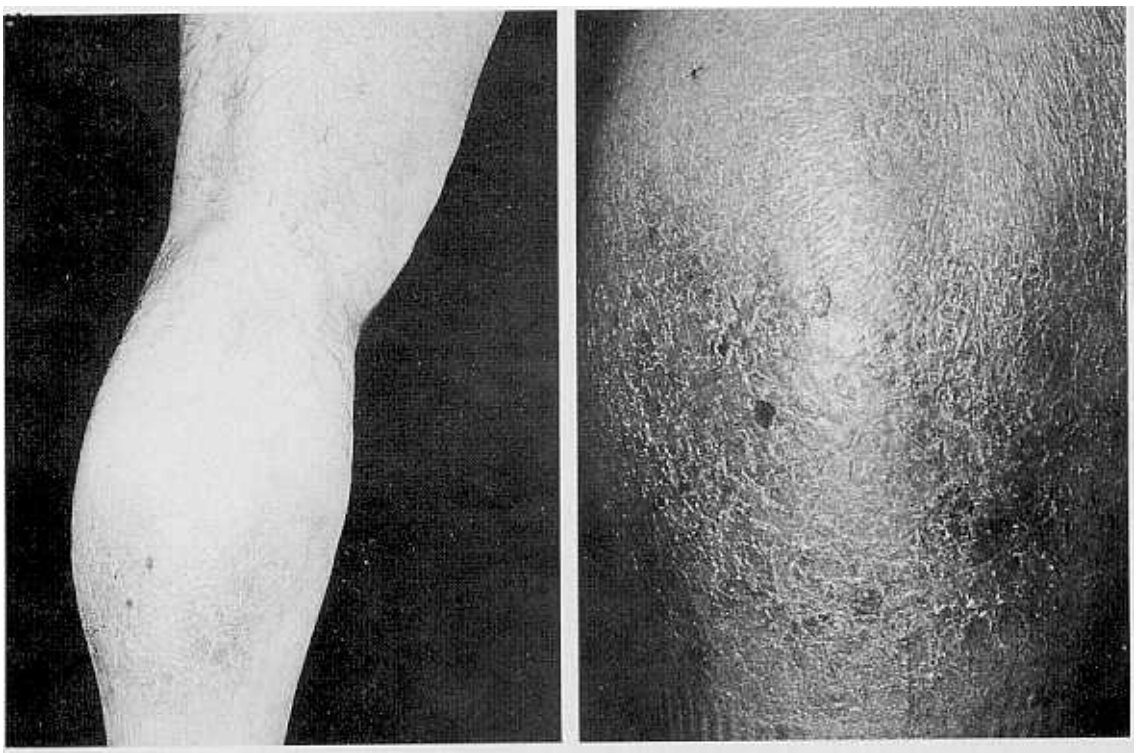

Fig. 6. *16 cmx14 cm sized, erythematous to dark-brown colored fine scaly large plaque with some induration on the left leg.*

and bone marrow study were all normal. The patient was diagnosed as Hodgkin's disease in stage IIB. After 1 cycle of ABVD regimen (Adriamycin 25 mg/m^2 day 1 and 8, Bleomycin 10 Unit/m^2 day 1 and 8, Vinblastine 5 mg/m^2 day 1 and 8, DTIC 250 mg/m^2 day 1 and 8), a clinical complete remission was achieved. A total 6 cycles of ABVD chemotheraphy was administered. Unfortunately, 2 months after finishing the chemotherapy, 16 cmx14 cm sized, erythematous dark-brown colored, fine scaly large plaques developed on the left leg and ill defined patches also developed on both thighs (Fig. 6). However, no lymphadenopathy was found on physical examination. The skin biopsy of the leg showed lichenoid inflammation with focal atypical T lymphocyte infiltration, consistent with mycosis fungoides. He is now being treated with topical application of mechlorethamine hydrochloride and electron beam radiotherapy with a partial response.

DISCUSSION

Mycosis fungoides is one of a spectrum of malignant T-cell lymphomas with a predilection for the skin (epidermis and upper dermis) (Lutzer *et al.* 1975; Broder and Bunn, 1980). The malignant cells in mycosis fungoides are mature, thymic-dependent (T) lymphocytes generally with helper/inducer (T4) phenotypes (Broder *et al.* 1976). Hodgkin's disease is a neoplastic disorder originating in lymphoid tissue and defined by the presence of the Reed-Sternberg cell. Controversy remains concerning the origin of the malignant cell of the Hodgkin's disease or the Reed-Sternberg cell. Initially, various observers suggested that the neoplastic elements were malignant histiocytes (Rappaport, 1966). However, immunoblasts and lymphocytes stimulated by an antigen or mitogen may resemble Hodgkin cells, and these findings lead to the proposal that Hodgkin cells are malignant B lymphocytes (Order 1972;

Table 1. Summary of 18 cases with mycosis fungoides and Hodgkin's disease

Case	Age/Sex	Sequence of diagnosis	Types of the HD	Duration of skin lesions prior to diagnostic skin biopsy(year)	Interval between the diagnosis	Status and survival
1	62/m	MF, HD	NS	8	2 year	5 year, died from MF
2	53/m	MF, HD	NS	13	2 year	3 year, alive with MF
3	46/m	MF, HD	NS	15	simultaneous	2 year, died from HD
4	51/m	MF, HD	MC	19	1 year	3 year, alive with MF
5	28/m	MF, HD	NS	6	15 year	15 year, alive (NED)
6	61/m	HD, MF	NS	?	7 year	8 year, alive (NED)
7	54/m	HD, MF	LP	11	12 year	12 year, alive with MF
8	63/m	MF, HD	MC	15	26 year	38 year, alive (NED)
9	39/m	MF, HD	MC	20	1 year	5 year, alive (NED)
10	66/m	HD, MF	MC	3	1 year	3 year, alive with MF
11	22/m	MF, HD	LD	20	1 year	14 month, alive (NED)
12	24/m	HD, MF	NS	22	8 months	8 month, alive with MF
13	46/m	MF, HD	MC	10	?	10 month, died
14	51/m	MF, HD	NS	13	?	6 year, alive
15	80/m	MF, HD	LD	25	?	6 month, alive
16	58/m	MF, HD	NS	4	?	5 year, alive
17	57/m	HD, MF	MC	1	1 year	6 year, died from MF
18	44/m	HD, MF	NS	3	2 year	3 year, alive (NED)

MF; mycosis fungoides, HD; Hodgkin's disease, NS; nodular sclerosis, MC; mixed cellularity, LP; lymphocyte predominant, LD; lymphocyte depletion, NED; no evidence of disease

De Vita 1973; Poppema *et al. 1982*). Therefore, mycosis fungoides and Hodgkin's disease are believed to be the distinct disease entities within the broad category of malignant lymphomas (Simrell *et al.* 1986).

During the past few years, an increasing number of reports of Hodgkin's disease following mycosis fungoides have appeared. And, previously, the Hodgkin's disease found in the lymph nodes of the patient diagnosed as mycosis fungoides was considered as a trasnformed form of mycosis fungoides. Recently, although the nature of lymphomas that develop in mycosis fungoides has been a subject of debate, Rappaport and Thomas (1974) concluded that earlier reports of mycosis fungoides evolving into the different types of lymphoma were unconvincing. Also, they concluded that mycosis fungoides retains its specific and distinctive histologic and cytologic features throughout the course of the disease. Moreover, Long and Mihm (1974) noted the difference that cutaneous lesions of mycosis fungoides usually occurs before the systemic disease, while, in Hodgkin's disease, the cutaneous dissemination usually occurs as a late sequelae of systemic disease. And finally, Simrell *et al.* (1986) showed the immunophenotypical proofs of the coexistence of the mycosis fungoides and Hodgkin's disease as two different disease entities.

During the literature review, we accumulated 18 reported instances of mycosis fungoides and Hodgkin's disease in the same patient (Table 1). We excluded the patients who were reported during the earlier period when the concept of transformation of mycosis fungoides to Hodgkin's disease was well accepted. With the exception of 7 cases, Hodgkin's disease followed the diagnosis of mycosis fungoides by months to years. And alomost all patients had a long history of skin lesions typical of mycosis fungoides. Reviewing these patients, some clinical pictures emerge; old patients except females, male preponderence, recurrent episodes of mycosis fungoides during the course. Our case emphasizes the importance of considering the diagnosis of another lymphoma in patients with mycosis fungoides who have lymphadenopathy. Practically, it is a very important point because, unlike the disseminated form of the nodal mycosis, Hodgkin's disease is curable. On the contrary, it also can be suggested that some cases of cutaneous mycosis fungoides may be misdiagnosed as a cutaneous recurrence of

Table 2. Distribution of composite lymphoma according to the histologic composition (Kim *et al.* 1977)

Non-Hodgkin's lymphomas		Hodgkin's disease and non-Hodgkin's lymphoma	
Histologic composition	Number of the patients	Histologic composition	Number of the patients
NLP+DH	7	LPHD+DMHL	1
NLPD+NH	2	LPHD+DH	1
NMHL+DH	2	NSHD+NLPD	2
NLPD+NMHL	1	NSHD+NH	1
		NSHD+DH	1
		MCHD+NLPD	1
		MCHD+NLPD UCHD+NMHL	1

NLPD; nodular lymphoma, poorly differentiated, DH; diffuse histiocytic lymphoma, NMHL; nodular lymphoma, mixed histiocytic lymphocytic, NH; nodular histiocytic lymphoma, NSHD; Hodgkin's disease, nodular sclerosing type, LPHD; Hodgkin's disease, lymphocyte predominant type, DMHL; diffuse lymphoma, mixed histiocytic lymphocytic, MCHD; Hodgkin's disease, mixed cellularity type, UCHD; Hodgkin's disease, unclassified

Hodgkin's disease in patients with systemic Hodgkin's disease. Therefore, such patients should be investigated and treated appropriately, because the cutaneous mycosis fungoides and Hodgkin's disease should be treated as independent disease.

Most of the reported cases showed the coexistences of mycosis fungoides and Hodgkin's disease during the disease course after the diagnosis of each disease with some intervals. But there is only one case with the simultaneous occurrence of both disease from the diagnosis similar to our case. The term-composite lymphoma' has been proposed for the occurrence of two different histologic types of lymphoma at the same time either in one organ or two separate organs (Custer *et al.* 1954). Although the term has been perpetuated by Rappaport *et al.* (1956) with the special reference to the non-Hodgkin's lymphomas, and broadened again to the Hodgkin's disease by Kim *et al.* (1977), the present case could be cited as an example of the composite lymphoma. It's true incidence is difficult to assess. Kim and Dorfman (1974) had reported 3 cases of composite lymphoma in 84 patients of non-Hodgkin's lymphoma, yielding an incidence of 3.5%. Kim *et al.* (1977) also reviewed 17 additional cases. According to them, the most frequent combination type was that of diffuse histiocytic lymphoma and nodular, poorly differentiated lymphocytic lymphoma based on the criteria of Rappaport. The combination of non-Hodgkin's lymphoma and non-Hodgkin's lymphoma was more common than that of non-Hodgkin's lymphoma and Hodgkin's disease (Table 2).

In our case, the Hodgkin's disease had coexisted with mycosis fungoides from the initial onset. But in 1985, we had considered the Hodgkin's disease of the axillary lymph node showing Reed-Sternberg cells as the transformation of mycosis fungoides, and treated our patient for mycosis fungoides with PUVA and radiotherapy. When Hodgkin's disease recurred after 4 years of remission, we reviewed the previous pathology slide; the skin biopsy showed a cell type with hyperchromatic, multiply-indented nuclei which is consistent with mycosis fungoides, and the lymph node biopsy showed infiltration of mature lymphocytes and eosinophils with scattered Reed-Sternberg cells, which are the characteristic findings of Hodgkin's disease with mixed cellularity. So, we concluded our final diagnosis as a composite lymphoma and to our knowledge, this is the first case of composite lymphoma combined with mycosis fungoides and Hodgkin's disease in Korea.

Reviewing the reported cases of the composite lymphoma, the prognosis was determined by the more aggressive type of the composite lymphoma. There was no difference between the single lymphoma and the composite lymphoma in the clinical course except for that the latter was somewhat complicated by anothers component of the composite lymphoma. We treated the patient as a independent disease when the Hodgkin's disease and mycosis fungoides recurred.

In conclusion, it is important to remeber the possibility of a coexisting other lymphoma, especially in patients with longlasting cutaneous mycosis fungoi-

des. Therefore, we should not consider a lymphadenopathy in mycosis fungoides patients as a nodal mycosis before nodal biopsy, because the nodal involvement of the mycosis fungoides is of poor grognosis, while the Hodgkin's disease is curable especially in the early stage.

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