Breast Carcinoma in Patients with Dermatomyositis: A Retrospective Analysis of Eight Cases

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Background: The association between dermatomyositis and breast carcinoma has not been fully evaluated yet. The aim of the study was to clarify characteristics of the association between these two diseases.

Methods: The medical records of 128 patients with dermatomyositis or polymyositis from 1990 to 1998 were retrospectively reviewed. Eight patients (6.3%) were identified with dermatomyositis which was associated with an underlying breast carcinoma. Clinical features, laboratory data, electromyograms, muscle biopsies, and the prognoses of these patients were assessed.

Results: The mean age of the 8 patients with breast carcinoma and dermatomyositis (62.1 ¡ 6.7 years) was larger than that of patients with breast carcinoma without dermatomyositis (48.5 ¡ 11.8 years). Dermatomyositis preceded breast carcinoma in 2 patients, was concurrent with breast carcinoma in 5 patients, and followed breast carcinoma in 1 patient. Of these 8 patients, 4 had TNM classification stage IV (M1) breast cancer, 1 had IIIA (T2N2M0) breast cancer, and 3 had IIB (T2N1M0) breast cancer. The follow-up period ranged from 2 to 79 (median, 21) months. Five patients died of recurrence or distant metastasis, and the remaining 3 patients had disease-free survival, with a follow-up period ranging from 11 to 28 (median, 20) months. Four of 5 patients had parallel improvement in dermatomyositis after surgical treatment of breast carcinoma.

Conclusion: In Taiwan, dermatomyositis is associated with an increased incidence of breast carcinoma. The mean age of the 8 patients with breast carcinoma and dermatomyositis was significantly larger than that of patients with breast carcinoma without dermatomyositis. If present, breast carcinoma can precede, occur concurrently with, or follow the diagnosis of dermatomyositis. Surgical treatment of breast carcinoma may alleviate the course of dermatomyositis and eliminate the need for steroids in some cases.

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Key words: breast carcinoma, dermatomyositis.

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Dermatomyositis is a rare disease of unknown origin. It is characterized by symmetric, proximal muscle weakness, and specific cutaneous findings such as Gottron's papules, heliotrope rashes, periungual telangiectasis, and so on. In 1916, Sterz first reported the association of dermatomyositis with gastric carcinoma.[1] Kankeleit reported the first case of breast carcinoma associated with dermatomyositis in the same year.[2] The rate of dermatomyositis associated with malignancy ranges from 3% to 60%.[3] In a large population-based study of 788 Swedish patients in 1992, increased incidences of cancer and mortality were found in patients with polymyositis and dermatomyositis. In the dermatomyositis group, the rate of breast cancer concurrent with or subsequent to the diagnosis was 2.04% (8 of 392 patients).[4]

However, the incidence of breast carcinoma with dermatomyositis, the influence of dermatomyositis on the clinical course, the associated complications, and the survival of patients with breast carcinoma after treatment still remain unclear. The aim of this study was therefore to retrospectively review the data of breast carcinoma patients with dermatomyositis to better understand the clinical courses of and relationship between these 2 diseases.

METHODS

From 1990 to 1998, there was a total of 2658 consecutive patients with histopathologically proven breast carcinoma treated at the Department of Surgery, Chang Gung Memorial Hospital, Taipei, Taiwan. Among them, 8 patients had concurrent dermatomyositis.

During the same time period, there was a total of 128 patients with dermatomyositis or polymyositis treated at the Department of Dermatology or Rheumatology. Dermatomyositis was diagnosed as defined by Bohan and Peter.[5] Electromyograms were performed and interpreted by neurologists, and muscle biopsy specimens were examined by pathologists.

Breast cancer occurred before, concurrently with, or following the diagnosis of the musculocutaneous disease. The condition that breast cancer and dermatomyositis occurred within 6 months of each other was defined as being concurrent. The breast cancer was staged according to the American Joint Committee on Cancer (AJCC) system for breast carcinoma. Clinical features, laboratory data, management, and long-term survival were assessed.

RESULTS

Description of patients

Forty (31%) of 128 patients with dermatomyositis or polymyositis had a concurrent malignancy (Table 1). Eight of these had breast carcinoma associated with dermatomyositis. Malignancies in the remaining 32 patients included nasopharyngeal carcinoma (12 cases), head and neck tumor (5 cases), lung cancer (4 cases), malignancy of unknown origin (3 cases), hepatocellular carcinoma (1 case), gastric carcinoma (1 case), and others (6 cases).

Table 1. Types of Malignancy Associated with Dermatomyositis

Type of associated malignancy	No. of cases (%)
Nasopharyngeal carcinoma	12 (30)
Breast cancer	8 (20)
Head and neck tumor	5 (12.5)
Lung carcinoma	4 (10)
Malignancy of unspecified site	3 (7.5)
Hepatocellular carcinoma	1 (2.5)
Gastric carcinoma	1 (2.5)
Other	6 (15)
Laryngeal carcinoma	1 (2.5)
Bone cancer	1 (2.5)
AML	1 (2.5)
Rectal carcinoma	1 (2.5)
Brain tumor	1 (2.5)
Pleura carcinoma	1 (2.5)
Total	40 (100)

Abbreviation: AML: acute myeloid leukemia.

The mean age of diagnosis of breast carcinoma of the 8 patients with breast carcinoma and dermatomyositis was significantly larger than that of patients with breast carcinoma without dermatomyositis (62.1 ¡ 6.7 vs. 48.5 ¡ 11.8 years) ($p < 0.0001$).

All 8 breast cancer patients with dermatomyositis had muscle weakness and scaly erythematous patches on the face, trunk, or extremities as well as

Table 2. Clinical Features of 8 Patients with Dermatomyositis and Breast Carcinoma

Case no.	1	2	3	4	5	6	7	8
Gender	F	F	F	F	F	F	F	F
Age at onset of dermatomyositis/breast cancer	61/58	59/59	62/62	58/58	54/54	65/68	63/63	74/75
Lag period to malignancy (months)	-32	5	-4	3	6	29	-6	10
Muscle weakness, heliotrope sign, and Gottron's papule	P	P	P	P	P	P	P	P
Muscle biopsy; EMG	ND/ND	P/P	P/ND	ND/ND	P/P	P/ND	ND/ND	P/P
CPK (IU/l)	ND	230	622	505	149	159	ND	32
Treatment of dermatomyositis with prednisolone (mg/day)	no	45	20	30	30	45	no	45
Breast lump	P	P	P	P	P	P	P	P
Breast echo	ND	P	ND	ND	P	P	P	P
Mammogram	ND	ND	ND	ND	P	P	P	P
Staging	IV (M1)	IIB (T2N1M0)	IV (M1)	IV (M1)	IIIA (T2N2M0)	IIB (T2N1M0)	IV (M1)	IIB (T2N1M0)
ER/PR	NA/NA	N/N	NA/NA	N/N	N/N	N/N	NA/NA	N/N
Management	MRM	MRM/C/T	C/T+R/T	C/T	induction C/T/ MRM	MRM/C/T	C/T	MRM
Influence on dermatomyositis after management	NA	stopped steroid use	rash subsided; no recovery from muscle weakness	NA	stopped steroid use	stopped steroid use and CPK:23	NA	stopped steroid use
Outcome (survival time/status)	37 mo/M	79 mo/M	22 mo/M	2 mo/M	28 mo/DFS	20 mo/DFS	15 mo/M	11 mo/DFS

Abbreviations: No: number; F: female; ND: not done; EMG: electromyogram; P: positive; CPK: creatine phosphokinase; IU: international units; NA: not available; ER: estrogen receptor; PR: progesterone receptor; N: negative; MRM: modified radical mastectomy; C/T: chemotherapy; R/T, radiotherapy; mo: months; M: mortality; DFS: disease-free survival.

other various cutaneous manifestations. Breast cancer occurred in 5 women within a mean period of 10.6 (range, 3 to 29) months after the diagnosis of dermatomyositis. The remaining 3 patients had breast carcinoma at a mean period of 14 (range, 4 to 32) months before the diagnosis of dermatomyositis. All 8 patients demonstrated a palpable breast lump during a breast examination (Table 2). One patient was diagnosed as having breast carcinoma before the diagnosis of dermatomyositis, and it was a stage IV breast carcinoma. Five patients were diagnosed as having breast carcinoma concurrent with dermatomyositis; 3 were at stage IV, 1 at stage IIB, and 1 at stage IIIA. Four of these 5 patients died of distant metastasis of the breast carcinoma in a median of 22 (range, 2 to 79) months. The other 2 patients were diagnosed as having dermatomyositis before the diagnosis of breast carcinoma, and they had stage IIB disease. Totally, 5 patients received a modified radical mastectomy among which 1 received induction chemotherapy and 2 received adjuvant chemotherapy. Five of the 8 patients died of distant metastasis of the breast carcinoma. Four of these 5 patients had stage IV disease, and 3 received only chemotherapy (Table 2).

Musculocutaneous characteristics and influence of management

Dermatological lesions occurred in all 8 patients. Skin lesions consisted of distinctive hyperkeratic, follicular, erythematous papules. In all patients, the face, neck, shoulder, and upper limbs were eventually involved. Table 2 summarizes the time intervals between the diagnosis of breast carcinoma and dermatomyositis and the influence of treatment of breast carcinoma on the course of the dermatomyositis.

Muscle weakness was found in all 8 patients with skin eruptions, and this was confirmed by electromyograms in 3 patients and by muscle pathology in 2 additional patients. Bilateral symmetrical muscular involvement is the rule. The histopathologic features included degeneration of muscle fibers and infiltration by inflammatory cells. Elevated creatine phosphokinase levels (CPK, 20-170 IU/l) were noted in 3 of 6 patients tested when dermatomyositis was suspected. The dosage of steroids for treatment of dermatomyositis is listed in Table 2. Four patients recovered from the skin rash and muscle weakness and discontinued steroid use after surgical treatment of the breast carcinoma (patients 2, 5, 6, and 8; Table 2). One patient recovered from the skin rash after concurrent chemoradiotherapy (patient 3).

Survival analysis

All 8 patients were followed up over a median period of 21 (range, 2 to 79) months. Of the 5 patients who received a modified radical mastectomy, 4 recovered from the dermatomyositis; in these patients, the skin rash subsided, normal muscle power was regained, and they discontinued steroid use (Table 2). Three of these 5 patients receiving operative intervention had a mean disease-free survival of 20 (range, 11 to 28) months (Table 2). Of the 8 patients, the 1-year survival rate was 87.5%, and the 2-year survival rate was 54.7% (Fig. 1).

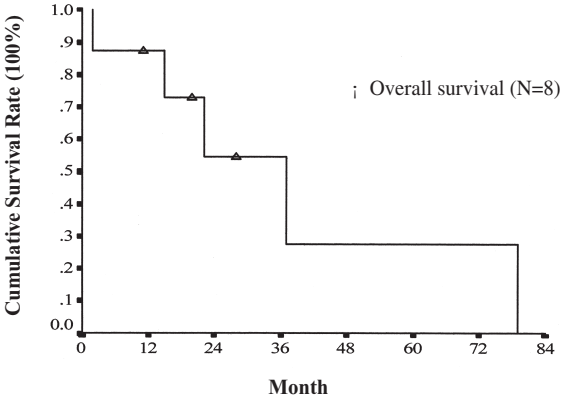

Fig. 1 Overall survival of the 8 patients with dermatomyositis and breast cancer.

DISCUSSION

Dermatomyositis is a disease of unknown etiology characterized by proximal muscle weakness and specific cutaneous signs. It has been reported that dermatomyositis is associated with an increased incidence of internal malignancy, ranging from 3% to 60%.[3] In our series, the incidence of internal malignancy associated with dermatomyositis was 31%. Regarding the associated tumor types, Callen and others found that the tumor types seem to roughly parallel those of the general population with carcinomas of the breast and lung being most common.[6] Similar to other reports from the Orient, nasopharyngeal carcinoma is the most common associated malignancy.[7-9] In our series, breast carcinoma was the second-most common associated malignancy.

In a large population-based study of 788 Swedish patients in 1992, increased incidences of cancer and mortality were found in patients with polymyositis and dermatomyositis.[4] In the dermatomyositis group, the incidence of breast cancer was 2.04% (8 of 392 dermatomyositis patients) concurrent with or subsequent to the diagnosis of dermatomyositis. In our series, the incidence of patients with dermatomyositis associated with breast cancer was 6.2%. In Taiwan, breast cancer is the second-most frequent malignancy in women and has become the fourth leading cause of death in women.[10] The incidence has been steadily increasing over the past few decades, as seen in other Asian countries.[8] The crude incidence of breast cancer in 1993 was 19.51 per 100,000, and it rose to 28.35 per 100,000 in 1996.[11] As seen in our study, the incidence of breast cancer in patients with dermatomyositis seems to be higher than that in the general population.

In our study, none of the 8 dermatomyositis patients had early-stage breast carcinoma, and this may explain the poor results in our series. Our recommendation is that all women presenting with dermatomyositis should have a thorough physical exam-

ination including a breast exam. Physical examination, breast ultrasonography, and a mammogram help make it possible to detect breast carcinoma early in patients with dermatomyositis.

The mean age of our 8 patients with breast carcinoma and dermatomyositis was larger than that of patients with breast carcinoma without dermatomyositis. This may partly explain the poor prognoses in our series. Basset-Seguin et al. reported that old age, the distribution of specific cutaneous signs, and an elevated erythrocyte sedimentation rate indicated a poorer prognosis for dermatomyositis with carcinoma.[12]

The relationship between the onset of dermatomyositis and the diagnosis of breast carcinoma is uncertain, as seen in the present study and in the literature.[13,14] Dermatomyositis may precede the occurrence of the malignancy by months to years, may be discovered concurrently with the malignancy, or may become evident several months after the malignancy is diagnosed. This investigation produced similar observations.

Like the temporal relationship between dermatomyositis and malignancy, the variability holds true for the influence of treatment of the associated malignancy on the clinical course of the dermatomyositis.[6] In our series, 4 of 5 patients who underwent surgical treatment of the breast carcinoma had parallel improvement in dermatomyositis, and 3 patients had disease-free survival. They recovered from the skin rash and muscle weakness, and discontinued using steroids.

Regarding the association between dermatomyositis and malignancies including breast carcinoma, the etiology and pathogenesis are not well understood. Several hypotheses have been proposed, including immune complex,[15] complement system,[16] cell-mediated immunity abnormality,[17] infectious diseases,[18,19] and HLA type.[20,21]

In conclusion, dermatomyositis is associated with an increased incidence of breast carcinoma in Taiwan. The mean age of patients with breast carcinoma and dermatomyositis being larger than that of patients with breast carcinoma might indicate that dermatomyositis is a poor prognostic factor. Physical examination may help detect the presence of breast carcinoma. If present, a breast carcinoma can occur before, concurrently with, or after the diagnosis of dermatomyositis. Surgical treatment of breast carcinoma may improve the myositic or cutaneous disease in a few cases.

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乳癌合併皮肌炎：8個病例的回顧性分析

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背 景： 皮肌炎與乳癌之間的關聯性仍未完全了解。這個回溯性的研究乃是分析一群乳癌病人合併皮肌炎的臨床特徵以進一步瞭解其相關性。

方 法： 對1990至1998年間128位患有皮肌炎或多發性肌肉炎患者做回溯性病例分析，其中有8位乳癌病人合併皮肌炎，我們就其臨床表現及預後做分析。

結 果： 患有乳癌合併皮肌炎之病人，其年齡比一般乳癌病患大，皮肌炎可以同時發生或是於發現乳癌之前或之後。2位病患發生於乳癌發現之前，5位病患與乳癌同時發現，1位病患發生於乳癌發現之後。這8位乳癌病人4位爲stage IV，1位爲stage IIIA及3位爲stage IIB乳癌，追蹤期限爲2至79個月。5位因爲乳癌復發或他處轉移死亡，其中3位乳癌病人接受手術後不僅乳癌不復發且皮肌炎獲得改善。

結 論： 在台灣，患皮肌炎病人其罹患乳癌之比例較高，外科處置乳癌後可以在一些病患改善皮肌炎之症狀並可以戒斷類固醇之使用。

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關鍵字：乳癌，皮肌炎。

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