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Dermatomyositis and malignancy: a retrospective study of 115 cases

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Abstract. – Aim of this study was to identify the association between dermatomyositis and malignancy in China.

Methods: **We retrospectively analyzed the clinical data of 115 cases of dermatomyositis associated with malignancy.**

Results: **From 1974 to 2008, there were 678 cases of dermatomyositis collected from the Second Affiliated Hospital, Sun Yat-Sen University, China. Among them, 115 cases (17.0%) were associated with malignancy. 7.4% (22/297) of patients under 40 years old were diagnosed with malignant tumor, while 24.4% (93/381) of patients aged 40 years or above were associated with malignancy. Malignancy preceded dermatomyositis in 14 cases. Dermatomyositis and malignancy were diagnosed at the same time in 22 patients. Another 79 patients were found to have cancer within 3 years after the dermatomyositis was diagnosed. Among them, cancer was detected in 66 patients in the first year, 11 patients in the second year and only 2 patients in the third year. Nasopharyngeal cancer made up 51.3% (59/115) of the associated malignancies, while lung cancer accounted for 17.4% (20/115). Other malignancies associated with dermatomyositis included liver cancer, ovarian cancer, cervical lymph node metastases of unknown origin, cholangial cancer, esophageal cancer, colon cancer, laryngeal cancer, renal cancer, tongue cancer and lymphoma.**

Conclusions: **Dermatomyositis associated with malignancy was more common in patients aged 40 years or above. Malignancy was often detected within the first year after the onset of dermatomyositis. The most common malignancy associated with dermatomyositis was nasopharyngeal cancer, followed by lung cancer in Guangdong, China.**

Key Words:

Dermatomyositis, Malignancy, Nasopharyngeal cancer, Lung cancer.

Introduction

Dermatomyositis is an idiopathic inflammatory myopathy with typical cutaneous manifestations. Bohan and Peter[1] divided the inflammatory myopathy into 5 groups: (1) primary idiopathic polymyositis; (2) primary idiopathic dermatomyositis; (3) dermatomyositis/polymyositis associated with neoplasia; (4) childhood dermatomyositis/polymyositis; (5) dermatomyositis/polymyositis associated with vasculitis and polymyositis/dermatomyositis associated with collagen vascular disease. Previous studies have suggested an association between dermatomyositis and malignancy. The most commonly reported tumors are ovarian cancer, breast cancer, melanoma, and colon cancer. However, it is a rare disease in China. There are only a few small studies reported. In order to identify the association between dermatomyositis and malignancy in China, we retrospectively analyzed the clinical data of 115 cases of dermatomyositis associated with malignancy, which were collected from our hospital from 1974 to 2008.

Materials and Methods

We retrospectively reviewed 678 cases of dermatomyositis that were examined in the Second Affiliated Hospital, Sun Yat-Sen University, China, from 1974 to 2008. There were 255 males and 423 females. All these cases met the dermatomyositis diagnostic criteria of Bohan and Peter[1]. Among them, 115 cases were associated with malignancy. We evaluated characteristics of dermatomyositis and their correlation with malignancy. Clinical manifestations, laboratory data, electromyography, muscular biopsy and the prognoses of these patients were assessed.

Comparisons of malignancy risk among different groups were done by Chi-square test. $P < 0.05$ was considered statistically significant.

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Results

In our study, 297 out of 678 cases were under 40 years old (98 males and 199 females); in this group, 7.4% (22/297) of patients were diagnosed with malignant tumor, including 8 males and 14 females. There was no significant difference in malignancy risk between male and female under 40 years old (8.2% versus 7.0%, $P > 0.05$). There were 381 cases aged 40 years or above (157 males and 224 females); 24.4% (93/381) of them were associated with malignancy, including 55 males and 38 females. Malignancy was more common in male than in female among patients aged 40 years or above (35.0% versus 17.0%, $P < 0.05$). Compared to patients under 40 years old, patients aged 40 years or above had a higher risk of malignancy (24.4% versus 7.4%, $P < 0.05$). In total, 115 out of 678 patients (17.0%) were associated with malignancy.

Nasopharyngeal cancer made up 51.3% (59/115) of the associated malignancies, while lung cancer accounted for 17.4% (20/115). Other malignancies associated with dermatomyositis included liver cancer (9 cases), ovarian cancer (7 cases), cervical lymph node metastases of unknown origin (3 cases), cholangial cancer (3 cases), esophageal cancer (3 cases), colon cancer (3 cases), laryngeal cancer (3 cases), renal cancer (3 cases), tongue cancer (1 case), and lymphoma (1 case).

Malignancy preceded dermatomyositis in 14 cases. Dermatomyositis and malignancy were diagnosed at the same time in 22 patients. Another 79 patients were found to have cancer within 3 years after the dermatomyositis was diagnosed. Among them, cancer was detected in 66 patients in the first year, 11 patients in the second year and only 2 cases in the third year.

The clinical manifestations of dermatomyositis included: blue-purple discoloration on the upper eyelids with edema in 80 cases, Gottron sign (scaly violaceous eruption over the extensor surfaces of joints: "Gottron's papules") in 70 cases, proximal muscle weakness in 84 cases, myalgia or muscle tenderness in 72 cases, amyotrophia in 15 cases, dysphagia in 68 cases, perionychial erythema in 20 cases, pruritus in 24 cases, necrotic ulceration of the skin in 16 cases, and blisters on extremities in 13 cases. In addition to the primary myopathy, some patient developed extramuscular manifestations, including interstitial pneumonia in 30 cases, cardiac disturbances in 19 cases, and gastrointestinal bleeding in 5 cases. Myopathy and rash didn't improve with corticosteroid therapy in 20 cases. Creatine phosphokinase (CK) level was elevated in 101 cases. Electormyologram demonstrated myopathic disorder in 98 cases. Muscle biopsy results were consistent with dermatomyositis in 96 patients. Erythrocyte sedimentation rate (ESR) was elevated in 58 cases and C-reative protein (CRP) was elevated in 34 cases. In 28 cases, serum albumin level was less than normal. Serum Epstein-Barr viral capsid antigen (VCA) IgA antibody was positive in 59 patients with nasopharyngeal cancer, ranging from 1:20 to 1:320. In 3 out of 7 patients with ovarian cancer, CA125 level was elevated (218 425 u/ml). Elevated serum alpha fetoprotein (AFP) was detected in 3 out of 9 patients with liver cancer, ranging from 240 to 1710 μg/L. Serum carcinoembryonic antigen (CEA) was higher than 15 μg/L in 5 out of 20 patients with lung cancer.

In our study, 75 patients died with a follow-up period ranging from 1 to 15 years. The causes of death included cancer metastasis (43 cases), pulmonary infection (18 cases), cardiac disturbances (7 cases), asphyxia caused by foreign body aspiration (3 cases), gastrointestinal bleeding (2 cases) and pulmonary interstitial disease (2 cases).

Discussion

Dermatomyositis associated with malignancy was first reported by Stertz in 1916, who described a case of dermatomyositis with coexisting gastric carcinoma. In the same year, Kankeleit reported another case of dermatomyositis associated with breast cancer. Since them, the relationship between dermatomyositis and malignancy has captured a lot of attention[2,3]. Dermatomyositis has been reported to be associated with malignancies in 15%-34% of patients in Western countries, but in as many as two-thirds of patients in Singapore[4]. In our study, there were 678 cases of dermatomyositis patients collected from our hospital from 1974 to 2008, and 17% of them (115 cases) were associated with malignancy.

Age plays an important role in whether dermatomyositis is associated with malignancy. The malignancy frequency in dermatomyositis patients is higher in elderly patients compared with younger patients. It is most frequent between 40

and 69 years of life[5]. In our study, 7.4% of patients under 40 years old had cancer. While the risk of malignancy was significantly increased to 24.4% in patients aged 40 years or above.

The reports of the association between gender and the risk of malignancy in dermatomyositis patients were inconsistent[5-8]. Dourmishev[5] and Sigurgeirsson et al[6] reported that malignancy was more common in women. However, Fung et al[7] and Selvaag et al[8] found that it was more common in men. In our study, there was no significant difference among the group under 40 years old. But it was more common in men than in women among patients aged 40 years or above (35.0% versus 17.0%).

Generally, tumor types associated with dermatomyositis seem to roughly approximate the frequencies of those in the general population[9]. Associated malignancies may differ with age, gender and regions. Marie et al[10] reported that 50% of malignancies were colon malignancies in dermatomyositis patients aged 65 years or over. Dourmishev[5] reported that associated malignancies were respiratory tract carcinomas in males, genital and breast carcinomas in females. Dermatomyositis was more frequently associated with nasopharyngeal carcinoma in Singapore[4], Taiwan[11] and Hong Kong[7]. Our study also showed that nasopharyngeal cancer was the most common tumor associated with dermatomyositis in Guangdong province (51.3%), followed by lung cancer (17.4%).

Previous studies in the last 10 years have reported some signs that indicated underlying malignancy in patients with dermatomyositis[8,10,12,13], which included: (1) old age; (2) necrotic ulceration of the skin; (3) pruritus; (4) perionychial erythema; (5) blisters on extremities; (6) dysphagia; (7) high ESR; (8) elevated CRP; (9) low Serum albumin level; (10) elevated CA_{125} level (prediction of ovarian cancer); (11) unresponsive to corticosteroid therapy. In our 115 cases of dermatomyositis with malignancy, 94 cases (81.7%) showed one or more signs listed above. Among them, a 74-year-old male patient had come to our attention. The patient presented with necrotic ulceration of the skin on his left leg (4 cm × 5 cm) when he was diagnosed with dermatomyositis in May 1987. No evidence of malignancy were found at that time. But he came back with an enlarged lymph node on the right side of the neck in April 1988, which was confirmed to be a metastatic squamous cell carcinoma by lymph node biopsy. The original tumor was not found after searching in the nasopharynx, esophagus and lung. The patient died of asphyxia by aspiration of foreign body in July 1988.

It is still controversial whether there is a causal relationship between dermatomyositis and malignant tumor. Some think that dermatomyositis may be a manifestation of a malignant tumor, which means that dermatomyositis is a kind of paraneoplastic syndrome when they are coexistent. For some patients, successful treatment of the tumor could relieve the dermatomyositis[14,15]. Mooney et al[16] demonstrated that a patient with prostate cancer presenting as dermatomyositis had autoantibodies to specific proteins produced by the neoplastic prostatic tissue, which was normally expressed in muscle tissue. It suggested that dermatomyositis might be a kind of immune reaction to the tumor. But other researchers have different views. In 1992, Sigurgeirsson et al[6] reported a population-based cohort study in Sweden from 1963 through 1983, in which the incidence of cancer in patients with dermatomyositis was compared with those for the general population. Among the 392 patients with dermatomyositis, there were 145 men and 247 women. The relative risk of cancer was 2.4 in the male patients and 3.4 in the female patients. It demonstrated that the risk of cancer was increased in patients with dermatomyositis. It is presumed that dermatomyositis and malignancy may share common pathogenesis or etiological factors, which included (1) immune system disbalance and a failure in immunological surveillance mechanism; (2) occupational exposure to risk factors which can cause both malignancy and dermatomyositis; (3) infection, especially EB virus infection. Some thought that the high risk of malignant tumor was related to the use of immunosuppressive agents.

Accompanied by malignant disease is an unfavorable prognostic factor for dermatomyositis. Since dermatomyositis is a systemic disease, it may present with symptoms of internal organs disorder. These sometimes covered the underlying malignancy. Most patients were in advanced stage when tumor was diagnosed. Some tumors were only found by autopsy[13]. In our study, there was a case of dermatomyositis with increased reticular marking on chest X ray, which was suspected to be interstitial pneumonia. But it didn't respond to corticosteroid therapy. Bronchoscopy and biopsy confirmed that it was bronchioalveolar carcinoma. Therefore, arousing the awareness of the association between dermatomyositis and

malignancy can help early diagnosis and treatment, and it is important to improve the prognosis of dermatomyositis.

In our 115 cases, dermatomyositis and malignancy were diagnosed at the same time in 22 patients. Cancer was detected in 66 patients in the first year after dermatomyositis was diagnosed. Totally, it accounted for 76.5% of the cases (88/115). Chow et al[17] had reported that the risk of malignancy in patients with dermatomyositis declined steadily with increasing years since initial diagnosis of dermatomyositis. The cancer risk was increased about six fold during the first year, but was 2.5 fold during the second year, with no significant increase in subsequent years of follow-up. Thus, malignancy should be suspected within the first two years after the onset of dermatomyositis, especially in the first year. Measures that lead to early detection of the malignant tumor include: (1) detail medical history and a system review, and a complete physical examination with rectal, pelvic and breast examinations; (2) laboratory tests with complete blood count, blood chemistry tests, fecal occult blood test, and urinalysis; (3) chest X-ray; (4) mammography in female. Any abnormal findings require further extent of search. Patients without abnormal findings should be followed up annually[18]. Patients with any inexplicable activation of myositis should be rechecked immediately. Examination of nasopharynx should be carried out in patients from the epidemic region of nasopharyngeal cancer. Currently, fiberoptic nasopharyngolarygnoscope has become a routine in our hospital for dermatomyositis patients.

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