

## Dermatomyositis Associated with Breast Cancer

DIMITRIOS PECTASIDES<sup>1,2</sup>, MARIA KOUMPOU<sup>2</sup>, ASIMINA GAGLIA<sup>1,2</sup>,  
MELINA PECTASIDES<sup>1,2</sup>, V. LAMBADIARI<sup>1</sup>, E. LIANOS<sup>1,2</sup>,  
G. PAPAXOINIS<sup>1,2</sup> and TH. ECONOMOPOULOS<sup>1,2</sup>

<sup>1</sup>Second Department of Internal Medicine-Propaedeutic, Oncology Section,  
University Medical School, Attikon University Hospital, Athens;

<sup>2</sup>Second Department of Medical Oncology, Metaxas Memorial Cancer Hospital, Piraeus, Greece

**Abstract.** *An increased risk of underlying malignancy has been found in patients with dermatomyositis (DM). The risk is increased even in patients with DM aged 45 or younger and remains high for many years after diagnosis. Breast carcinoma does not represent the most common solid tumor associated with this autoimmune disorder. In the present report, two new cases of DM associated with breast cancer are described, together with an extensive literature review.*

An increased incidence of cancer in patients with dermatomyositis (DM) and polymyositis has been reported in many studies, though with wide variations in the estimated risks. We report two cases of dermatomyositis associated with breast cancer. In our first patient, DM had developed one year before diagnosis of breast cancer and in the second one, on relapse of the malignancy.

### Case Report 1

A 43-year-old female was admitted to the hospital with a palpable mass over the right breast. During self-examination two years previously, the patient had found a palpable nodule in the external upper quadrant of her right breast. A bilateral low-radiation dose mammography had not revealed any abnormal findings. One year later, she developed erythematous papules accompanied by itching over the ear lobules, the shoulders, the skin of the anterior thoracic wall and the nose. She consulted a dermatologist and received treatment which did not ameliorate her symptoms. Over the following year, she developed extension of the erythematous papules over the dorsal aspects of her hands and elbows. She was examined by a rheumatologist

and the laboratory investigations revealed: anti-nuclear antibodies (ANA) =1:320 and CPK= 457, constituting abnormal values. An electromyography (EMG) of the upper and lower limbs did not reveal any abnormal findings. She then received treatment with dihydro-chloroquine (Plaquenil) and indomethacin. She did not experience any improvement of her skin and other symptoms and progressively developed diffuse myalgias over the feet, difficulty in rising from a sitting position and in walking. Thereafter, she was admitted to a rheumatology department where a full investigation was performed. Clinical examination revealed a 5x5 cm palpable firm mass over the right breast. Laboratory investigations revealed the following: ANA=1:640 positive, C3=105, C4=24.8, CPK=662, anti-Jo antibodies: negative, CEA=0.3, CA-15.3=45. She underwent a new EMG, which revealed myopathic changes and a skin-muscle biopsy was consistent with DM.

Mammography demonstrated a shadow in the right breast and enlarged homolateral axillary lymph nodes. A fine-needle aspiration was taken from the lump on the right breast and the cytological examination revealed an infiltrating ductal carcinoma of the breast. Soon after this diagnosis, she was admitted to our hospital. The full investigation tests (including CT scans of the chest, abdomen, pelvis and a bone scan) were negative for metastatic disease. She underwent a right modified radical mastectomy and axillary lymph node dissection. Histology was consistent with an infiltrative ductal carcinoma, grade III, with metastatic invasion in seven out of 19 resected axillary lymph nodes. She was then treated with adjuvant chemotherapy with cyclophosphamide, doxorubicin and 5-fluorouracil (CAF) x six cycles. Following mastectomy and CAF chemotherapy, she experienced remarkable improvement of the dermal erythematous papules and muscle symptoms. The only skin lesion that was apparent on completion of chemotherapy was a small erythematous papule of the left eyelid. She then received ovarian suppression with an LHRH analog, goserelin, for 2 years. One year later, while continuing goserelin, she had a

*Correspondence to:* Dimitrios Pectasides, MD, 5B Gravias, Ag. Paraskevi 15342, Athens, Greece. Tel/Fax: +30 210 600 8610, e-mail: pectasid@otenet.gr

*Key Words:* Dermatomyositis, breast cancer.

complete remission of her skin and muscle disease. Thereafter, she continued treatment with tamoxifen and has remained disease-free from breast cancer and symptom-free from DM for more than 10 years.

### Case Report 2

A 59-year-old woman was examined in our hospital for a palpable nodule in the left breast. Mammography revealed a 1x1 cm soft tissue mass in the central portion of the left breast and enlarged ipsilateral axillary lymph nodes. CT scans of the chest, abdomen and pelvis and a bone scan were negative for metastatic disease. She underwent an axillary lymph node biopsy. Histology revealed metastatic adenocarcinoma, grade III, with the possible primary originating from the breast. A few days later, a left modified radical mastectomy with axillary node dissection was performed. Histology revealed metastatic invasion by a ductal adenocarcinoma in five out of 17 resected axillary lymph nodes. She was then treated with adjuvant chemotherapy with high-dose epirubicin (110 mg/m<sup>2</sup>) administered biweekly. After three cycles with high-dose epirubicin every 2 weeks, she received cyclophosphamide (840 mg/m<sup>2</sup>), methotrexate (57 mg/m<sup>2</sup>) and fluorouracil (840 mg/m<sup>2</sup>) (Mega-CMF) every 2 weeks with G-CSF administration. She then underwent radiotherapy to the chest wall, left axilla and left supraclavicular fossa with a total dose of 5000 cGy. After completing radiotherapy, she received tamoxifen and remained disease-free.

Three years later, she developed diffuse erythema over her face and the dorsal aspects of her hands, and periorbital edema and telangiectasias. She also developed muscle weakness and dysphagia. She underwent an electromyography which revealed only nerve conduction abnormalities consistent with radiculopathy and no myopathic changes. Laboratory investigations revealed: ANA=1:80 positive, anti DNA: (-), CPK=124. A skin-muscle biopsy of her left shoulder was performed. Histology revealed sclerodermatous changes of the skin specimen and a limited inflammatory infiltration between muscle fibers associated with edema and fibroblast proliferation. These findings were compatible with DM. Treatment was instituted with prednisolone and methotrexate orally for 1 month and she experienced improvement of her symptoms. At the same time, a CT scan of the abdomen and pelvis revealed metastatic disease of the liver. She underwent chemotherapy with an experimental protocol consisting of carboplatin, paclitaxel and cefitinib orally. After completing the first cycle, she had complete regression of the dermal lesions and her muscle symptoms. On completion of six cycles of chemotherapy, she developed progressive liver disease and second-line treatment was instituted with trastuzumab, pegylated liposomal doxorubicin and

Table I. Bohan and Peter criteria for diagnosis of DM.

Individual criteria	
1.	Symmetric proximal muscle weakness
2.	Muscle biopsy evidence of myositis
3.	Increase in serum skeletal muscle enzymes
4.	Characteristic electromyographic pattern
5.	Typical rash of dermatomyositis
Diagnostic criteria	
Definite:	5 plus any three of 1-4
Probable:	5 plus any two of 1-4
Possible:	5 plus any one of 1-4

docetaxel. She completed three cycles with no response, and died 2 months later from progressive disease with no apparent recurrence of DM.

### Discussion

A diagnosis of DM and polymyositis in elderly patients strongly suggests the possibility of an underlying malignancy. Based on a meta-analysis of the available literature, Callen *et al.* (1) concluded that pure polymyositis carries an increased risk of malignancy compared with the general population, although the incidence is significantly lower when compared with DM. Cancers that are more strongly associated with DM are ovarian, lung, gastric, colorectal and pancreatic cancers and non-Hodgkin's lymphoma. However, more rarely there has also been an association with a broad range of other malignancies, such as breast cancer (2).

Malignancy in adult women with DM was reviewed in a report by Callen (3). The frequency of breast, uterine, cervical and ovarian cancers in DM patients with malignancies accounted for 36% of all malignancies in adults and almost 65% of the malignancies in women with DM.

DM is an autoimmune disorder characterized by inflammatory muscular and cutaneous disease. Clinically, the most frequent problem is insidious, progressive painless symmetric proximal muscle weakness over the course of 3-6 months before the first visit to a physician. Other features presented may be attributable to muscle weakness. Other symptoms, each occurring in approximately 5% of patients, are pitting edema of the extremities as a result of lack of muscle tone needed to promote central venous return, hoarseness or dysphagia as a result of bulbar muscle weakness, nasal regurgitation of liquids or aspiration pneumonia and dyspnea. Gottron's papules and heliotrope rash are considered pathognomonic cutaneous features of DM (4).

In 1975, Bohan and Peters presented criteria for the diagnosis of polymyositis and DM (Table I) (5). According to these criteria, our first case report was a definite DM and

the second one was a probable DM. Both patients presented here had typical dermal and muscular symptoms, the EMG findings were compatible with myositis and both had histological findings consistent with DM. However, there have been certain case reports in the literature of so-called amyopathic DM, associated with breast cancer, characterized by the absence of muscular symptoms, EMG and histological findings of myositis (6-8). It has been suggested that amyopathic DM is not responsive either to steroid treatment or to specific treatment of the underlying malignancy (6).

In contrast, typical DM associated with breast cancer demonstrates a parallel course with breast cancer evolution after surgery, local radiotherapy and systemic therapy with cytotoxic agents or hormones, as exhibited in both cases under study here. Both patients experienced a complete regression of the dermal lesions and their muscular symptoms.

The fact that DM has been noted to improve after treatment of cancer suggests a paraneoplastic origin (9, 10). Moreover, in one of our cases, DM was diagnosed at relapse, suggesting a consistent relationship between the course and evolution of the underlying malignancy (11).

However, there is speculation concerning the biological basis of a possible association between DM and malignancy. It has been suggested that a common environmental factor might act as a trigger of inflammation and as a carcinogen at the same time. Some investigators have implicated an antitumoral immune reaction that evolves into an autoimmune syndrome through cross-reaction with muscle and skin antigens (12); while others suggest a possible involvement of tamoxifen therapy itself, or tumor regression by this agent at the onset of DM (13).

There seem to be differences in the clinical features of DM associated with malignant disease. Patients with cancer-associated DM are more likely to have normal creatinine kinase values and digital vasculitides, and less likely to have myositis-specific autoantibodies than those without cancer (14, 15).

Classic reviews have emphasized that malignancy tends to occur in adult patients with DM, in particular those over 40 years in age. Hill *et al.*, concluded that the risk of malignant disease was increased even in DM patients aged 45 or younger (2).

In conclusion, the increased risk of malignant disease for patients with DM remains high for many years after diagnosis. For those patients, in addition to routine examination and laboratory screening, CT scan of the chest, abdomen and

pelvis, mammography and gynecological examinations are justified. Even if mortality is not prevented or survival prolonged for these malignant diseases, disability from myositis could be alleviated if the cancers were detected and treated early enough.

## References

- 1 Callen JP: Myositis and malignancy. *Curr Opin Rheumatol* 6: 590-594, 1994.
- 2 Hill CL, Zhang Y *et al*: Frequency of specific cancer types in DM and PM. *Lancet* 357: 96-100, 2001.
- 3 Callen JP: DM and multiple malignancies in a patient treated with MTX. *J Surg Oncol* 24: 113-116, 1983.
- 4 Oddis CV and Medsger TA Jr: *Rheumatology*, 3rd edn. London: Mosby, 2003.
- 5 Bohan A and Peter JB: Polymyositis and dermatomyositis. *N Engl J Med* 292: 344-347, 403-407, 1975.
- 6 Stonecipher MR, Jorizzo JL, White WL, Walker FO and Prichard E: Cutaneous changes of DM in patients with normal muscle enzymes: DM sine myositis? *J Am Acad Dermatol* 28: 951-956, 1993.
- 7 Euwer RL and Sontheimer RD: Amyopathic DM (letter). *J Am Acad Dermatol* 26: 506-508, 1992.
- 8 Goyal S and Nousari HC: Paraneoplastic amyopathic DM associated with breast cancer recurrence. *J Am Acad Dermatol* 41(5 Pt 2): 874-875, 1999.
- 9 Verducci MA, Malkasian GD, Friedman SJ and Winkelmann RK: Gynecologic carcinoma associated with DM-PM. *Obstet Gynecol* 64: 695-698, 1984.
- 10 Sunnenberg TD and Kitchens CS: DM associated with malignant melanoma: parallel occurrence, remission, and relapse of the two processes in a patient. *Cancer* 51: 2157-2158, 1983.
- 11 Tsavaris N, Karagyris G, Pikazis D, Vadiaka M, Kosmas C, Sakellaropoulos N and Vaiopoulos G: Adenocarcinoma of the colon presenting as PM: case report. *J Chemother* 14: 102-105, 2002.
- 12 Stone OJ: DM/PM associated with internal malignancy: a consequence of how neoplasms alter generalized extracellular matrix in the host. *Med Hypotheses* 41: 48-51, 1993.
- 13 Harris AL, Smith IE and Snaith M: Tamoxifen-induced tumour regression associated with DM. *Br Med J* 284: 1674-1675, 1982.
- 14 Fudman EJ and Schnitzer TJ: DM without creatine kinase elevation: poor prognostic sign. *Am J Med* 80: 329-332, 1986.
- 15 Klippel JH and Dieppe PA: *Rheumatology*, 2nd edn. London: Mosby, 1998.

Received February 3, 2006

Accepted March 17, 2006