Breast cancer and dermatomyositis: a case study and literature review

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ABSTRACT

A 49-year-old woman presents with an extensive violaceous rash, rapidly progressive proximal muscle weakness, and dysphagia to solids, consistent with a diagnosis of dermatomyositis. Two weeks later, she palpates a mass in her left breast and is diagnosed with HER2-positive metastatic invasive ductal carcinoma of the breast.

There is a well-established association between dermatomyositis and malignancy. However, the specific association between breast cancer and dermatomyositis has not been well characterized. No guideline for oncologists managing these patients has been established. Recently, 3 cases of breast cancer and dermatomyositis were diagnosed at our institution. A review of the literature was pursued to characterize the association between breast cancer and dermatomyositis.

A review of 178 papers identified 22 cases of breast cancer with dermatomyositis. Most patients (71%) presented with stage III or IV breast cancer. The median time between the diagnosis of breast cancer and the onset of dermatomyositis symptoms was 1 month. Three quarters of the patients were steroid-responsive and able to taper. Half the women with follow-up data experienced a documented cancer relapse associated with a new flare of cutaneous symptoms.

The presence of dermatomyositis appears to be associated with more-advanced breast cancer stage and is most commonly associated with invasive ductal carcinoma. In our review, treatment of cancer alone is insufficient to adequately control the cutaneous and myopathic manifestations of dermatomyositis, which can significantly affect quality of life. A multidisciplinary approach, including close collaboration with rheumatologists and dermatologists, is therefore important in the diagnosis and management of oncology patients with dermatomyositis.

Key Words Dermatomyositis, cancer-associated myositis, breast cancer, idiopathic inflammatory myositis, breast neoplasms

INTRODUCTION

Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by proximal muscle weakness, rash, and other systemic manifestations (Table I). The cutaneous manifestations of DM include pathognomonic papules on the extensor surfaces of the hands, elbows, and knees (Gottron’s sign), eye edema and erythema (heliotrope sign), and a diffuse violaceous photosensitive rash (shawl sign, V-sign, holster sign), all of which can be very similar to skin findings in acute cutaneous lupus. The rash of DM can be highly variable, and the diagnosis of DM can be challenging, especially in patients who do not have muscle weakness or elevated creatine kinase (amyopathic DM).1,2 Electromyography and muscle magnetic resonance imaging (MMI) can assist in the diagnosis, with subsequent tissue confirmation on muscle biopsy.

The association between DM and malignancy is well-established, with 15%–30% of DM patients having an underlying malignancy.3 Although the frequency of the various tumour types found in patients with DM generally reflects the epidemiology in the general population, lung, ovarian, and breast cancers appear to be the most common.4,5

In collaboration with the myositis clinic at our centre, we identified three cases of DM in women with breast cancer. Here, we describe one case in detail and present a summary table of all three cases. Combining those cases with a comprehensive literature review, we aimed to better characterize clinical and pathologic features so as to guide the management of DM associated with breast cancer.

CASE DESCRIPTION

A 49-year-old woman presented with a violaceous rash of the upper back, chest, and arms (Figure 1), accompanied by progressive proximal muscle weakness. Within 1 week, the
rash covered 80% of her body surface area. She was treated with 3 days of oral prednisone 50 mg daily and topical corticosteroids for a presumed atopic dermatitis, achieving minimal improvement. Two weeks later, she palpated a left breast mass and presented to the emergency department.

Because of progressive dysphagia to solids and skin and muscle weakness, the woman was admitted to hospital. Her dermatology exam showed heliotrope rash, Gottron papules, periungual erythema, abnormal nail-fold capillaries, and diffuse violaceous rash throughout her body. Her proximal muscle strength was decreased (rated as 4/5) in a symmetrical pattern around her shoulder and pelvic girdle, including neck flexors, but was preserved (5/5) in distal muscle groups. She had a normal cranial nerve exam, sensory exam, and deep tendon reflex test. On breast exam, she had 2 firm 4 cm masses in the left breast, with palpable left axillary lymphadenopathy. She was seen by the rheumatology and dermatology services, who felt that her symptoms were consistent with DM.

A breast MRI showed 3 masses in the left breast (the largest being 4.4 cm in diameter and invading into the areola and skin), together with grossly abnormal left lymph nodes measuring 1.7×2 cm, with ill-defined margins. Computed tomography of abdomen and pelvis, and a bone scan, demonstrated metastatic lesions throughout the axial skeleton. After serial imaging, 4 indeterminate hypodense liver lesions were felt to be benign.

A left breast biopsy showed a multifocal invasive ductal carcinoma that was positive for the estrogen and progesterone receptors and HER2 (the human epidermal growth factor receptor). The other mass was triple-negative. Her tumour staging was T3M1 or stage iv.

Liver enzymes, creatinine, and complement levels were normal; antinuclear antibodies were negative. Creatine kinase was normal (<130 U/L) at the time of rash onset, but peaked at 1527 U/L, corresponding to the development of muscle weakness.

This patient’s DM workup also consisted of skin biopsy and a pelvis and thigh-muscle MRI. Skin biopsy showed a significant vacuolar interface change in a thinned epidermis, consistent with a diagnosis of DM (Figure 2). A myositis antibody panel including Mi-2, TIF1, MDA5, Jo-1, and PM/Scl was negative. The MRI demonstrated a diffuse and symmetrically increased T2 signal in multiple muscle groups of the pelvis and thighs (Figure 3).

For stage iv breast cancer, the patient was started on docetaxel chemotherapy and monoclonal antibodies against the HER2 oncogene (trastuzumab and pertuzumab). After 4 cycles of chemotherapy and targeted therapy, the breast tumours were no longer clinically palpable, and a marked reduction in the primary tumour and metastatic disease by more than 50% was observed on mammography and computed tomography imaging.

After 7 cycles of chemotherapy, the patient underwent ultrasound-guided left breast lumpectomy and sentinel node resection. The largest mass had decreased in size from 4.4 cm to 1.9 cm, and pathology confirmed an invasive ductal carcinoma with negative margins. Sentinel lymph node resection was positive for extranodal extension without evidence of treatment effect.

### TABLE I

Systemic manifestations of dermatomyositis

| Organ system    | Findings                                   |
|-----------------|--------------------------------------------|
| Peripheral vasculature | Abnormal nail-fold capillaries |
|                  | Raynaud phenomenon                         |
| Respiratory      | Interstitial lung disease                  |
|                  | Respiratory muscle paralysis               |
| Gastrointestinal | Dysphagia (upper esophagus)               |
| Cardiac          | Myocarditis                                |
|                  | Conduction abnormalities                   |
|                  | Arrhythmias                                |
| Muscle weakness  | Symmetric proximal muscle weakness         |
|                  | in shoulder and pelvic girdle              |
|                  | Myalgias                                   |

**FIGURE 1** The patient’s poikiloderma took a shawl distribution.

**FIGURE 2** Skin biopsy shows significant vacuolar interface change in this relatively thinned epidermis, which is consistent with the diagnosis of dermatomyositis.
Because of the response to chemotherapy and sclerotic bony lesions on computed tomography imaging, the patient was sent for postoperative radiation therapy. At 18 months after her initial diagnosis, she remains very stable, with minimal residual disease on maintenance monoclonal antibody treatment (trastuzumab and pertuzumab), with minimal residual disease on maintenance monoclonal antibody treatment (trastuzumab and pertuzumab), tamoxifen, and pamidronate.

For DM, the patient was concomitantly prescribed prednisone 30 mg twice daily. She was subsequently started on intravenous immunoglobulin (ivig) at 1 g/kg daily for 2 consecutive days every 4 weeks. She received intravenous methylprednisolone with each ivig infusion.

Despite the patient’s clinical response to the chemotherapy, her DM remained active for more than 6 months, with ongoing skin rash. She was started on oral weekly methotrexate as a steroid-sparing agent, and topical steroid creams, together with hydroxychloroquine for active skin DM. At 8 months after diagnosis, her skin rash and muscle weakness have improved, but are not yet back to normal.

This woman’s case demonstrates an aggressive subtype of HER2-positive breast cancer and the effectiveness of chemotherapy and targeted therapy in patients with advanced HER2-positive disease.

The other two patients seen at our institution had different tumour types; Table II summarizes their cases.

DISCUSSION

In patients with breast cancer, DM is a rare diagnosis, and no guidelines for the management of DM in breast cancer have been established. We conducted a literature review in MEDLINE, PubMed, and EMBASE using the terms “dermatomyositis,” “cancer associated myositis,” “idiopathic inflammatory myopathy,” and “breast neoplasm” for 1999–2016. We identified 44 previously published cases of DM in patients with breast cancer; however, only 22 patients had specific staging and a confirmed DM diagnosis. After including our institution’s 3 patients (25 patients total), we looked for trends of DM in these patients with breast cancer.

Median age at the time of initial breast cancer diagnosis in the identified cohort was 58 years (range: 39–74 years), and the most common type of breast cancer was invasive ductal carcinoma (12 of 16 patients with available tumour pathology, 75%). The median time to diagnosis of breast cancer from presentation with DM was 1 month (range: 29–36 months). Most patients were diagnosed with cancer before they were diagnosed with DM; only 6 of the 25 (24%) presented with myositis symptoms first. The presence of DM was associated with late-stage tumours, 72% of the patients (18 of the 25) having presented with stage III or IV disease. No trends in hormone receptor status were observed in these breast cancer patients with DM. The distribution of triple-negative, HER2-positive, and estrogen or progesterone receptor–positive breast cancers was relatively even.

The heterogeneity of presentation in these patients and the exclusion of patients with cancer from randomized controlled trials makes it difficult to define the optimal treatment regimen for DM in this setting. The goal of treatment is to ameliorate muscle inflammation and restore muscle strength, to address extramuscular involvement, and to resolve cutaneous manifestations. The cutaneous symptoms of DM can be challenging to manage and can cause discomfort because of intense pruritus. Sunscreen can be a helpful adjuvant therapy because the cutaneous symptoms are often photosensitive.

High-dose glucocorticoid is the cornerstone of treatment, typically starting at a daily dose of 1.5 mg/kg. In severe cases, ivig is added at 1 g/kg daily, given for 2 consecutive days monthly. Some patients can require additional intravenous glucocorticoids. Methotrexate and azathioprine are common steroid-sparing agents. Oral hydroxychloroquine and topical therapies are sometimes used to address active cutaneous involvement.

All but 1 of the 22 cases identified in our literature review were treated with corticosteroids. The exception was a patient with limited cutaneous disease and ductal carcinoma in situ, who responded to hydroxychloroquine alone. The literature review demonstrated that, of the 20 patients successfully treated for their breast cancer, 75% (n = 15) were subsequently able to eventually taper their steroids.

Cutaneous manifestations were a useful marker for cancer recurrence. Of the 10 patients for whom long-term follow-up information was available, 5 had a documented cutaneous relapse of DM. All had either stage III or IV breast cancer at the time of initial diagnosis. In all of the patients with relapse, recurrence or worsening of their rash reflected underlying cancer activity. Currently, no specific screening guidelines have been established for DM patients without a known cancer diagnosis.

SUMMARY

Breast cancer patients presenting with proximal muscle weakness, skin rashes, or other systemic manifestations suggestive of DM should receive prompt evaluation, including muscle enzymes, MRI, electromyography, and muscle biopsy for tissue confirmation. Myositis-specific antibodies are not always positive, but can assist in the diagnosis and subtyping of DM. Treatment of underlying malignancy alone is usually insufficient; patients require treatment...
for DM. That treatment typically involves high-dose corticosteroids, steroid-sparing agents, and early initiation of IVIG therapy in severe cases. A multidisciplinary approach including a rheumatologist is recommended to manage treatment and systemic involvement.

CONFLICT OF INTEREST DISCLOSURES
We have read and understood Current Oncology’s policy on disclosing conflicts of interest. There are no relevant disclosures for the present work. RH has received honoraria as an advisory board member for Janssen, Pfizer, Novartis, Bristol–Myers Squibb, Boehringer Ingelheim, and Merck outside the submitted work. RH’s institution receives funding from Roche, Celldex Therapeutics, and Bristol–Myers Squibb for trials in which she is co-investigator outside the submitted work. OV has received honoraria as an advisory board member for Grifols. EH and HF have no conflicts outside the submitted work. RH has received honoraria as an advisory board member for Janssen, Pfizer, Novartis, Bristol–Myers Squibb, and the present work. RH has received honoraria as an advisory board member for Grifols. EH and HF have no conflicts to disclose.

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