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Other full case

Dermatomyositis presenting as a paraneoplastic syndrome due to underlying breast cancer

Nicole P Sandhu,[1] Shaheen Zakaria,[2] Amy C Degnim,[3] Judy C Boughey[3]

[1]Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA;
[2]The Chrysalis, Rancho Mirage, California, USA;
[3]Department of Surgery, Mayo Clinic, Rochester, Minnesota, USA

Correspondence to Nicole P Sandhu, sandhu.nicole@mayo.edu

Summary

Breast cancer most often presents as a palpable mass or with an abnormal mammogram. Much less commonly, breast cancer may present as a paraneoplastic syndrome. Dermatomyositis (DM) is a rare disease most often considered a complement-mediated idiopathic inflammatory myopathy manifested by classic skin findings and proximal muscle weakness. However, DM may also be due to a paraneoplastic syndrome associated with an underlying malignancy. The authors present a case report of a woman with presumed contact dermatitis who was diagnosed with breast cancer in the setting of progressive fatigue and muscle weakness. DM was subsequently diagnosed. Treatment of DM simultaneous with treatment of the breast cancer led to regression of DM. The diagnosis of DM in an adult should raise suspicion of an underlying malignancy. Breast cancer is a common disease that may rarely present with uncommon features that may divert attention from the underlying malignancy.

BACKGROUND

Dermatomyositis (DM) has an incidence of approximately 1/100 000. The majority of cases are idiopathic, but in approximately 15–30% of cases of adult-onset DM, an underlying malignancy is the cause of a paraneoplastic syndrome manifested as DM.[1 2] The lifetime incidence of breast cancer in the USA is 1/8 and is the most common cancer in women. In nearly 20% of cases of malignancy-associated DM, an underlying breast cancer is the case.[1] We present this case as a reminder that a common disease (breast cancer) may present with uncommon features (DM as a paraneoplastic syndrome), and physicians must consider malignancy as the underlying systemic process when an adult patient presents with DM.

CASE PRESENTATION

A 49-year-old premenopausal woman with no family history of significant medical problems presented to her local physician for evaluation of a generalised pruritic macular rash occurring after application of a body luster lotion followed by sun exposure. The rash was initially diagnosed as photocontact dermatitis and treated with topical steroids followed by oral steroids and cephalexin with minimal improvement. Over the subsequent 2 weeks, she developed significant fatigue and progressive proximal upper extremity muscle weakness in a symmetric distribution. Around this time, she coincidentally noticed a left axillary mass prompting diagnostic breast evaluation. A diagnostic mammogram showed extensive suspicious calcifications in the left breast. Stereotactic breast biopsy revealed invasive ductal carcinoma, grade III, and fine needle aspiration biopsy of the left axillary lymph node revealed metastatic adenocarcinoma of breast origin. CT scan of the chest, abdomen and pelvis and a bone scan showed no distant metastases.

She was referred to our institution for additional dermatologic evaluation and care given her failure to improve. Infectious eczematoid dermatitis was thought to be the underlying skin problem. However, examination revealed a heliotrope rash, oedema and erythema of her face and lower eyelids. Marked dermatitis in the sun-exposed areas of the trunk (figure 1A), accompanied by herpetic lesions on the buttocks and thighs as well as infectious papular and nummular eczema of the forearms was noted. Gottron's papules were also identified (figure 1B). Given the clinical findings, additional evaluations were undertaken in the setting of her fatigue and muscle weakness to evaluate the possibility of DM.

Given the outside diagnosis of breast cancer simultaneous with her referral to our institution, she was also referred to our Breast Clinic for further evaluation. Clinical breast examination revealed an area of nodularity in the upper outer quadrant of the left breast consistent with invasive malignancy and a single large, mobile, pathologic lymph node was identified in the left axilla.

INVESTIGATIONS

Serologic tests revealed elevated alanine aminotransferase (61 U/l), aspartate aminotransferase (78 U/l), creatine kinase (747 U/l) and aldolase (11.3 U/l). Ig panel and connective tissue serologies were within normal limits, including antinuclear antibody, antibody to extractable nuclear antigens and Jo-1 antibody. Electromyogram (EMG) demonstrated findings consistent with a proximal myopathy likely because of an inflammatory process. The EMG findings in the setting of the clinical findings were felt to be strongly suggestive of DM. Histologic findings on skin punch biopsy were consistent with DM (figure 2), with concordant vacuolar interface dermatitis and lichenoid reaction seen by direct immunofluorescence. Due to the

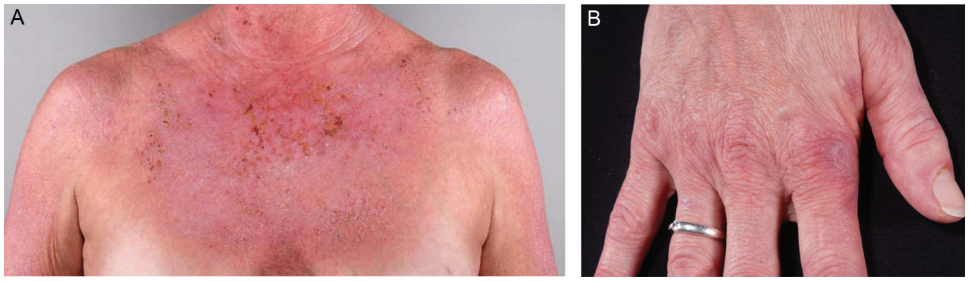

Figure 1 (A) Marked dermatitis involving sun-exposed areas of the trunk. (B) Gottron's papules overlying the knuckles.

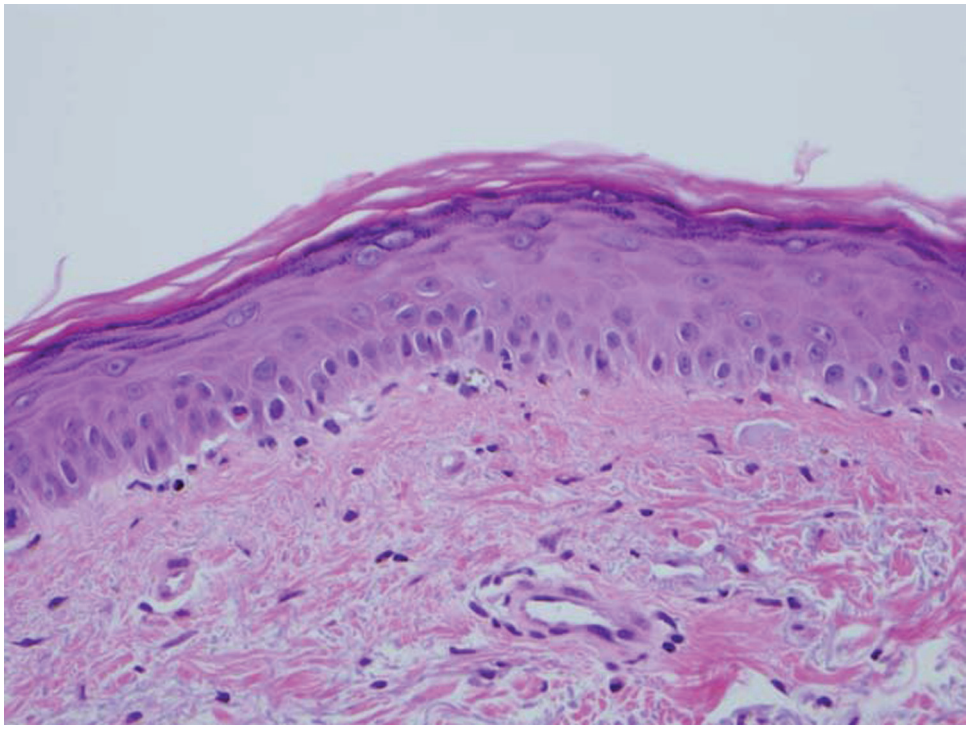

Figure 2 Interface dermatitis with basal vacuolar degeneration at the dermal-epidermal junction, apoptotic keratinocytes and pigment incontinence (original magnification 400×, H&E staining).

accumulated evidence felt to be consistent with a diagnosis of DM based on diagnostic criteria, a muscle biopsy was not pursued.

The patient's outside breast imaging was reviewed by a Mayo radiologist and revealed malignant-appearing calcifications throughout the left breast and an area of focal asymmetry in the upper outer quadrant. The tumour was found to be strongly oestrogen receptor and progesterone receptor positive. *Her-2/neu* expression was negative by immunohistochemistry. Fluorescent in situ hybridisation results were controversial, demonstrating no evidence of gene amplification, but the *Her-2/neu* gene was found to be duplicated.

OUTCOME AND FOLLOW-UP

The patient was initiated on treatment for her DM with topical and oral corticosteroids, moxifloxacin and valacyclovir, controlling the skin changes within 1 week. She underwent mastectomy and axillary dissection with concomitant bilateral salpingo-oophorectomy without complication for a T1N3M0 tumour. Of 18 axillary lymph nodes, 13 were positive for metastatic adenocarcinoma, including 2 level III lymph nodes. She tolerated her breast cancer therapy well, with all manifestations of DM resolving after her surgery. She was treated with adjuvant chemotherapy with doxorubicin and cyclophosphamide followed by paclitaxel and trastuzumab and postmastectomy radiation and adjuvant tamoxifen. Four years have passed since surgical treatment and there is no evidence of breast cancer recurrence. The patient reports that the skin manifestations of DM occasionally recur in association with significant stressors, but she has experienced no recurrence of symptoms suggestive of myositis since her mastectomy. She continues to do well medically and has completed reconstructive surgery. At this time, completion of a 5-year course of adjuvant tamoxifen is planned, and she continues routine clinical follow-up.

DISCUSSION

DM is generally considered an idiopathic inflammatory myopathy because of an autoimmune disorder. It is characterised by a heliotrope rash, Gottron's papules (violaceous, thickened, scaly papules over the knuckles) and proximal muscle weakness. Other symptoms may include pitting

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oedema, dysphagia secondary to bulbar muscle weakness and nasal regurgitation of liquids or aspiration pneumonia and dyspnoea.[3]

DM is associated with an underlying malignancy in 6–60% of cases,[4 5] and in which case, it is considered a paraneoplastic syndrome. DM is strongly associated with malignant disease, in particular ovarian, lung, pancreatic, stomach, colorectal cancers and non-Hodgkin's lymphoma.[6] The risk of malignancy is highest in patients aged 45–74 years at the time of diagnosis.[7]

Table 1 describes the diagnostic criteria for DM.[3 8] The underlying mechanism of the autoimmune process of DM in the idiopathic setting remains undefined. Multiple trigger mechanisms have been proposed in the literature, including infections, drugs, environmental factors and malignancy.[9] No differences have been found between the idiopathic presentation of DM and that associated with malignancy.[10] Our patient's signs and symptoms of DM resolved after surgical treatment of her breast cancer. This is consistent with published reports of DM associated with breast cancer demonstrating regression of DM with treatment of the underlying breast cancer.[3 11]

Standard breast cancer therapies are recommended for patients with DM and breast cancer. It seems logical to extrapolate data from available clinical trials on treatments for invasive breast cancer, keeping in mind that involvement of the skin with the typical rash of DM is not equivalent to malignant skin involvement and that treatment of DM generally results in regression of the dermatologic abnormalities. In patients with breast cancer and DM, the role of neoadjuvant chemo/hormonal therapy is debatable, and there are no data available in this setting. Wound healing after surgery is a concern if the skin condition is poor, but this has not been assessed scientifically. When possible, it seems reasonable to attempt to improve the skin condition before surgical resection followed by adjuvant treatment for patients who are appropriate candidates for this approach. Alternatively, neoadjuvant chemo/hormonal therapy may be considered in appropriate cases if the skin is clear of infection.

It has also been observed that myopathy may relapse in the setting of recurrent malignancy, further supporting a paraneoplastic origin of malignancy-associated DM.[10 12] This suggests that appropriate clinical follow-up of patients previously diagnosed with malignancy-associated DM should include observation for evidence of recurrent malignancy as well as for symptoms and signs of recurrent myopathy.

Table 1 Criteria for diagnosis of DM

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

With permission from Pectasides *et al*[3].

Learning points

- DM is an uncommon diagnosis, with an incidence of 1/100 000.
- DM presenting in an adult should raise clinical suspicion of an underlying causative malignancy (paraneoplastic syndrome).
- The development of DM as a paraneoplastic syndrome may be simultaneous with identification of an underlying malignancy or may present months to years before clinical manifestation of the malignancy.
- When an underlying malignancy is causative of DM, treatment of the malignancy generally results in regression of DM.
- Recurrence of DM may herald recurrence of the underlying malignancy.

In summary, although DM is an uncommon autoimmune process that most often presents as an idiopathic disease, the diagnosis of DM in an adult patient should prompt consideration of an underlying cancer. In female patients, breast cancer must be considered as it is so common among women. It should also be remembered that DM due to an underlying malignancy may present concurrent with, or at a time separate from, the diagnosis of cancer by an average of 2 years, but increased incidence of malignancy has been observed for at least 5 years after diagnosis.[7 13]

Competing interests None.

Patient consent Obtained.

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