

Case Report

Sudden Onset of Dermatomyositis as a Sign of Recurrence of Breast Cancer along with Regional Metastasis

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Abstract

Dermatomyositis is an idiopathic connective tissue disease characterized by specific cutaneous findings and inflammatory lesions in the muscle biopsy. An association between dermatomyositis and malignancy, including breast, ovarian, lung, and colon cancer has been identified many years ago. Paraneoplastic dermatomyositis is diagnosed in up to 30% of cases.

Here we report a case of a 51-year old woman with dermatomyositis whose clinical onset was apparently concomitant with recurrence of previously diagnosed and treated breast cancer along with newly developed regional metastasis.

Thus we underline that dermatomyositis can occur as paraneoplastic disease not only in association with the primary tumor but also in case of recurrence and/or progression of the tumor disease. The presence of dermatomyositis in a patient with previous cancer in the medical history can indicate recurrence or progression of the cancer and is associated with poor outcome. Therefore physicians should be aware of this association and perform a thorough tumor screening by patients with cutaneous manifestations and myopathy compatible with dermatomyositis and in particular if they have a history of malignancy. The treatment of dermatomyositis in such patients constitute the management of both cancer and dermatomyositis. An early detection and appropriate therapy is crucial for a favorable outcome.

INTRODUCTION

Dermatomyositis is an idiopathic inflammatory disease of the connective tissue characterized by cutaneous manifestations and weakness of the proximal muscles. The exact pathomechanism of the disease is not clear but it is supposed that trigger factors such as viral infections, drugs or malignancy lead to an immune response. The characteristic skin manifestations include erythema over the face, neck and upper trunk known as "neckline V sign" and slightly elevated erythematous papules located on the metacarpophalangeal and proximal interphalangeal joints, called "Gottron's papules". These can be found in up to 60-80% of the patients. Further findings are purple-red discoloration of the upper eyelids with or without associated eyelid edema and nail changes such as capillary teleangiectasia along the distal nailfold, periungual erythema and hyperkeratosis. Calcinosis or hyperkeratotic lesions on the fingers known as "Mechanic's hand" can also occur in some cases. Photosensitivity and pruritus have also been described in conjunction with the disease [1].

Myositis presents with mild to severe weakness of the

proximal muscles accompanied by pain in one third of the patients who claim about difficulties raising their arms or climbing stairs. Dermatomyositis is usually idiopathic, but in approximately 15-30% of adults with dermatomyositis there is an association with underlying malignancy which is usually diagnosed within a year of the onset of dermatomyositis [2]. In about 20% of patients with malignancy-associated dermatomyositis there is an association with an underlying breast cancer. Other related types of cancer are ovarian, lung [3] and colon cancer. Among women with paraneoplastic dermatomyositis breast and ovarian cancer are the most common types of cancer.

It should be taken into consideration that dermatomyositis can present not only on a later time point but also at the same time point and also prior to malignancy. A sudden onset of dermatomyositis as paraneoplastic syndrome can also occur in case of recurrent malignancy or metastatic disease [4]. Thus clinicians should be aware of the fact that dermatomyositis may indicate progress or recurrence of malignancy in patients with a previously diagnosed and treated cancer disease.

CASE PRESENTATION

A 51-year old female patient presented to our clinic with an erythema of the face and upper trunk accompanied by a severe itching sensation at her whole body. Before the presentation the patient had been treated with short courses of low dose oral prednisone, topical steroids and sunscreen with no significant improvement.

The physical examination revealed erythematous plaques on the face and proximal extremities together with reddish-livid papular lesions over the metacarpophalangeal and proximal interphalangeal joints of the hands of our patient. Additionally, we detected an approximately 2 cm palpable hard lymph node on the right axilla of the patient which had been previously detected from her gynecologist and treated as a cyst. The rest of the physical examination was normal. Her medical history revealed pain and weakness in the muscles of proximal extremities and neck flexor muscles leading to difficulty raising her arms and climbing stairs. At the same time she reported unexplained fatigue and reduced appetite in the last two months.

One year ago the patient had been diagnosed with a ductal carcinoma in situ. Following initial diagnosis she underwent a right modified partial mastectomy and subsequently an implant reconstruction of the right breast. In order to establish the diagnosis we enhanced our diagnostic approach with laboratory examination and biopsy.

The laboratory findings revealed slightly elevated serum levels of myoglobin 69 µg/l (normal range 25-58), aldolase 9.4 U/l (normal range until to 7.6 U/l) and LDH 341 U/l

(normal range 0-247 IU/L). Antinuclear antibody (ANA 1/160) was weakly positive while extractable nuclear antibodies (ENA) including U1-snRNP, RNP-Sm, Sm, SS-A/ Ro, SS-B/ La, Scl-70 and CENP were negative. Interestingly the anti-Jo-1 antibody was also negative. Creatine phosphokinase (CK), liver enzymes and other laboratory parameters were also normal.

The histopathologic examination of the skin/muscle biopsy showed vacuolar degeneration of the basal membrane with perivascular inflammatory infiltration together with a lymphohistiocytic infiltration. Furthermore extensive mucin deposition in the dermis and linear atrophy of the muscle layer could also be detected. The morphologic features were compatible with dermatomyositis.

Because of the palpable lymph node on the right axilla of our patient and her history of malignancy we performed an intense tumor screening. The patient underwent a mammography, a lymph node biopsy, a bone scintigraphy and a computer tomography (CT) of head/neck, thorax and abdomen. The mammography revealed a suspicious mass 7x11x4 mm on the right chest attached to the breast implant such as three irregular, hypochoic masses 30x18x32 mm, 14x11x4mm and 18x9 mm defined as suspicious lymph nodes on the right axilla. The patient underwent a biopsy of the suspicious breast mass and a sentinel lymph node biopsy of the suspicious lymph nodes on the right axilla. The histopathology revealed a stage 3 poorly differentiated invasive ductal carcinoma (pT2N1) positive for HER2 receptors. The CT and bone scintigraphy revealed no abdominal or cerebral metastases.

The patient was diagnosed with paraneoplastic dermatomyositis as the first sign of a recurrence of breast cancer along with onset of regional metastasis.

In collaboration with gynecologists the patient was initiated on treatment for her dermatomyositis with oral corticosteroids (methylprednisolone initially 40 mg/day and gradually tapered off) along with topical corticosteroids (mometasone furoate 0.1% cream) and oral antihistamines. One week after the beginning of this regimen, the patient's lesions remained unresponsive and only an improvement of pruritus had been reported. The patient underwent mastectomy and axillary dissection without complications.

She tolerated her breast cancer therapy well, with all manifestations of her dermatomyositis resolving after her surgery. She was treated with adjuvant chemotherapy with epirubicin/cyclophosphamide followed by paclitaxel and herceptin with good tolerability. In the one-year follow up examination the patient showed a complete remission of her dermatomyositis with no skin lesions and muscle symptoms.

DISCUSSION

Dermatomyositis is an idiopathic inflammatory disease which affects muscles and skin and is characterized by skin rash and inflammation. Dermatomyositis is associated with an underlying malignancy in up to 15-20% of patients [5] and is then considered as paraneoplastic syndrome. These patients present symptoms of dermatomyositis and cancer at the time of the diagnosis or at some point during the follow-up [6]. Patients aged 45-74 years at the time of diagnosis have a higher risk of malignancy [7].

Paraneoplastic dermatomyositis is most commonly associated with ovarian, lung, pancreatic, stomach, colorectal cancers and non-Hodgkin's lymphoma [8]. The risk of malignancy seems to be higher in the first year after the diagnosis of dermatomyositis and reduces gradually over the following years [9]. Overall show patients with dermatomyositis a significantly higher risk of malignancy through all years of follow-up compared to the general population [6,9]. Dermatomyositis can also present as a sign of recurrent malignancy or progression by patients with previous cancer in their medical history, as in our case. This association is rather rare and only few cases have been reported so far [10,11].

This suggests that appropriate clinical follow-up of patients which had been previously diagnosed with malignancy should be performed. In case of sudden onset of cutaneous manifestations or myopathy in these patients a paraneoplastic dermatomyositis should be suspected. The diagnostic approach should definitely include a thorough tumor screening in order to exclude new tumors or recurrence or/and progression of previously diagnosed malignancy, as in our patient.

The pathogenetic mechanism of dermatomyositis related to underlying malignancy remains undefined. It is hypothesized that the onset of paraneoplastic dermatomyositis is a result of an immune disorder or an abnormal immunologic response to substances secreted by neoplastic cells or to newly presented tumor associated antigens.

The clinical symptoms of dermatomyositis vary in severity and number and usually cannot precede the diagnosis of

malignancy. Interestingly, no differences have been found between the idiopathic presentation of dermatomyositis and the paraneoplastic one [12]. In paraneoplastic dermatomyositis it is remarkable that the clinical symptoms can be extremely therapy-resistant as long as malignancy co-exists. Our patient is a perfect example of this relationship as she showed no improvement of her symptoms before the surgery despite systemic therapy with corticosteroids. However she showed a complete resolution of her signs and symptoms after surgical treatment of her breast cancer. This is consistent with previous reports of cases with dermatomyositis associated with breast cancer who demonstrated regression of dermatomyositis only after treatment of the underlying malignancy [13].

Although several cases of paraneoplastic dermatomyositis have been reported no standard treatment regimen has been established yet. Patients with dermatomyositis associated with breast cancer are treated with the standard breast cancer therapies including surgery and neoadjuvant chemo/hormonal therapy according to the severity and grade of the primary tumor and the presence of metastatic disease. As first-line therapy is a therapy with high-dose corticosteroids suggested along with local corticosteroids for a short time after the diagnosis of dermatomyositis. In patients with no response to corticosteroids an immunosuppressive therapy with azathioprine, cyclosporine, rituximab, mycophenolate, methotrexate such as with anticalcineurinic drugs (tacrolimus, pimecrolimus) may lead to an improvement of symptoms and better disease control. The therapy with human intravenous immunoglobulins (IVIG) is suggested as second-line therapy [14].

The response of each patient to the therapy should be individually examined by the physician. When it comes to therapy-resistant cases the risks associated with immunosuppression by underlying malignancy should be seriously balanced. In some cases it is reasonable to stop the systemic immunosuppressive therapy and may maintain the local steroid and anti-pruritic therapy until the surgery of the underlying cancer. The local steroid therapy should again not be given for longer time as adverse effects of local corticosteroids such as skin atrophy may impair the postoperative wound healing. It is recommendable to try to improve the skin condition of these patients if possible before the surgical resection. Alternatively, neoadjuvant chemo/hormonal therapy may be considered in appropriate cases if the skin is clear of infection. In any case, the control of the underlying malignancy remains the most important part of the therapy of paraneoplastic dermatomyositis as symptoms of dermatomyositis improve or completely resolve after cancer treatment, as in our case.

To summarize, although dermatomyositis often presents as an idiopathic disease, when it occurs in adult patients should alert for possible underlying malignancy. Patients with previous cancer in the medical history who develop suspicious signs of dermatomyositis should be examined for a possible recurrence or/and metastatic disease. In female patients, breast and ovarian cancer must be considered as they are common among women. It should also be taken into consideration that paraneoplastic

dermatomyositis may present concurrent with, or at a time separate from the diagnosis of cancer. The highest incidence is however observed within the first year after cancer diagnosis, as happened with our patient.

As the prognosis of paraneoplastic dermatomyositis depends on the underlying malignancy an early recognition and awareness of this entity is not only important for a prompt diagnosis and therapy of the tumor but also for a better prognosis and quality of life of these patients.

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