Our Dermatology Online

Case Report

Dermatomyositis related to the relapse of cervical cancer

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ABSTRACT

Dermatomyositis (DM) is a rare syndrome which belongs to the group of idiopathic inflammatory myopathies (IIM). The diagnosis of DM in adults is an indication for diagnostic evaluation towards malignancy. The exacerbation of clinical symptoms or laboratory markers of DM may indicate the relapse of neoplasm, therefore close follow-up visits of patients are obligatory. We present the case of a woman with a two-month history of progressive muscle weakness, dysphagia and oedemo-erythematous skin lesions limited to the face and trunk. The patient was diagnosed with DM associated with the relapse of cervical cancer.

Key words: cervical cancer, dermatomyositis, paraneoplastic syndrome

INTRODUCTION

Dermatomyositis (DM) is a rare syndrome which belongs to the group of idiopathic inflammatory myopathies (IIM). Clinical manifestation includes progressive muscle weakness and characteristic skin lesions. The association between DM and malignancy has been confirmed by many reports [1-3].

We present the case of a woman diagnosed with DM associated with the relapse of cervical cancer and review the current literature on DM as a paraneoplastic syndrome - characteristic clinical symptoms, that may indicate the coexistence of malignant process.

CASE REPORT

A sixty-seven-year-old woman was admitted to the Dermatological Department in Medical University of Gdańsk in June 2013 for the evaluation of a symmetrical eyelid oedema, confluent oedematous-erythematous skin lesions of lilac colour localized on the forehead, neckline and neck as well as erythomatous skin lesions and scaling in the area of hand nail folds were observed (Fig. 1). The skin lesions were accompanied by progressive muscle weakness and swallowing difficulties. Furthermore, there was a severe oedema of left lower leg and single, indolent lymph nodes were palpable in the right groin region.

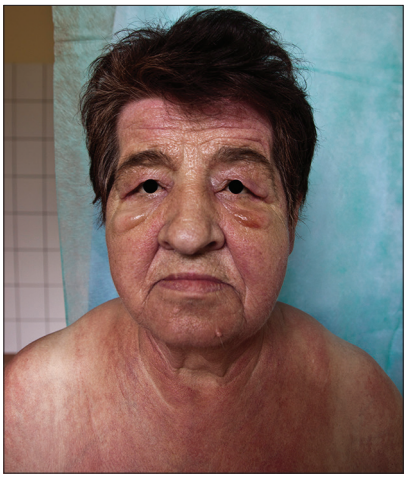

Figure 1: A sixty-seven-year-old female patient with dermatomyositis. Erythematous lesions of lilac colour located symmetrically in the area of eyes accompanied by exudation in the lower eyelids. Erythematous lesions of lilac colour in the skin of forehead and neckline

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The first skin lesions had appeared symmetrically in the area of eyelids in May 2013 and presented as oedema and erythematous lilac-coloured eruptions. The skin lesions were asymptomatic. Similar lesions had appeared shortly after on the skin of the neck and decolletage. During the two-weeks period prior to the hospitalization the patient had started to complain because of progressive muscle weakness manifested by difficulties in performing simple activities, such as combing hair, getting out of bed or climbing stairs. At the same time, symptoms of dysphagia had appeared.

The patient was treated with surgery and radiotherapy combined with chemotherapy due to cervical cancer in the G3 stage at the time of diagnosis in 2006. There were also a history of deep vein thrombosis of left lower limb in 2012 and depression, treated since 2013 with orally administered escitalopram at the dose of 5 mg per day. The patient was regularly controlled by Mental Health Outpatients' Clinic.

The laboratory investigations revealed elevated levels of creatine kinase (CPK) – 1262 U/l, aspartate transaminase (AST) - 108 U/L and lactate dehydrogenase (LDH) - 521 U/L. The peripheral blood smear showed an increased monocytosis, lymphopenia, hyperkalaemia, accelerated erythrocyte sedimentation rate (ESR) - 35 mm/h, high level of D-dimer - 3580,45 mg/l and fibrinogen – 3,78 g/l. Cardiac markers (CK-MB mass, Troponin I) and tumor markers (alpha-fetoprotein, Ca 125, Ca 15.3, Ca 19.9, carcinoembryonic antigen) were within normal limits. The urinalysis did not reveal any pathology. Antinuclear antibodies test on Hep2 cell substrate (ANA-Hep2) was at titer 1:2560 and immunoblot analysis led to detection of anti-Ro-52 antibodies. The myogenic dysfunction was recorded in electromyography (EMG) of quadriceps muscle. Echocardiography did not reveal any significant pathology, whereas the chest radiograph showed an intensified interstitial lung drawing. Lower limbs venous Doppler ultrasound imaging revealed features of superficial vein thrombosis. Due to the patient's history of malignancy, the diagnostic tests concerning the detection of neoplastic disease were performed. The gynecological examination and transvaginal ultrasound imaging did not show any significant pathology. Based on presented clinical features and diagnostic tests performed so far DM was diagnosed. Due to progressive muscle weakness and deterioration of patient's general condition, methylprednisolone pulse therapy was introduced. A single pulse of intravenously administered methylprednisolone at the total dose of 3000 mg resulted in a slight improvement in muscle strength and reduction of dysphagia symptoms. The maintenance therapy included orally administered prednisone at the initial dose of 40 mg per day, whereas the anticoagulant therapy was based on subcutaneously administered dalteparin sodium at the daily dose of 15 000 international units. Along with the treatment we continued diagnostics of neoplastic disease. A contrast-enhanced computed tomography (CT) of abdomen and pelvis showed multiple small lymph nodes along the abdominal aorta, iliac vessels and in the right groin region (Fig. 2). Histopathological examination of the lymph node biopsy (right inguinal region) had revealed metastases of squamous cell carcinoma. In the Regional Oncology Centre in Gdansk a palliative chemotherapy with 5 -fluorouracil and cisplatin was introduced, however after the second cycle of therapy, a deterioration in muscle strength, exacerbation of skin lesions and dysphagia symptoms recurred. The control laboratory tests results of muscle enzymes were normal. After oncological consultation, the palliative chemotherapy (5-fluorouracil, cisplatin) and prednisone were completed by orally administered methotrexate at the dose of 15 mg per week. The improvement in muscle strength, reduction of dysphagia symptoms and resolution of skin lesions were noted.

DISCUSSION

The association of DM with malignant tumors was described nearly 100 years ago by two investigators independently – Kankeleit and Stertz.

DM is considered to be an autoimmune disease. The mechanism of its association with malignancy remains unclear [3]. According to some authors, mediators produced by tumor cells may play role in the initiation

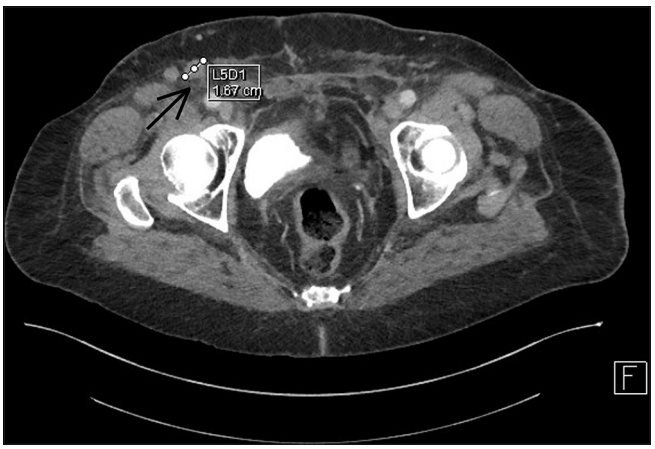

Figure 2: Patient's CT scan of pelvis. Pathological lymph nodes in the right groin region (arrow)

of abnormal immune response against cells of striated muscle and skin [2].

The incidence of cancer in the population of adult patients with DM is estimated at 13-42% [2]. Neoplastic process may precede, appear at the same time or after the onset of DM [4]. The greatest risk of malignancy occurs in a period of first 3 years after diagnosis of DM [5]. The clinical course of the disease correlates with the course of malignant process, however it is difficult to determine whether the resolution of DM symptoms results from tumor remission after oncological treatment or due to immunosuppressive effect of chemotherapy itself [6].

Distribution of tumor incidence associated with DM does not differ from the incidence in the general population, with the exception for ovarian cancer. For this reason, some researchers recommend annual screening towards ovarian cancer in women with diagnosis of DM in the first five years after the diagnosis [7]. In a study population of 618 patients with DM from Sweden, Denmark and Finland, in 198 cases a neoplastic process was diagnosed. A higher incidence of malignant neoplasms of the ovary, lung, stomach, colon and rectum, pancreas and non-Hodgkin's lymphomas was observed in the group of patients with DM compared to the population without DM [8].

The diagnostic criteria of DM introduced by Bohan *et al*. in 1975 have been still actual and include typical for DM skin lesions and three out of four of the following symptoms: symmetrical proximal muscle weakness, abnormal EMG test indicating primary changes in muscle tissue, increased serum levels of muscle enzymes, inflammatory infiltration, degeneration or regeneration and atrophy surrounding muscle bundles in histopathological examination. Pathognomonic for DM skin eruptions include - heliotrope rash, manifested by erythematous-oedematous lesions of lilac colour located symmetrically in the eyelids and Gottron's papules, characterized by the presence of violet papules and plaques over the metacarpophalangeal and interphalangeal hand joints. Similar oedematous-erythematous lilac coloured skin lesions may be also present in the skin of cheeks, knees, elbows, hands, nail folds and the neck, decolletage and shoulders (the shawl sign). In the later stages of the disease skin thickening in the palms of hands (mechanic's hands) as well as linear telangiectasia and splinter hemorrhages in the areas of nails may be observed. The pressure within the nail folds may provoke tenderness (Keining's sign). Skin lesions may either precede or occur at the same time of muscle weakness [9]. In the presented case, the physical examination revealed specific for DM heliotrope rash and less typical erythematous-oedematous lilac coloured eruptions in the skin of forehead, cheeks, neck and neckline.

Progressive muscle weakness is manifested by difficulties in performing daily activities such as getting up from chair, climbing stairs, combing or lifting objects. Fine motor disorders usually occur in an advanced stage of the disease and their severity depend on the initial strength of distal muscles. In the course of DM the involvement of internal organs, including esophagus, respiratory system and heart may appear. DM associated with malignant process may have more fulminant course which can quickly lead to patient's disability or even death.

Clinical observations indicate that in the population of patients with DM, malignancy occur more frequently in males, in the late age of onset, in patients with dysphagia or necrotic skin changes, while in patients with DM presenting arthritis and/or interstitial changes in lungs, naoplasia is rarely found [10].

The histological examination of a biopsy taken from an involved striated muscle reveals characteristic perivascular and perimysial lymphocytic infiltration, which secondarily leads to the perifascicular atrophy [11]. In the presented case the muscle biopsy was not necessary, because the number of required diagnostic criteria fulfilled the diagnosis of DM.

The laboratory findings in patients with DM include numerous non-specific abnormalities, like accelerated erythrocyte sedimentation rate, increased leukocytosis with lymphopenia and eosinophilia. The most characteristic for DM laboratory abnormalities are increased serum levels of enzymes indicative for muscle damage, such as creatine phosphokinase (CPK), which concentration may exceed tens of times the reference value. Moreover, its level correlates with the activity of the disease, however in some cases it may be normal. High serum levels of alanine transaminase (ALT), aldolase and lactate dehydrogenase (LDH) as well as increased level of creatinine in 24-hour urine collection especially at the initial stages of the disease may be also observed. In the presented case, the laboratory assessments performed in the initial stage of the disease showed a significant increase of serum levels of enzymes indicating skeletal muscle damage (CPK, LDH, AST).

Immunological tests reveal positive antinuclear antibodies (ANA) in approximately 50% of adult patients with DM and in 20% of cases the antibodies specific for inflammatory myopathies (MSA) can be found [12,13]. Anti-Mi-2 antibodies are characteristic for DM. Interesting results of a multi-center study by Azuma *et al*. showed that patients with DM associated with malignancy present rather low serum levels of muscle enzymes and the lack of MSA antibodies [14]. Recent independent studies proved that the presence of antibodies against lately described protein with a mass of 155 kDa, may be a negative prognostic marker, which means that in patients with positive above-mentioned antibodies the risk of cancer associated with myopathy is low [15,16]. In our case high titer of ANA was showed. Immunoblot analysis revealed the presence of antibodies against the antigen Ro-52 (anti- Ro52). The antibodies against the antigen Mi -2 (anti -Mi -2) were not detected. The results of immunological tests in the presented case are consistent with the observations by Menéndez *et al*., who showed a higher incidence of malignancy in patients with DM presenting an isolated presence of anti- Ro52 antibodies, without a diagnosis of autoimmune disease [17].

Treatment of DM associated with malignancy includes primarily the therapy of neoplastic process (oncological, surgical). Immunosuppressive therapy used in autoimmune DM is supportive in malignancy associated DM and aims at the improvement of clinical symptoms that result from the involvement of internal organs, striated muscle tissue and skin.

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