

A case report of a patient with dermatomyositis as a prodromal sign of lung cancer

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Abstract: Dermatomyositis (DM) is a connective tissue disease characterized by specific inflammatory lesions in muscle biopsy. It is caused by vasculitis determined by humoral factors with subsequent inflammatory cell accumulation, mainly T CD4+ and B cells, which infiltrate myocytes leading to its vacuolization and degeneration (mainly in the skeletal muscles, rarely in the smooth muscles). The incidence of DM is estimated at 1–10 per million in adults and at 1–3.2 per million in children. The autoimmune mechanism of disease induction is not fully recognized. Several lines of evidence showed the link between DM and neoplastic disease. The first report of dermatomyositis associated with stomach cancer, by Stertz, comes from 1916. In the same time, Kankeleit reported DM associated with breast cancer. Presumably, it is the result of immune reaction against antigens common for muscle and neoplastic cells or some paraneoplastic syndrome underlying mechanism. The report presents the case of a 52-year-old woman with DM (diagnosed according to the Bohan and Peter criteria) and with coexistent squamous lung cancer *in situ*. The left upper lobectomy was performed. No complications in postoperative period were observed. During more than 2 years of follow-up after the surgery, the patient remained in good condition, without DM symptoms, or cancer relapse. Considering that DM may be associated with lung cancer; extensive diagnostic work-up to exclude neoplastic lesions should be performed. Patients aged 40 years or more should be particularly screened.

Key words: dermatomyositis, lung cancer, paraneoplastic symptoms

INTRODUCTION

Dermatomyositis (DM) is a connective tissue disease characterized by *perivasculitis* type inflammation lesions with immune complex deposit formation in endomysial capillaries and with subsequent inflammatory cell accumulation, mainly T CD4+ and B, which infiltrate myocytes leading to its vacuolization and degeneration (mainly in skeletal muscle, rarely in smooth muscle). Muscle cells are damaged by focal phagocyte infiltrations and this leads to muscle fiber loss. Besides a role of viral infections or medications as a trigger, clinical reports showed a relationship of the disease with cancer [1,2]. The first report of dermatomyositis associated with stomach cancer, by Stertz, comes from 1916. In the same time, Kankeleit reported DM associated with breast cancer [3]. Andreev [4] found that

DM coexists with pulmonary cancer rather than with any other neoplastic disease. However, only few papers reported this correlation and no one describes DM together with lung cancer *in situ* when a total recovery with dermatomyositis symptoms resolving after upper lobectomy was observed. The purpose of this paper is to present a case of a patient with DM and *in situ* cancer of the left lung surgically treated.

CASE REPORT

A 52-year-old female with diabetes, previously working in a distillery (exposure to toxic inhalers, including formalin), was treated with amoxicillin 3 × 500 mg due to the upper respiratory tract infection on the ambulatory basis. After the 5th dose of antibiotic, symmetric erythematous lesions on the face and neck occurred. The patient was admitted to the Dermatology Ward because of unclear general signs and symptoms – increasing dyspnea with reduced exertion tolerance. The patient was then referred to the Surgical Ward with sudden and severe upper abdominal pain. The symptoms were associated with nausea and vomiting. In laboratory tests

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CASE REPORTS

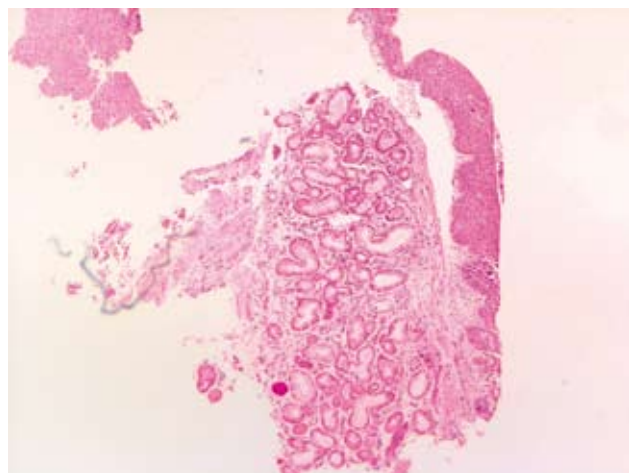


Fig. 1. Squamous carcinoma *in situ* with different grade of atypia (magnification 10x)



Fig. 2. Computed tomography of the thorax (May 25, 2004). Thickening of pleura in apex both side, bilateral pleural-diaphragmatic adhesions. Enlarged lymph node in front of tracheal bifurcation (2.99 × 1.25 cm), upper few lymph nodes (size <1.24 cm)

leukocytosis (14500/mm³) and increased aminotransaminase serum levels (AlAT – 539 U/l; AspAT – 195 U/l) were observed. Because of the presence of intestinal air-fluid level in the left upper abdomen and in the lower abdomen on the X-ray presenting subileus and because of increasing leukocytosis (20180/mm³) the classic cholecystectomy was performed on the day of admission. After the surgery the patient general condition deteriorated; she was not able to walk, sit, and, subsequently, to elevate the upper limbs and even keep the head upright, due to increasing weakness. The patient with severe dyspnea and biochemical parameters suggesting multi-organ failure (creatinine 325 μmol/l, creatine phosphokinase [CPK] 29,550 U/l) was referred to the Internal Ward and then, due to respiratory insufficiency – to the Intensive Care Unit. The patient was 2 times treated with intubation and assisted

mechanical ventilation (from April 17 to April 28 and from May 5 to May 12, 2004).

Laboratory data showed as follows: CPK 59,695–98,520 U/l, lactate dehydrogenase 1392 mg/dl, AlAT 621–26 U/l, AspAT 1316–18 U/l, cardiac troponin I 0.4 ng/ml, C-reactive protein 45.50 mg/ml. Cardiac causes of the patient's severe general condition were excluded (echocardiography was normal, ECG – normogram with negative T wave in I, II, aVF, V2-V6 leads). Because of predominant clinical and biochemical myolysis features which were present, the immune diagnostic work-up was performed and histidyl-tRNA-synthetase antibody (Jo-1) was found (9.7 U/ml). The skeletal muscle antibody test was positive (screening test for antinuclear antibody and bile capillary antibody – negative). The electromyography showed severe myogenous damage mainly in proximal muscle and DM was diagnosed. Screening tests for carcinoembryonic antigen 2.0 ng/ml and α-fetoprotein 1.72 ng/ml were performed with no further diagnostic tests for the detection of cancer. The treatment with 1 g cyclophosphamide pulse and steroids was introduced. After the second dose peripheral leukocytopenia occurred with a subsequent instant recovery. In the bone marrow biopsy regeneration features were present. The third dose of cyclophosphamide was administered. During physical rehabilitation gradual improvement of skeletal muscle function was observed. The patient was referred to the local hospital at the end of May 2004; she could then easily manipulate with upper limbs and move with assistance. Prednisone 20 mg/24h was administered. The consultations by specialists were performed and some abnormalities on physical examination were found: rheumatologic examination – pain and symmetric edema of metacarpophalangeal and proximal interphalangeal joints of both hands, dermatologic examination – erythematous papular lesions on the skin of hand joints, neurologic examination – muscle weakness. The skin/muscle biopsy was performed and histopathologic examination showed vacuolar degeneration of the basement membrane with lymphohistiocytic infiltration of the dermis; striation atrophy in the muscle layer with partial muscle fiber atrophy. Despite immunomodulatory treatment and continuous rehabilitation, the patient's condition deteriorated during her stay in the local hospital.

In June 2004 the patient was referred to the Pulmonary Clinic because of bilateral pneumonia. Bronchofibroscopy showed patent bronchi with mucosal edema and redness, mainly in the left segment 1+2, covered with purulent secretion and with areas of pale necrotic epithelium. Histopathology of biopsy specimen – carcinoma *planoepitheliale in situ*, in the muscular layer of bronchi – interstitial, mainly perivascular lymphocyte infiltrations were shown, which are morphologic characteristics of autoimmune process and belong to polymyositis histopathology features (Fig. 2). Computed tomography of the chest showed no abnormalities except the pleural thickening in both pulmonary apices and bilateral pleurodiaphragmatic adhesion; in front of tracheal bifurcation an enlarged lymph node 2.99 × 1.25 cm and several lymph nodes in the mediastinum ≤1.24 cm (Fig. 1) were shown. Since no cardiologic or anesthesiologic contraindi-

cations were found, the patient was assessed to be eligible for surgery. Because of enlarged mediastinal lymph nodes, the mediastinoscopy was performed (histopathology did not confirm metastatic lesions in the lymph nodes) and subsequently the left upper lobectomy (August 12, 2004) was done (Fig. 3). No complications in the postoperative period were observed. During consecutive 12 weeks 20 mg of prednisone was administered in tapering doses.

During more than 2 years of follow-up, the patient remained in good condition, without DM symptoms, local relapse of lung cancer or other cancer development (Fig. 4).

DISCUSSION

Dermatomyositis is an idiopathic inflammatory myopathy with muscle weakness, creatine kinase elevation, electrophysiologic abnormalities and inflammatory lesions in muscle biopsy. Clinical feature characteristics are progressive symmetric proximal muscle weakness; in serious cases DM may involve respiratory muscles and may lead to the fatal outcome.

In the case described muscle weakness, fully pronounced at the beginning, was dominated by acute abdomen symptoms with subsequent cholecystectomy. Diffused intestinal air-fluid levels (described as subileus) could be the symptom of smooth muscle atrophy. A characteristic skin lesion of dermatomyositis is heliotrope erythema around the eyes. The erythematous rash may occur on the face, the neck, the upper trunk and the posterior surface of arms; it is called a neckline V sign – and that was the reason for the first hospital admission of our patient. In the case presented, skin lesion dynamics was diversified: at the beginning erythema on the face and the neck was more pronounced, while later, when the muscle function improved and respiratory tract “infection” occurred, a papular rash on hands appeared. The clinical feature of muscle involvement caused inability to move and raise the head and (because of muscle of the chest myopathy) – respiratory insufficiency which required mechanical ventilation, with amply pronounced biochemical muscle damage [5,6].

Diagnostic criteria for DM (Bohan, Peter) [7] are as follows:

- 1) progressive symmetric muscle weakness of the inferior and superior extremity girdle with dysphagia (or not) or with respiratory muscle involvement
- 2) muscle biopsy confirming myositis
- 3) increase in muscle enzyme serum levels
- 4) EMG abnormalities indicating primary muscle damage
- 5) characteristic skin lesions.

The presence of 3–5 symptoms in this case confirms the diagnosis of DM.

Nowadays however some investigators claim that the Bohan and Peter criteria from 1975 should be supplemented by immunohistochemical evidence for myositis (muscle-specific aminoacyl-tRNA synthetase antibody, mainly anti-Jo-1 histidyl-tRNA synthetase), with only Jo-1 in the case described [5]. Those criteria despite their shortcomings are however still



Fig. 3. X-ray image of the chest (August 12, 2004). State after upper left-side lobectomy

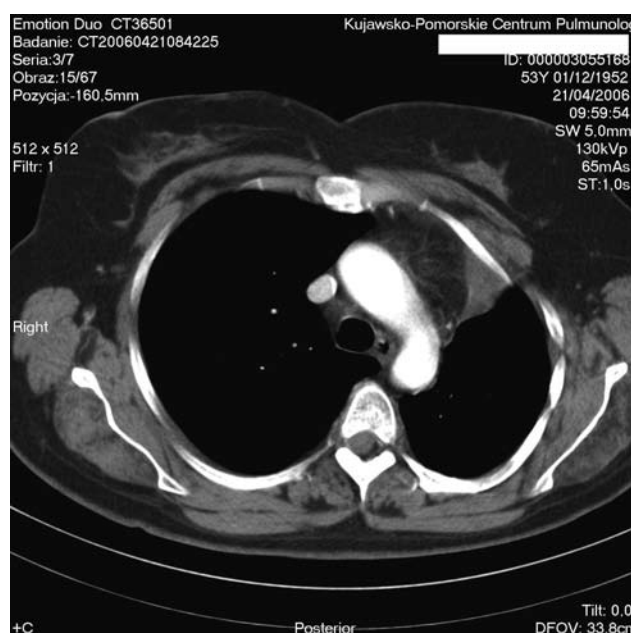


Fig. 4. Computed tomography of the chest (April 21, 2006). State after upper left-side lobectomy. Dislocation of the mediastinum in the left side. Frontal pleural adhesions (pericardial and diaphragmatic) on the left side

accepted and sufficient to diagnose DM or polymyositis, the more so because the immunosuppressive treatment of both these diseases remains similar [8].

In DM, internal organs may be involved and interstitial lung fibrosis can be seen [6,8]. However the most important feature in adults with DM is an increased incidence of malignancies. Several authors reported coexistence of DM with various cancers (especially that of the lung, stomach, colon, ovary or non-Hodgkin lymphoma), with the prevalence of 6–45% of cases [1,5].

CASE REPORTS

There are several hypotheses regarding concurrent occurrence of cancer and DM – immune disorder (humoral and cell-mediated), angiopathy, viral infections facilitating abnormal immunologic response, substance secretion by neoplastic cells or as a response to neoplasm in cross-reaction to newly presented “exposed” antigens. The symptoms of DM usually precede the diagnosis of cancer. In the extensive study by Hill et al. [1] among 618 patients with DM, 198 had cancer and in 115 cancers were found after DM was diagnosed. A similar coincidence was shown by Fujita et al. [9] with focus on the small cell cancer, squamous cancer and adenocarcinoma. The majority of malignancies are diagnosed after DM, usually in two years since the onset of myositis symptoms. Given the probable malignant trigger mechanism of DM, the tumor may be diagnosed before or together with DM. For example, in lung carcinoma that is possible in the case of the preceding occurrence of paraneoplastic syndrome which is present in about 10% of cases. Paraneoplastic symptoms are clinical abnormalities associated to neoplastic disease, not directly related to primary tumor or metastases [10-12]. The symptoms resolve after the malignant tumor is completely removed.

In this case report, DM was the paraneoplastic syndrome coexisting with squamous cancer of the left lung. Available data show that it is one of the most common cancers associated with dermatomyositis [1,9]. The diagnosis of cancer in the case described was made 4 months after the sudden beginning of DM. Surgical treatment of cancer in some cases may lead to a significant decrease in symptoms, or a recovery from DM, also in cases resistant to pharmacological treatment [12]. In the case presented DM occurred in the *in situ* phase of the disease, which allowed radical surgical treatment and a complete recovery from DM. Keeping in mind that DM may be associated with lung cancer, extensive diagnostic work-up to exclude neoplastic lesions should be performed. Patients aged 40 years or more should be particularly screened.

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