

## Case Report

# Dermatomyositis as presenting feature of ovarian cancer, treated with neo-adjuvant chemotherapy and interval debulking surgery<sup>☆</sup>



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## Introduction

Dermatomyositis is a rare, idiopathic, inflammatory myopathy with reported incidences varying from 0.5–0.89 per 100,000 (Robinson and Reed, 2011). There is a well documented relationship with malignancies such as breast, lung or ovarian cancer (Sigurgeirsson et al., 1992; Hill et al., 2001) and it has previously been reported as a presenting feature of ovarian cancer. However, previous reports in ovarian cancer are of cases treated with primary de-bulking surgery. We believe this to be the first report of a case treated with neo-adjuvant chemotherapy and interval debulking surgery.

## Case

A 57 year old Caucasian lady presented to her General Practitioner with a pruritic rash on her anterior chest, upper arms, hands and face. Two weeks later proximal myalgia and stiffness of all four limbs developed and a dermatology opinion was sought. On physical examination there was an erythematous maculopapular rash affecting the

face, trunk and upper limbs which was more prominent in photo-exposed areas, with flat-topped scaly lesions on the dorsum of both hands and wrists thought likely to be Gottron's papules. Serum creatine kinase (CK) was elevated at 3012 IU/L (n = 30–135).

Medical history included hypothyroidism, hypertension, osteoporosis, depression and previous lumbar discectomy for degenerative disease. She was prescribed levothyroxine, fluoxetine, amitriptyline, calcium carbonate, alendronic acid, lisinopril, paracetamol and omeprazole. There was a history of ovarian cancer in the patient's mother.

Dermatomyositis was suspected and a skin biopsy was performed under immunofluorescence. The skin biopsy revealed a vacuolar interface dermatitis consistent with a collagen vascular disease or dermatomyositis [Fig. 1].

One week later the patient was admitted to hospital with progressive proximal muscle weakness. CK had risen to 11,608 and erythrocyte sedimentation rate was elevated at 46. Temperature was elevated at 38.2 °C. Physical examination revealed a rash affecting her chest, back and upper arms (shawl distribution), muscle weakness predominantly affecting hip flexion and shoulder abduction, and a palpable mass in the right iliac fossa.

Prednisolone 40 mg was commenced with a dose increase to 60 mg after 10 days due to lack of response. CK fell to 2279 but without any symptomatic improvement and she remained bedbound in hospital.

CT scan of chest, abdomen and pelvis revealed a 9.5 cm × 8.8 cm lobulated, cystic adnexal mass with multiple peritoneal deposits. Biopsy of the pelvic mass was consistent with a high grade serous carcinoma of ovarian or primary peritoneal origin.

Neo-adjuvant chemotherapy with Carboplatin AUC-6 and Paclitaxel 175 mg/m<sup>2</sup> was commenced as an in-patient 1 month after presentation. Ca125 fell from 2231 KU/L to 172 after 3 cycles of chemotherapy, all given as an in-patient. CK rose to 3256 during week 1 of chemotherapy but was within normal range at 51 by cycle 3. Muscle weakness improved during chemotherapy and she was mobilising independently on the ward after 2 cycles. A relapse of her photosensitive rash responded to hydroxychloroquine. Prednisolone was gradually reduced to a dose of 30 mg.

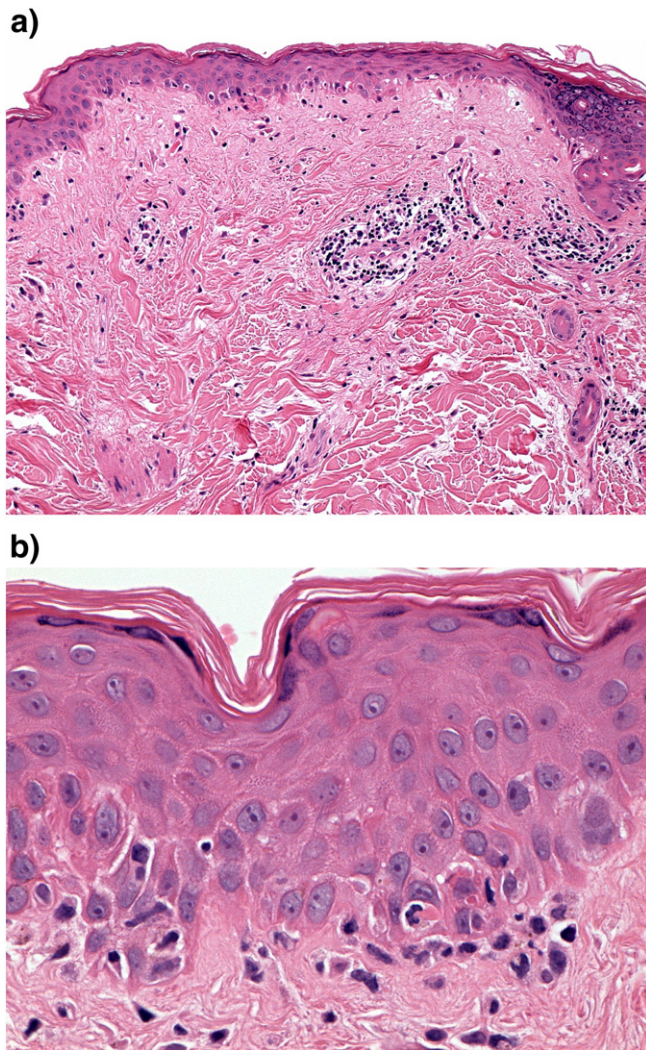
CT scan after 3 cycles showed a good partial response to treatment and a fourth cycle of neo-adjuvant chemotherapy was given as an out-patient.

She proceeded to a laparotomy, anterior resection of the rectum with re-anastomosis, bilateral salpingo-oophorectomy, hysterectomy and omentectomy without intra-operative complications. Post-operatively,

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**Fig. 1.** Images of the skin biopsy showing the vacuolar interface dermatitis at 10 $\times$  (a) and 40 $\times$  (b).

a flare of the rash affecting her shoulders, back, elbows and knees, and subsequent mild proximal muscle weakness, responded after increasing prednisolone to 40 mg.

Following cytoreductive surgery, a 1 cm peritoneal deposit remained in an inaccessible area beneath the right hemi-diaphragm. Her post-surgery CT scan 6 weeks later identified diffuse low volume peritoneal disease in the right and left paracolic gutters. Two further cycles of post-operative carboplatin and paclitaxel were given, with a further response but persistent low volume peritoneal disease on her end of treatment CT, and Ca125 of 54. No dose reductions or delays were required during chemotherapy and the only grade 2 toxicity experienced was alopecia. Prednisolone was gradually reduced to a maintenance dose of 10 mg.

The patient experienced exacerbation of her skin rash 3 months after completion of chemotherapy, but remained asymptomatic of her ovarian cancer. There was a rise in Ca125 and CK, and restaging CT scan revealed new low volume ascites and an increased volume of peritoneal disease. There was a subsequent relapse of proximal muscle weakness. Prednisolone was increased to 40 mg, with an improvement of the skin rash and fall in CK, although muscle weakness persisted.

Chemotherapy for relapsed disease with weekly carboplatin and paclitaxel and 3-weekly bevacizumab was commenced 5 months after completion of her post-operative chemotherapy. Bevacizumab was stopped after the first cycle due to haematuria. Ca125 levels were rising after 4 months of second-line chemotherapy, with

disease progression confirmed on CT. Although CK levels continued to fall, disease progression coincided with worsening proximal muscle weakness and new difficulties swallowing.

Chemotherapy was stopped and the patient died from progressive disease 18 months after initial presentation.

## Discussion

The association between dermatomyositis and malignancy is now well recognised. In one Swedish series, 15% of patients presenting with dermatomyositis were subsequently found to have a malignancy (Sigurgeirsson et al., 1992) while a later pooled analysis of Scandinavian studies identified a malignancy in 32% of patients with dermatomyositis (Hill et al., 2001). The increased risk of ovarian cancer is also recognised with a reported incidence in dermatomyositis of 13.3% (Cherin et al., 1993), and a reported standardised incidence ratio of 10.1 (Hill et al., 2001). Ovarian cancer is commonly advanced at the time of diagnosis; in one case series of 14 patients, all had stage III or IV disease at presentation (Davis and Ahmed, 1997).

Clinical features of dermatomyositis include photosensitivity affecting the upper back, chest, and shoulders (shawl sign), face, ears and hands. Further cutaneous features include Gottron's papules, a heliotrope rash and periungual telangiectasia. Muscle weakness predominantly affects proximal muscles and is symmetrical. Skin and muscle disease may occur concurrently or independent of each other. Other features include dyspnoea due to weakness of the intercostal muscles or interstitial lung disease; myocarditis leading to heart failure or arrhythmias; and dysphagia due to oesophageal involvement. CK levels are commonly elevated and used to monitor disease activity, but can be normal in active disease. (Callen, 2000; Stone, 2010; Smith et al., 2009).

The pathogenesis is that of a microangiopathy, characterised by complement deposition in the microvasculature of the muscle and antibody mediated capillary destruction. Confirmation of the diagnosis requires tissue biopsy of the skin or muscle. Skin biopsy reveals an 'interface dermatitis' on immunofluorescence, with vacuolar changes at the dermal-epidermal junction and a perivascular lymphocytic inflammatory infiltrate (Stone, 2010; Smith et al., 2009). Muscle biopsy demonstrates a perivascular inflammatory infiltrate, capillary obliteration, capillary thrombosis, endothelial cell damage and perifascicular atrophy (Robinson and Reed, 2011; Stone, 2010).

Treatment with high dose glucocorticoids, such as prednisolone 0.5–1 mg/kg, may result in an improvement of CK levels within the first couple of weeks. There is often a delay before muscle strength returns. Muscle weakness may respond better than skin rash. However, steroid induced proximal myopathy is common and can present similarly to active disease. Second line treatment with azathioprine, methotrexate or cyclophosphamide may be required for aggressive disease. Hydroxychloroquine may be useful as a steroid sparing agent (Robinson and Reed, 2011; Callen, 2000; Vermaak and McHugh, 2012).

Independent of an underlying malignancy dermatomyositis may have a poor prognosis with reported rates of remission range from 25%–77%. Recent series report a 5 year OS of 75–90%. Underlying malignancy is an established risk factor for poor prognosis in dermatomyositis, with lung, cardiac and oesophageal involvement also poor prognostic factors (Robinson and Reed, 2011; Marie, 2012).

There is little evidence to guide treatment of dermatomyositis in the presence of ovarian cancer, although historically this has involved surgical debulking with or without post-operative chemotherapy. Prognosis is poor with mortality reported at 100% for patients with ovarian cancer and dermatomyositis in one series (Davis and Ahmed, 1997). Our case demonstrates that dermatomyositis in this setting can improve with neo-adjuvant chemotherapy and interval debulking surgery, in conjunction with corticosteroid therapy and physiotherapy. Skin rash may persist despite improvement in muscle function and treatment of the underlying ovarian cancer. Worsening of the skin rash may also be the first sign of relapsing disease.

Recognition of the high risk of ovarian cancer in the dermatomyositis population, particularly in females aged over 40, can expedite diagnosis.

#### Conflicts of interest

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