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Case report

Dermatomyositis - key to diagnosing ovarian cancer, monitoring treatment and detecting recurrent disease: Case report

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1. Introduction

Dermatomyositis is an idiopathic inflammatory myopathy characterized by proximal skeletal muscle weakness, muscle inflammation and distinct cutaneous eruptions. The disease is rare, with an incidence of 0.5–0.89 per 100,000 with a female to male predominance of 2:1 (Mammen et al., 2013). There is an association between dermatomyositis and malignancy. The most common cancers in female patients are ovarian (13.3–26%) and breast cancer (13.5%) (Sigurgeirsson et al., 1992).

In this case report, we describe two premenopausal women with skin and muscle symptoms consistent with dermatomyositis. They were started on high-dose immunosuppressive therapy without resolution of symptoms and were subsequently diagnosed with stage III ovarian cancer. After debulking surgery and adjuvant chemotherapy their symptoms associated with dermatomyositis resolved.

2. Case 1

Case 1 is a 38-year-old G0 healthy female presenting with an erythematous facial rash, muscle pain and weakness in her shoulders and hips and swelling in the proximal nail folds [Fig. 1a]. She was diagnosed with dermatomyositis and started on mycophenolate mofetil 1000 mg BID, prednisone 30 mg daily and topical tacrolimus. Labs showed an elevated anti-p155/140 autoantibody. PET-CT showed a hyper-metabolic left para-aortic mass and lymph node (SUV 15.6 and SUV 4.6, respectively) with a focus of uptake in the right ovary (SUV 8.1). A retroperitoneal biopsy of the left para-aortic lymph node showed metastases from a Mullerian primary with serous differentiation. CA-125 level was 65. Prior to surgery, mycophenolate mofetil was held and prednisone was decreased to 20 mg daily. The patient underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy and argon beam ablation. Intraoperatively, there was a right ovarian mass and disease in the para-aortic region requiring radical dissection for optimal cytoreduction. Stress dose steroids were given during surgery and for 24 h postoperatively and she was continued on prednisone 20 mg daily. Final pathology revealed stage IIIAi2 high-grade serous carcinoma. The patient was of Ashkenazi Jewish ancestry and had a maternal great-grandmother with ovarian cancer. Her genetic testing was negative. She received adjuvant chemotherapy with IV carboplatin and paclitaxel. Her symptoms and rash resolved after surgery and two cycles of chemotherapy [Fig. 1b]. Her CA125 trended down to 55.6. After surgery and two cycles of chemotherapy, she developed a pelvic abscess that required drainage and antibiotic therapy. Cycle 3 of chemotherapy was delayed due to infection. At the time of this report, the patient had completed chemotherapy and has no evidence of disease.

3. Case 2

Case 2 is a 43-year-old G1P0010 healthy female, who presented with a 6-week history of flu symptoms, muscle and joint pain and skin rash. Her OBGYN history was notable for one prior termination of pregnancy and OCP use for 20 years. She had a paternal and maternal grandmother with breast cancer. She was started on high-dose

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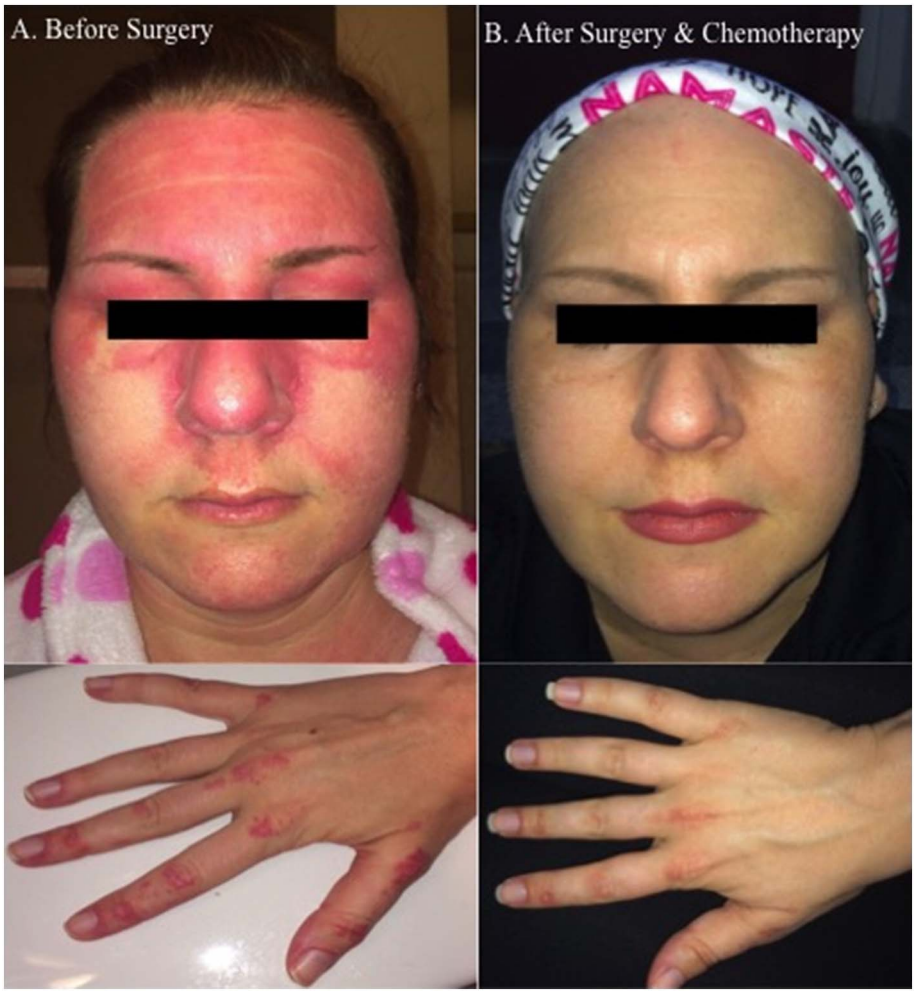

Fig. 1. A) Case 1 - Dermatomyositis skin manifestations including Gottron's papules, heliotrope facial rash and periorbital edema prior to surgery and chemotherapy B) Case 1 - Resolution of skin manifestations after surgery and chemotherapy.

prednisone and antibiotics. Symptoms did not improve and she continued to have a macular erythema over shoulders, neck and face with periorbital edema. A MRI of bilateral thighs and muscle biopsy showed changes consistent with dermatomyositis. CT imaging revealed a right adnexal mass with omental caking. Immediately before surgery, CA125 was 338. She underwent exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy and radical ovarian tumor debulking. She was sub-optimally debulked. Intraoperatively, there were bilateral complex adnexal masses, extensive omental caking with numerous small implants on the mesentery of the small bowel. Stress dose steroids were given during surgery and for 24 h postoperatively. She was continued on prednisone 60 mg daily. Final pathology revealed Stage IIIC high-grade serous ovarian carcinoma. Genetic testing confirmed BRCA2 mutation. She received adjuvant chemotherapy with 6 cycles of IV carboplatin and paclitaxel with bevacizumab starting cycle 2. She had improvement in symptoms and remained on maintenance bevacizumab for 16 months, but it was discontinued due to toxicity. About 1 year later, she had recurrence of her rash and muscle symptoms and was noted to have an elevated CA125. CT imaging confirmed recurrence and she was started on carboplatin and doxorubicin. She had an excellent response with downtrending CA125 and resolution of dermatomyositis symptoms. She is currently enrolled in a clinical trial with randomization between oral PARP inhibitor rucaparib versus placebo. Recent imaging shows no evidence of recurrent disease.

4. Discussion

Dermatomyositis is an autoimmune connective tissue disease that presents with cutaneous eruptions including discoloration on the eyelids with edema, a flat rash on the face and upper trunk, and erythema of the knuckles with raised violaceous scaly eruptions (Mammen et al., 2013). Most patients also have symmetric proximal muscle weakness (Mammen et al., 2013). An elevated creatine kinase, aldolase, AST, ALT and lactate dehydrogenase, which are released from damaged muscle, are often present, but not required for diagnosis (Mammen et al., 2013). Other myositis-specific autoantibodies can be associated with dermatomyositis including anti-Mi-2, anti-Jo-1, anti-U1-RNP and anti-155/140 (Mammen et al., 2013; Wolff et al., 2017). The anti-p155/140 autoantibody increases the risk of an underlying malignancy by 18-fold and previous reports have shown that 71% of patients with this antibody will be diagnosed with cancer (Mammen et al., 2013; Selva-O'Callaghan et al., 2010).

The most common malignancies associated with dermatomyositis are ovarian, breast and colon cancer, melanoma and non-Hodgkin's lymphoma (Dalakas, 2014; Hill et al., 2001). Ovarian cancer was found in 8.3% of patients with dermatomyositis (Dobloug et al., 2015). Cancer is most commonly diagnosed simultaneously with or during the first year after the diagnosis of dermatomyositis although there continues to be an elevated risk of malignancy even after 5 years (Hill et al., 2001). Malignancies are usually identified through a history, physical exam, basic labs and/or age-appropriate screening tests (Dalakas, 2014). In women, a transvaginal ultrasound and CA125 may be helpful to identify ovarian cancer (Mammen et al., 2013). If malignancy is clinically

suspected, a whole body PET scan can be considered (Dalakas, 2014). It has been proposed that patients with dermatomyositis and anti-p155/140 autoantibody should have a whole body PET scan due to the high association of this antibody with underlying cancers (Selva-O'Callaghan et al., 2010). Other studies have shown that malignancy is increased in all patients with dermatomyositis, even those less than 45 years old (Hill et al., 2001). Our patients were both under 45 and highlight the importance of maintaining a high clinical suspicion regardless of age. Patients who have a negative malignancy screen initially should have careful surveillance. Current recommendations for ovarian cancer surveillance in women with dermatomyositis include pelvic exam, CA125 level and transvaginal ultrasound at 6–12 month intervals for at least 2 years after diagnosis, but observation for up to 5 years may have benefit (Sontheimer et al., 2012).

In patients with dermatomyositis, there are some important considerations regarding preoperative and postoperative management due to immunosuppression. Preoperatively and postoperatively, our patients were continued on their outpatient oral steroid regimen along with supplemental perioperative IV steroids. In patients with functional adrenal insufficiency from high dose steroids, there is concern for adrenal crisis induced by the stress of surgery and historically patients have received preoperative stress dose steroids (Marik and Varon, 2008). For an ovarian debulking surgery, the patient would continue their outpatient regimen of steroids and receive hydrocortisone 100 mg IV once and continue hydrocortisone 50 mg IV q8hours for 24 h postoperatively (Jackson et al., 2015).

High dose steroids have negative impacts including poor wound healing, risk of infection, fluid retention and hyperglycemia. In one of our patients, steroids may have contributed to the development of a postoperative wound abscess. New evidence suggests that if patients continue their outpatient steroid regimen, no preoperative stress dose steroids should be required to prevent adrenal crisis (Marik and Varon, 2008; Kelly and Domajnko, 2013). A Cochrane review showed that supplemental perioperative steroids did not decrease adverse effects or complications in patients with adrenal insufficiency undergoing surgery, although results were limited by small number of patients (Yong et al., 2012). The team should be aware that the patient has been on high-dose corticosteroids, but clinicians may consider giving stress dose steroids only if the patient develops volume refractory hypotension consistent with adrenal crisis (Marik and Varon, 2008).

Dermatomyositis symptoms can lead to the initial diagnosis of ovarian cancer, but can also be used to monitor treatment and recurrence. Both of these patients and other case reports describe resolution of symptoms after surgery and chemotherapy that parallel down trending CA125 levels (Chao and Wei, 2009; Christie et al., 2013). In a similar fashion, relapse of dermatomyositis can be the first sign of recurrent ovarian cancer (Chao and Wei, 2009; Christie et al., 2013). In Case 2, the patient represented with recurrent skin manifestations, followed by muscle symptoms and was then found to have a rising CA125. During ovarian cancer surveillance in patients with dermatomyositis, it is important to be vigilant in asking about recurrent skin manifestations or muscle weakness, as this could be the first indication of recurrent malignancy.

Dermatomyositis patients who are diagnosed with breast or ovarian cancer should have genetic testing for BRCA mutations. Case 2 in this case report was positive for the BRCA2 gene mutation, while the other patient's genetic testing returned negative. There is only one other case report related to dermatomyositis and ovarian cancer in which genetic testing has been reported and was positive for BRCA1 mutation (Arshad and Barton, 2016). Other patients with dermatomyositis who were subsequently diagnosed with breast cancer have been found to have BRCA1 gene mutations (Selva-O'Callaghan et al., 2010). Genetic testing is an important component in caring for these patients to ensure they have appropriate risk reduction surveillance if they have positive testing.

Clinicians should have a high clinical suspicion for underlying ovarian cancer, especially with an elevated anti-p155/140 autoantibody, in women of all ages diagnosed with dermatomyositis. Dermatomyositis patients are often immunosuppressed, which can present unique challenges at the time of surgery for ovarian cancer. Treatment response and recurrence of disease can be monitored with dermatomyositis symptoms. All women diagnosed with dermatomyositis and ovarian cancer should have genetic testing.

Consent

Written informed consent was obtained from the patients for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

The authors have no conflicts of interest.

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