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Case Report

Two fatal cases of dermatomyositis and ovarian cancer

二個同時患皮肌炎和卵巢癌的死亡個案

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Dermatomyositis (DM) is known to be associated with an increased incidence of internal malignancies. Initial diagnosis is often made by dermatologists because of distinctive skin signs of this serious disease. Ovarian cancer is the second most common and the leading cause of death from gynaecologic malignancies in Australia. Seventy percent of patients have metastatic disease at the time of diagnosis. We present two cases to highlight the importance of a proactive approach to the management of ovarian cancer in adult female DM patients.

皮肌炎與內在惡性腫瘤的關聯一向爲人所知。皮膚科醫生常能根據這個嚴重疾病獨特的皮膚表徵而首先作出診斷。在澳洲卵巢癌是第二位最常見及死亡率最高的婦科惡性腫瘤，七成的病患在確診時已有癌細胞轉移。我們報告兩個病例以顯示進取的卵巢癌治療方案對成年女性皮肌炎患者的重要性。

Keywords: CA125, dermatomyositis, fatal outcome, ovarian neoplasms

關鍵詞：CA125 ，皮肌炎，致命結果，卵巢腫瘤

Patient A

Time to diagnosis of ovarian cancer from the onset of symptoms: 11 months

Patient A was an 85-year-old woman who was referred for the management of an eight week history of weakness, rash, dysphagia and dyspnoea. A dermatologist had been consulted because of a progressive rash.

On arrival at the emergency department, her face was oedematous as were both legs. There was generalised erythema with a v-shaped photo-distributed rash over her neck and upper chest. Nail fold erythema, paronychia, and Gottron's papules over her metacarpophalangeal and proximal interphalangeal joints bilaterally were present, as were conjunctival injection and heliotrope rash (Figures 1 and 2). Several mobile inguinal lymph nodes were palpable bilaterally.

A provisional diagnosis of dermatomyositis (DM) was made and she was admitted for investigations. Patient A remained dyspnoeic and hypoxic on the ward. High-resolution chest

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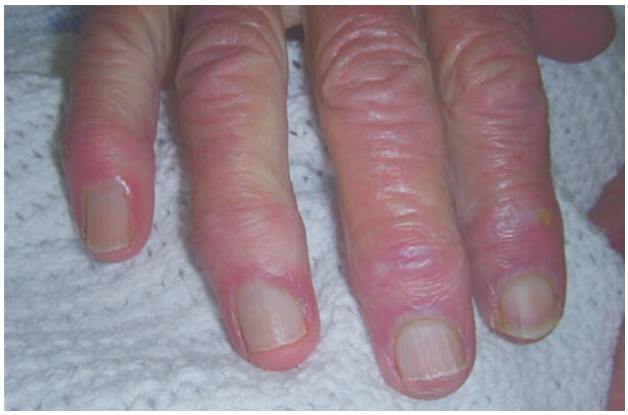

Figure 1. Gottron's papules.

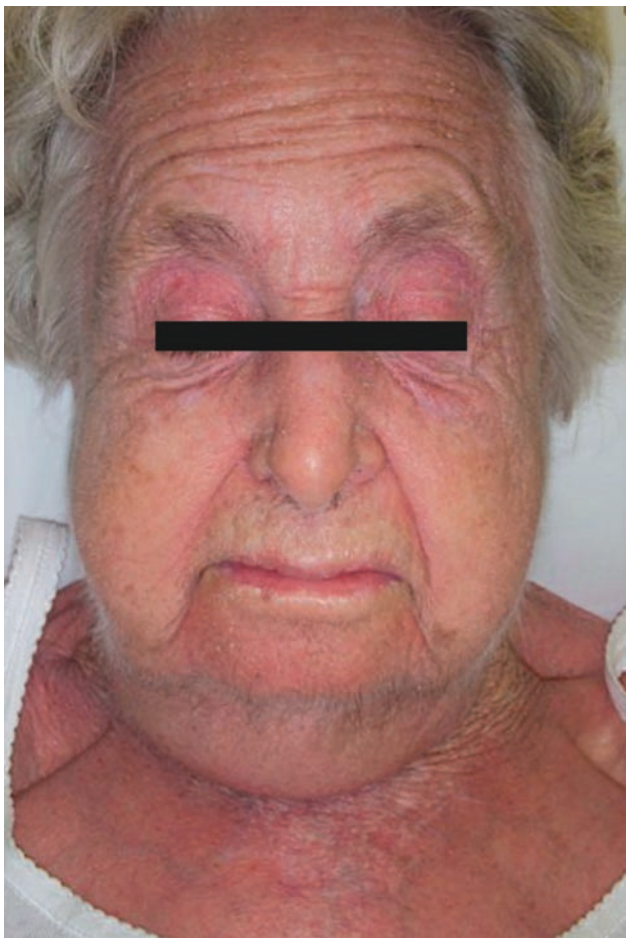

Figure 2. Heliotrope change in the eyelids and photosensitive change on the upper chest.

computed tomography showed bilateral pulmonary fibrosis. The diagnosis of interstitial lung disease secondary to DM was made. Oral prednisolone 60 mg daily and betamethasone ointment were initiated. Meanwhile the rash remained prominent and pruritic.

Skin biopsy showed changes consistent with a lichenoid reaction with negative immunofluourescence. The muscle biopsy showed no inflammation and a normal myosin heavy chain 1 (MHC1) pattern with some neurogenic features which made autoimmune myositis unlikely. Cancer antigen 125 (CA125) was 1795 kU/L at the time (Figure 3). Transvaginal ultrasound showed a mass measuring 28×29×32 mm in the left adnexal region. The gynaecologist was unsure if it was a malignant process.

Patient A was discharged home with follow-up. Unfortunately, she remained dependent on high doses of prednisolone for her dyspnoea and hypoxia. Azathioprine was added as a steroid-sparing agent. Even though the proximal weakness improved significantly with the immunosuppression, persistent skin lesions on the hands were causing significant discomfort and distress. At six months, the option of explorative laparoscopy was declined by the patient. At nine months, Patient A presented with a new swelling in her left cervical region. The biopsy showed poorly differentiated large cell carcinoma with weak CA125 staining which was consistent with ovarian cancer. CA125 was 5815 kU/L (Figure 3). Oral cyclophosphamide was initiated for her metastatic ovarian cancer. She tolerated the chemotherapy well with a slight improvement in her neck swelling and skin rash. CA125 was 216 kU/L after six cycles (Figure 3). On follow-up at 15 months, she complained of new right sided abdominal pain and fatigue. CA125 was 1077 kU/L (Figure 3). One week later, Patient A was re-admitted to hospital, critically ill. Further imaging showed gastric outlet obstruction secondary to metastatic serosal disease

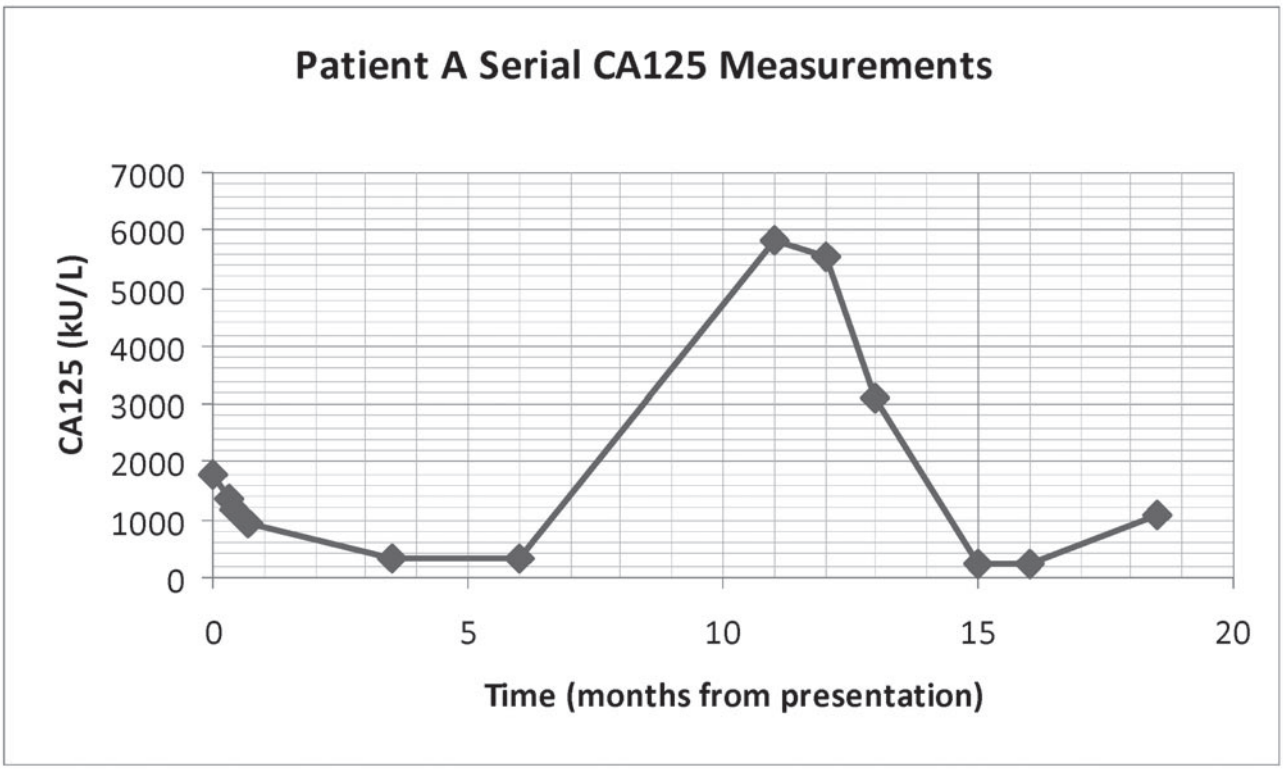

Figure 3. Patient A's CA125 over time.

complicated by aspiration pneumonia. Sadly, she died three weeks later.

Patient B

Time to diagnosis of ovarian cancer from the onset of symptoms: 8 months

Patient B was a 57-year-old woman who was referred for management of a worsening rash. The rash affected the upper limbs mainly, and had been present for eight months along with six months of fatigue and a weight loss of 12 kg. She noticed that it was becoming more difficult to comb her hair. A dermatologist was consulted three months earlier and suggested psoriasis as a possible cause. Skin biopsies were unremarkable at the time. Patient B was investigated 18 months prior for post-menopausal vaginal bleeding. Repeat transvaginal ultrasound 6 months prior to presentation was unremarkable.

On examination, the patient had an erythematous and scaly scalp which extended onto the forehead. She had early non-scarring alopecia (Figure 4). No heliotrope rash was noted. She had bilateral and well demarcated erythema with mild scaling on the sun exposed areas of the arms. On the hands, there was a symmetrical erythematous rash with rugged cuticles and Gottron's papules around the metacarpophalangeal joints. Painful digital ulcers on her toes were evident (Figure 5).

She was admitted to hospital for further management of her general symptoms and the rash, which was initially treated with topical steroids. Skin biopsies showed lichenoid changes and immunofluorescence was negative. The diagnosis of DM was made and oral prednisolone 60 mg daily was started with significant improvement of the proximal weakness.

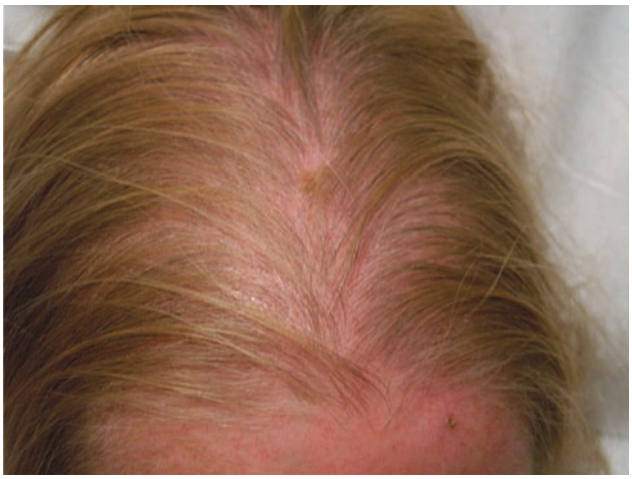

Figure 4. Erythematous and scaly scalp with non-scarring alopecia.

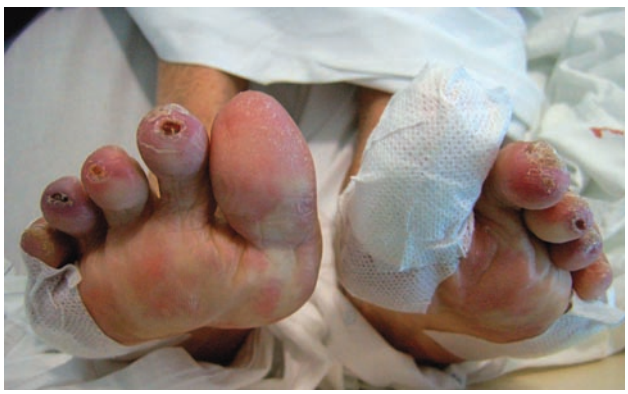

Figure 5. Painful digital ulcers of the toes.

A full malignancy screen was performed. Computerised tomography (CT) of the pelvis showed a large mixed cystic and solid pelvic mass with displacement of the upper rectum and effacement of adjacent fat planes. Transvaginal ultrasound showed a large heterogeneous myometrial mass arising from the uterine fundus with invasion into the endometrial cavity and a smaller left adnexal complex cystic mass. CA125 was 2035 kU/L at the time (Figure 6). The gynaecologist felt that the pelvic lesions had a low chance of resectability and a high risk for operative complications. Fine needle aspirate showed adenocarcinoma, cytokeratin 7 (CK7) and CA125 positive, suggestive of malignancy arising from the female genital tract.

Neoadjuvant chemotherapy with paclitaxel and carboplatin was commenced and it was well tolerated. Follow-up CT after five cycles showed almost complete clearance. CA125 decreased significantly (Figure 6). However, despite moderate daily oral prednisolone (10-20 mg) throughout this period, she continued to be troubled by the ulcerating lesions on the hands and elbows which were very debilitating at times.

Unfortunately, prior to her assessment for surgery, she was readmitted to hospital critically ill and deteriorated rapidly before succumbing to aspiration and respiratory arrest. CA125 was 2209 kU/L at the time of her death (Figure 6).

Discussion

The incidence of dermatomyositis is 10 per million people and the average age of diagnosis is 40. Women are twice as likely to be affected.[1] DM has been associated with malignancies, especially ovarian, lung, pancreatic, stomach, colorectal, non-Hodgkin lymphoma and nasopharyngeal cancers in Asians.[2,3] The relative risk is highest in the first year after diagnosis and among patients older than 49.[4]

In Australia, ovarian cancer is the second most common gynaecological malignancy and the leading cause of death from gynaecologic malignancies.[5] Seventy percent of patients have metastatic disease at the time of diagnosis.[6] Despite current multimodal therapy, including aggressive cytoreductive surgery and combination chemotherapy, five-year survival rates are poor.[7] The lifetime risk of a woman being diagnosed with ovarian cancer by the age of 75 is approximately 1%. However, it is important to note that ovarian cancer has been recorded in up to 13% female DM patients.[8]

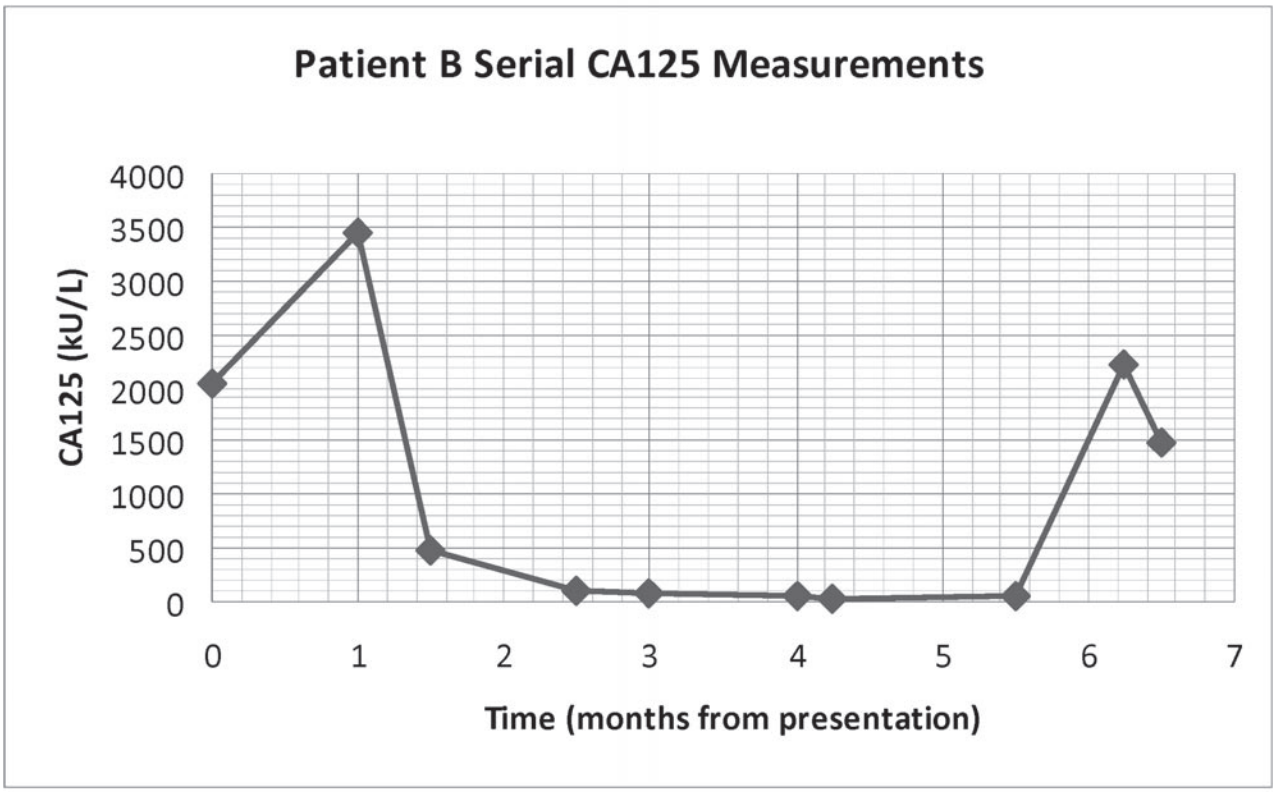

Figure 6. Patient B's CA125 over time.

The onset of DM is often insidious. It has been recognised that cutaneous lesions precede muscle disease in one third to one half of patients and myositis follows within 3-6 months in most patients.[9] Pathognomonic Gottron's papules occur in approximately 70% of patients and heliotrope rash in 30-60% of patients during the course of the illness.[10] It is of interest that, the heliotrope sign derives its name from the vivid lavender flowers of a genus of flower plants, Heliotropium. Other manifestations include mechanic's hands, periungual telangiectasias, dysphonia and dysphagia. Not all patients have these problems. However, if they are present, they should prompt clinicians to consider skin and muscle biopsies to help with reaching a definitive diagnosis.[11]

Once the diagnosis of DM has been made in a mature female patient, the clinician should proceed to investigate as to the possibility of an underlying malignancy. Hill et al[2] suggests that in addition to routine examination and laboratory screening, CT imaging of the chest, abdomen and pelvis, ultrasound scan of the abdomen and pelvis, mammography, and gynaecological examination, are justified. CA125 was used in both of our patients for diagnosis, monitoring chemotherapy effectiveness and recurrence indication.

CA125 is a measure of epithelial antigen protein derived from coelomic epithelium. It is also raised in pancreatic cancer as well as non-malignant condition such as endometriosis, benign ovarian cysts, cirrhosis and pericarditis.[12] CA125 is readily available; it can be repeated at appropriate intervals and is minimally invasive. CA125 has a sensitivity of 53%-89% and specificity of 98% for the diagnosis of ovarian cancer.[13] Interestingly,

over 90% of advanced ovarian cancer have elevated CA125 but only 50% of stage I ovarian cancers have abnormal CA125.[14] CA125 should be measured if a patient becomes generally unwell, with symptoms suggestive of progression, to confirm recurrent disease and as a baseline for future therapy.[15]

In many countries, the average life span has been increasing. In itself, older age should no longer be a barrier to necessary and appropriate clinical management, particularly in light of ever improving medical technologies. In the case of Patient A, when she was discharged home, she was able to ambulate fairly independently and her quality of life was relatively good. Lawton[16] argues that primary surgery for gynaecological malignancies in older women can be carried out with low morbidity and mortality and suggests that biological age which equates with performance status and general fitness for surgery is a much more important predictor of surgical risk than chronological age.

The two patients reported here bring home, once again, the message that dermatology is not just skin deep and dermatologists can and do save lives. Furthermore, we hope that these two cases will remind clinicians of the importance of skin signs of internal malignancy. Dermatologists are privileged clinicians. They need to remain vigilant and continue to contribute to cancer medicine through early clinical diagnosis of problems such as malignancy associated dermatomyositis. Finally, dermatologists and trainees should remember that no patients are too young to be seriously ill and no patients are too old for us to lose hope!

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