CASE REPORT

Three differently timed presentations of dermatomyositis associated with advanced ovarian cancer

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SUMMARY

Each of the three patients reported in this article presented with dermatomyositis at various stages of their advanced ovarian cancer. Dermatomyositis was the presenting feature and preceded the diagnosis of ovarian cancer by several months in one patient. In another patient, dermatomyositis occurred just prior to the scheduled third cycle of palliative chemotherapy after surgical debulking for stage 4 disease. The third patient presented with pathognomonic diagnostic features of dermatomyositis after ovarian cancer recurrence. Diagnosis was delayed in at least two of these patients; however, once appropriately diagnosed, each patient responded well to immunomodulatory treatment. In one patient, initiation of oral prednisolone seemed to correlate with a steady improvement in her proximal myopathy. A pulsed methylprednisolone approach was used in another patient with conversion to a tapering dose of oral prednisolone to good effect. In the patient in whom the most severe myopathy affecting bulbar muscle groups was demonstrated, an infusion of 5 days of intravenous immunoglobulin produced an eventual improvement in her steroid-refractory myopathy.

BACKGROUND

The three cases reported in this article illustrate presentations of dermatomyositis at various stages of advanced ovarian cancer disease, suggesting that the pathogenesis of dermatomyositis is not necessarily linked to the course of ovarian cancer. They also demonstrate how clinical history and examination as well as simple biochemical tests can be used for diagnosis and for monitoring of response to treatment. All patients improved during the course of their treatment, with the use of immunomodulator drugs, supporting the immunopathogenesis of the disease. In the severest case in which bulbar muscles were affected, the use of intravenous inmmunoglobulin (IVIG) seemed to correspond with a treatment response and supports retrospective evidence for its use in this setting.

CASE PRESENTATION

Patient 1 is a 50-year-old woman who presented with a 3-month history of skin rash and muscle weakness. This manifested by difficulty in her activities of daily living (lifting household objects and walking upstairs) which had been getting progressively worse. During this time, she had been investigated with serum autoantibodies for a series of autoimmune conditions; none of which were confirmatory. Eventually, a CT scan of her chest, abdomen and pelvis demonstrated evidence of advanced ovarian cancer with a markedly elevated cancer antigen (CA) 125 tumour marker of 3169. The diagnosis of high-grade serous carcinoma was confirmed from a left pelvic lymph node biopsy.

Patient 2 is a 43-year-old woman who had primary debulking surgery for ovarian cancer with optimal debulking and unfortunately developed a postoperative malignant pleural effusion. She was seen in the chemotherapy clinic prior to her third cycle of palliative carboplatin/paclitaxel/bevacizumab. Over the preceding 2 weeks, she had developed particular difficulty walking up stairs and a heliotrope rash on her face and limbs associated with periorbital swelling and Gottron's papules.

Patient 3 is a 56-year-old woman who had been treated with neoadjuvant carboplatin/paclitaxel/bevacizumab 1 year previously which had been complicated by a bowel perforation after her first cycle. After recovery, she completed five further cycles of carboplatin/paclitaxel before proceeding to optimal debulking surgery and a further two cycles of adjuvant chemotherapy. Unfortunately, a few weeks after initiating carboplatin and liposomal doxorubicin for recurrent disease, she presented with a 1-week history of a diffuse rash first affecting hands and arms, then back and associated shoulder girdle pain and weakness. Her examination demonstrated a heliotrope rash and Gottron's papules, thought to be pathognomonic of dermatomyositis.

INVESTIGATIONS

Additional tests done for each patient

(1) One year previously, generalised arthralgia had been investigated with a rheumatoid factor serum test which had measured <20 (normal). During her diagnostic workup, a panel of autoantibodies had been sent off including: anti-Jo-1/Jo-1, PL-7, PL-12, SRP, Ku, Mi-2, PMScl, C3, C4 all of which were in the normal range.

(2) Due to significant dysphagia in this patient, a gastrograffin swallow was performed during her inpatient admission showing stasis in the valleculae with a small amount of penetrating aspiration, which ultimately necessitated percutaneous endoscopic gastrostomy (PEG) insertion. Follow-up video fluoroscopy as an outpatient demonstrated impaired pharyngeal constriction in the pharyngeal phase of swallowing resulting in reduced anterior excursion of the hyoid

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and incomplete epiglottic deflection. All of this was consistent with proximal oesophageal myopathy.

DIFFERENTIAL DIAGNOSIS

The delay in diagnosis in two of the patients was perhaps because alternative diagnoses were more enthusiastically considered initially.

For patient 1, initial consideration of systemic lupus erythematosus and other autoimmune conditions had been considered, but ultimately imaging revealed the likely ovarian-cancer-associated dermatomyositis.

Patient 2 had also presented with severe hypertension and a bevacizumab-associated rash and arthropathy was considered. However, her protein–creatinine ratio was normal (<15 mg/mmol), and her blood pressure normalised with amlodipine treatment. Her myopathy and dysphagia symptoms progressed leading to creatine kinase (CK) serum measurements supporting the diagnosis of dermatomyositis.

TREATMENT

Patient 1 was started on prednisolone 60 mg with calcichew, alendronate and lansoprazole, with a slow wean to 50 mg and then 40 mg orally once a day. She was treated with palliative chemotherapy comprising carboplatin/paclitaxel and bevacizumab.

Patient 2 was admitted as her dysphagia deteriorated and she was initially treated with pulsed intravenous methylprednisolone 500 mg intravenously for three consecutive days which made no significant difference to her proximal myopathy or her CK/aspartate transaminase levels. She required PEG feeding during this admission and due to concerns about worsening dysphagia associated with hypophonia, a 5-day course of IVIG was initiated. Just prior to discharge, the steroid-sparing agent, oral methotrexate 15 mg/week was initiated. She continued on her systemic therapy with carboplatin/paclitaxel and bevacizumab.

Patient 3 was also initially treated with pulsed intravenous methylprednisolone and continued on oral prednisolone 40 mg, which was then gradually weaned. She continued treatment on carboplatin and liposomal doxorubicin.

OUTCOME AND FOLLOW-UP

Table 1 demonstrates the trend in improvement in biochemical markers in each of these three patients.

Patient 1's dermatomyositis improved significantly during the course of treatment, but flare-up of dermatitis appeared to be temporally related to periods of disease progression. She did not have interval debulking surgery as she had had such a dramatic response to chemotherapy with little residual disease demonstrated post-treatment. She continued on maintenance bevacizumab and clinical surveillance. Her myopathy improved, but when her skin rash flared up, she was commenced on hydroxychloroquine 200 mg two times per day. This predated a significant change in her CA-125 by several months, a rise in which prompted a restaging CT scan which showed small volume nodal progression. A follow-up surveillance CT 3 months later demonstrated multiple retroperitoneal nodes and corresponded to a further flare of her dermatitis symptoms. She started second-line chemotherapy with carboplatin and gemcitabine. She had a partial response to this treatment, but 5 months later, further progression occurred, with initiation of liposomal doxorubicin planned. Dermatitis symptoms currently remain stable.

Patient 2 had a good biochemical (CA-125) and radiological response to treatment. Her proximal myopathy continued to improve and her PEG was removed. However, she experienced recurrent symptoms of dermatomyositis with muscle weakness, rash and dysphagia at the time of her 17th cycle of maintenance bevacizumab. CT scan at the time did not show relapse but a positron emission tomography/CT was done and confirmed recurrent disease. She commenced carboplatin and liposomal doxorubicin and has had a symptomatic response after two cycles.

Patient 3 continued to experience improvement in her predominantly shoulder girdle myopathy associated with an ongoing good clinical and radiological response to chemotherapy. Her end of treatment CT scan, however, showed low volume peritoneal disease progression. She was initiated on weekly paclitaxel after a period of observation, through which she progressed, and was deemed unfit for further treatment. There was no recurrence of her myopathy during this period of her disease course.

DISCUSSION

Although the timing of development of dermatomyositis differed in each patient, most myositis-associated malignancies are indeed diagnosed within 2 years before or after development of myositis.[1] Unrecognised malignancy may consequently be a cause of failure of treatment response.

These case presentations highlight both the variable way in which dermatomyositis may present as well as its fluctuating clinical course which may or may not relate specifically to treatment response or disease progression. Unfortunately, there is an absence of epidemiological data which may relate to the lack of a consistent use of diagnostic criteria for dermatomyositis, its rarity and indolent clinical course.[2] Consequently, there are no large-scale series that can retrospectively be used to permit an analysis on whether the presence or absence of dermatomyositis is a good or adverse prognostic sign.[3]

The use of prednisolone 1 mg/kg to a maximum of 80 mg/day is recommended as first-line treatment for dermatomyositis.[4] This should be continued for 4–6 weeks with cautious weaning. The recommendation for severe myositis which was considered for patients 2 and 3 is the use of pulsed methylprednisolone for 3 days. More than 80% of patients are thought to respond to steroids alone. Muscle enzymes tend to normalise within 6 weeks which was demonstrated in each of these patients. However, typically, muscle strength improvement tends to lag behind by several months with the majority of patients not returning to normal muscle strength.

Table 1 Use of ESR, CK and/or AST, as biochemical markers of responsiveness in three patients (1, 2 and 3) with dermatomyositis; measurements taken at diagnosis and on improvement of myositis symptoms

	1			2			3		
	ESR	CK	AST	ESR	CK	AST	ESR	CK	AST
Diagnosis	28	2366	ND*	58	16596	616	85	544	47
Clinical improvement	ND	64	ND*	21	1187	81	77	162	38

Normal ranges in reference laboratory: ESR (0–12 mm/hour), CK (25–200 U/L), AST (<32 U/L).
*Not done (ND): patient treated at a different hospital in which AST is not routinely measured.
AST, aspartate transaminase; CK, creatine kinase; ESR, erythrocyte sedimentation rate.

This seems to have been the pattern experienced by each of these patients.

The use of glucocorticoid (GC)-sparing agents is a practical strategy to consider for all patients who may be anticipated to remain on steroids for several months. A dose of dose 15 mg/week of oral methotrexate is a reasonable choice and is supported by retrospective series in which a response rate of 71%–82% in patients with dermatomyositis is reported including in patients who failed GC.[5]

Learning points

- The diagnosis of dermatomyositis should be considered early in patients presenting with muscle weakness and rash, and malignancy should be excluded.
- Although reports of confirming diagnosis using electromyography, muscle biopsy and anti-Jo antibodies may be relevant in refractory cases, they add limited value to the routine management or surveillance of patients in which the diagnosis is clinically likely.
- In severe dermatomyositis, for example, those cases affecting bulbar muscles, admission for speech and language assessment and percutaneous endoscopic gastrostomy feeding as well as intravenous immunoglobulin may prove necessary.
- The use of steroid-sparing agents such as methotrexate can be implemented safely even during chemotherapy treatment for malignancy.
- The course of ovarian cancer and response to treatment are not necessarily correlated with the course of dermatomyositis.

Patient 2 was initiated on IVIG due to concerns about her worsening dysphagia after pulsed methylprednisolone. The use of IVIG has been described in a case series of 73 patients supporting its use in the first-line setting in combination with GC for life-threatening oesophageal impairment complicating steroid-resistant polymyositis/dermatomyositis. Its use has been associated with infusion reaction and prolongation of hospitalisation,[6] highlighting the importance of selective use of IVIG.

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