



## Case report

## Paraneoplastic myositis secondary to poorly differentiated serous carcinoma of ovarian/tubal origin

Zachary Raizman<sup>c</sup>, Boshra Hosseini<sup>a</sup>, Sarah Kean<sup>b</sup>, Alon D. Altman<sup>a,b,\*</sup><sup>a</sup> Department of Obstetrics Gynecology and Reproductive Sciences, University of Manitoba, Canada<sup>b</sup> Cancer Care Manitoba, Division of Gynecologic Oncology, Manitoba, Canada<sup>c</sup> Rady Faculty of Health Sciences, University of Manitoba, Canada

## ARTICLE INFO

## Keywords:

Paraneoplastic myositis  
Serous carcinoma  
Ovarian cancer

## 1. Introduction

Myositis is characterized by proximal muscle weakness and pain, with possible cutaneous lesions and dysphagia. The incidence of ovarian cancer in the setting of dermatomyositis has been reported to be as high as 13–26%, which is much higher than the 1% risk in the general population (Cherin et al., 1993). Conversely, the risk of ovarian cancer in polymyositis does not seem to be greatly increased (Hill et al., 2001). Despite this, the association between myositis and ovarian cancer is rarely recognized by gynecologists.

The majority of cases of myositis are considered to be idiopathic; however, there is a strong association between myositis and malignancy. Among patients diagnosed with either dermatomyositis (DM) or polymyositis (PM) there is an increased incidence of malignancy. The incidence is highest in patients with DM and within the first year of myositis diagnosis. It is estimated that the risk of malignancy increases three-fold following the diagnosis of DM compared to 30% increase in patients diagnosed with PM. Ovarian, lung, pancreatic, stomach and colorectal cancers are types of malignancies associated with dermatomyositis. On the other hand, cancers most often associated with polymyositis are non-Hodgkin's lymphoma, lung and bladder cancer (Hill et al., 2001).

Inflammatory myopathies can be primary or present as part of a paraneoplastic syndrome that develops as a consequence of a primary malignancy. The pathogenic molecular mechanisms underlying malignancy and myositis are still unclear, however, it is thought that patients with a primary tumour express high levels of myositis autoantigens which result in the subsequent myopathy (Casciola-Rosen et al., 2005). In paraneoplastic myositis, treatment of the cancer usually results in the

regression of the myopathy, although it is sometimes difficult to distinguish between primary and paraneoplastic myositis, especially when the malignancy is advanced or resistant to treatment. This poses a challenge in determining the prevalence of paraneoplastic myositis.

This case report describes a case of paraneoplastic myositis caused by poorly differentiated serous carcinoma of ovarian/tubal origin that improves after treatment of the cancer. To our knowledge, there are 35 reported cases of paraneoplastic myositis as a consequence of a primary ovarian cancer. Pubmed was the data base that was utilized for our search and “Myositis” [MeSH] AND “Ovarian Neoplasms” [MeSH] were the terms used to gather our sources. The majority of these cases present as paraneoplastic DM with classic skin lesions. Our case presents as paraneoplastic PM, of which there are only two other cases in the literature. Moreover, our patient had significant symptoms and signs of paraneoplastic myositis with a low volume of malignant disease (stage IIIA), compared to other reports of similar presentations with more advanced disease.

This case highlights the importance of including ovarian malignancy in the differential diagnosis for a female patient presenting with signs of myositis. Ovarian cancer can be present in this context even with mildly elevated levels of CA125 and minimal imaging evidence of disease.

## 2. Case

A 63 year old female presented with a three week history of progressive proximal muscle weakness, edema, and pain that severely limited her functional status. Laboratory investigations showed elevated creatinine kinase (CK) (26,995 U/l), erythrocyte sedimentation

\* Corresponding author at: RS 406, 810 Sherbrook St., Winnipeg, MB R3A-1R9, Canada.  
E-mail address: [alon.altman@cancercare.mb.ca](mailto:alon.altman@cancercare.mb.ca) (A.D. Altman).

<http://dx.doi.org/10.1016/j.gore.2017.04.001>

Received 19 February 2017; Received in revised form 24 March 2017; Accepted 4 April 2017

Available online 05 April 2017

2352-5789/© 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

rate (ESR) (65 mm/h) and myoglobin (5182 ng/ml). A cause for myositis could not be elucidated from the history.

She was treated with both oral and intravenous glucocorticoids. This caused a decline in her CK levels, but no improvement in her functional status. An MRI of the pelvis and thighs showed extensive edema within the hip flexors and extensors, the anterior gluteus medias, and the piriformis muscles bilaterally. Additionally, there was an incidental finding of bilateral complex ovarian masses. Ultrasound showed bilateral ovarian masses with cystic and solid components, measuring  $4.9 \times 3.7 \times 3$  cm on the right and  $6.7 \times 4.4 \times 3.9$  cm on the left. There was no identification of advanced disease, including omental caking, retroperitoneal lymphadenopathy, ascites or peritoneal nodularity.

The patient underwent laparoscopic bilateral salpingo-oophorectomy, partial omentectomy, and biopsy of an omental adhesion. Full surgical staging/debulking was limited by her clinical condition. In the days prior to surgery, her CK and myoglobin levels were 30,649 U/l and 9146 ng/ml, respectively. Her Ca-125 was only mildly elevated at 89 U/ml. The day following surgery, these values had decreased to 1676 U/l, 502 ng/ml, 26 U/ml for CK, myoglobin and Ca-125 respectively. Pathology showed a high grade serous adenocarcinoma of ovarian primary, consistent with surgical stage IIIA, with apparent optimally debulked disease.

The patient completed 3 cycles of chemotherapy with carboplatin and paclitaxel and was then switched to carboplatin and caelyx due to severe peripheral neuropathy (grade 3) and pancytopenia. She had prolonged admission for decreased functional status and severe deconditioning, requiring intense physiotherapy. Her CK was 207. Her functional status continues to improve and her most recent imaging showed no evidence of recurrent disease; she continues to have ongoing mild weakness and neuropathy 5 months after completion of treatment.

### 3. Comment

Among the 35 reported cases of paraneoplastic myositis secondary to ovarian cancer in the literature, the majority were treated surgically with either primary debulking or bilateral salpingo-oophorectomy. The myositis paralleled the course of the ovarian cancer. Complete removal of the tumour usually resulted in an improvement in symptoms and biomarkers of myositis (Hong et al., 2015; Nakanishi et al., 1999).

In most of the published case reports, the diagnosis of ovarian cancer occurs shortly after the diagnosis of myositis, as is the case here. Subsequent to the diagnosis of myositis, the risk of identifying an ovarian cancer is reported to be 16.7% over the ensuing 5 years (Sigurgeirsson et al., 1992). One case reports ovarian cancer diagnosed 6 years after the finding of myositis (Scheinfeld, 2008). With increasing time interval between the two diagnoses, it becomes more difficult to differentiate primary vs paraneoplastic myositis.

Other cases in the literature are similar to this case report. These women presented with proximal muscle weakness that significantly hindered their functional capacity. Blood results revealed significantly elevated CK levels. The majority of patients were tried on a round of steroids that minimally improved the weakness and pain and were found to have bilateral ovarian masses on imaging. In one case, the Ca-125 was significantly elevated at 543 U/ml and the pathology report showed stage IIIC high grade serous carcinoma. This is supported by a retrospective analysis performed on 14 cases of ovarian malignancy in patients with DM and PM by Davis and Ahmed. Two out of the 14 cases had PM, which presented months before an underlying malignancy was discovered by imaging. Dissimilar to our case, one patient in Davis and Ahmed's report had a significantly elevated Ca-125 at 1447 U/ml. However, similar to our case, had stage 3 ovarian cancer. On the other hand, in another case report, the patient did not have a significantly elevated Ca-125 at 44 U/ml. Elevated Ca-125 was not seen in our case. In one of these cases, the patient's presentation was remarkably similar to our patient, but with more advanced disease. In that report, the

patient died within 3 months of her ovarian cancer diagnosis after choosing to abstain from any cancer treatment (Hong et al., 2015; Nakanishi et al., 1999; Ghosh et al., 2007; Davis and Ahmed, 1997).

To assist in the differentiation of primary vs paraneoplastic myositis, Braverman proposes that the presence of Raynauds phenomenon in an individual with DM can possibly exclude ovarian cancer (Braverman, 1998). In their study, the presence of Raynauds phenomenon was documented in 40 adults with DM (25 without concurrent malignancy, 15 patients with concurrent malignancy). Five out of the 25 patients without cancer had presentation of Raynauds phenomenon compared to 0 of the 15 patients with cancer (Braverman, 1998). Furthermore, paraneoplastic myositis commonly resists classic myositis treatment and usually only remits when the underlying malignancy has been removed, as was seen in this case.

The clinical features and laboratory findings seen in paraneoplastic myositis are generally congruent to those observed in idiopathic conditions. Patients older than 50 years old who have a poor response to immunosuppressive treatment should prompt further investigation into an underlying malignancy (Shah et al., 2015). In women presenting with refractory symptoms of myositis, ovarian cancer should be ruled out. Interestingly, the Ca-125 in our patient was lower than would be expected in a patient with her level of disease. We are uncertain of the significance of this and have not observed a similar pattern in the majority of other case reports. However, this finding could possibly be due to the lower volume of disease. In other paraneoplastic PM case reports, the ovarian cancer was more advanced.

There have been multiple attempts at explaining the mechanism of paraneoplastic myositis, however, there has not been one proven hypothesis. It is thought that the tumour may secrete a myotoxic factor that causes inflammation within the muscles, thus, the serum from affected patients should be tested for that factor. Alternatively, the tumour antigen might resemble a muscle cell surface antigen, so that an immune response to the tumour might result in a myositis (Casciola-Rosen et al., 2005).

As this case report shows, a workup for coexisting malignancies should be considered in patients who present with signs and symptoms of myositis. In female patients this should include ovarian cancer, as the treatment of the malignancy improves the symptoms of myositis. This should be considered even in patients with mildly elevated levels of CA125 and minimal imaging evidence of disease.

### Disclosures

There are no conflicts of interest or financial disclosures.

### References

- Braverman, I.M., 1998. *Skin Signs of Systemic Disease*, third ed. WB Saunders Co, Philadelphia.
- Casciola-Rosen, L., Nagaraju, K., Plotz, P., Wang, K., Levine, S., Gabrielson, E., et al., 2005. Enhanced autoantigen expression in regenerating muscle cells in idiopathic inflammatory myopathy. *J. Exp. Med.* 201 (4), 591–601.
- Cherin, P., Piette, J.C., Herson, S., Bletry, O., Wechsler, B., Frances, C., et al., 1993. Dermatomyositis and ovarian cancer: a report of 7 cases and literature review. *J. Rheumatol.* 20 (11), 1897–1899 (Nov).
- Davis, M.D., Ahmed, I., 1997. Ovarian malignancy in patients with dermatomyositis and polymyositis: a retrospective analysis of fourteen cases. *J. Am. Acad. Dermatol.* 37 (5 Pt 1), 730–733 (Nov).
- Ghosh, A., Malak, T.M., Pool, A.J., 2007. Polymyositis and ovarian carcinoma: a case report. *Arch. Gynecol. Obstet.* 275 (3), 195–197 (Mar).
- Hill, C., Zhang, Y., Sigurgeirsson, B., Pukkala, E., Mellekjær, L., Airio, A., et al., 2001. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet* 357 (9250), 96–100.
- Hong, M.-K., Lee, M.-H., Ding, D.-C., Chu, S.-C., Chu, T.-Y., 2015. High grade serous ovarian carcinoma with serous tubal intraepithelial carcinoma in a case presented with atypical glandular cell favor neoplasm cervical cytology and dermatomyositis. *Taiwan J. Obstet Gynecol.* 54 (2), 183–186 (Apr).
- Nakanishi, K., Cualing, H., Hussein, N., 1999. Dermatomyositis as a presenting symptom of ovarian cancer. *Obstet Gynecol.* 94 (5 Pt 2), 836–838 (Nov).
- Scheinfeld, N., 2008. A review of the cutaneous paraneoplastic associations and metastatic presentations of ovarian carcinoma. *Clin. Exp. Dermatol.* 33 (1), 10–15

(Jan).  
Shah, A.A., Casciola-Rosen, L., Rosen, A., 2015. Review: cancer-induced autoimmunity in the rheumatic diseases. *Arthritis Rheum.* 67 (2), 317–326 (Feb).  
Sigurgeirsson, B., Lindelöf, B., Edhag, O., Allander, E., 1992. Risk of cancer in patients

with dermatomyositis or polymyositis. A population-based study. *N. Engl. J. Med.* 326 (6), 363–367 Feb 6.