Clear cell ovarian carcinoma following polymyositis diagnosis: a case report and review of the literature

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Abstract
Background: The association of ovarian malignancy with dermatomyositis (DM) is well established from previous reports, while the relationship with polymyositis (PM) is rare.
Case report: We report a case of a 50 years old nulliparous woman who developed clear cell ovarian cancer four years after the PM diagnosis. The patient presented with deep lower abdominal pain and distension. CA-125 was elevated and the preoperative MRI showed pelvic tumor occupying the Douglas pouch. Exploratory laparotomy revealed a gross mass of clear cell ovarian carcinoma.
Conclusion: Physicians must be alert of the possibility of malignancy in patients with a previous diagnosis of polymyositis. Hippokratia 2008; 12 (3): 181-185

Key words: polymyositis, dermatomyositis, inflammatory myositis, ovarian cancer

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Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies with characteristic cutaneous and muscle manifestations. Skin and muscles are the most commonly affected organs. Several studies have documented an increased rate of malignant diseases associated with DM and PM1-3. Ovarian cancer presents more commonly in patients with DM, whereas correlation with PM is rare1-3. The diagnosis of myositis most often precedes the diagnosis of malignancy a few months to several years (mainly the first three years). The detection of ovarian cancer at an early stage is very crucial for patient survival. The physician must be alert of the possibility of malignancy in patients with a previous diagnosis of myositis, especially of ovarian carcinoma in the female population. However, screening of such carcinoma including pelvic examination, transvaginal ultrasonography and CA-125, is not always effective.

Because of the rare correlation between ovarian carcinoma and the PM, we present our case and review the literature.

Case report
A 50 years old nulliparous woman was admitted in Hippokratio Hospital on October 2002 because of proximal muscle weakness, limb extremities pain and tenderness, muscle weariness and arthralgy. Elevated serum level of creatine phosphokinase (CPK) 255 IU/L (normal range 0-145 IU/L), positive antinuclear antibody (ANA: 1/80), electromyogram (EMG) and muscle biopsy (quadriiceps muscle) confirmed PM diagnosis.

The patient was placed on corticosteroid therapy (methylprednisolone 16 mg X 2, daily). Within two months of the initial therapy serum CPK was normalized, while clinical symptoms significantly improved. Four months later because of partial clinical recovery of the PM symptoms, the patient was further treated with the immunosuppressive agent (azathioprine 50 mg × 2, daily). The patient was regularly examined every six months in the Outpatient Department for the PM disease and for occult malignancy. Pelvic examination, PAP smear, transvaginal ultrasonography and serum CA biomarkers (CA-125, CEA, CA-15-3 and CA-19-9) were used for detection of genital malignancy. No signs of cancer were observed during the next four years after the diagnosis of PM.

On December 2005 while the patient was under steroid and immunosuppressive therapy because of incomplete remission of the PM symptoms, she was admitted complaining for lower abdominal pain and distension. Pelvic examination and transvaginal ultrasonography revealed a gross pelvic mass filling the Douglas pouch. Magnetic resonance imaging (MRI) confirmed the diagnosis (ovarian tumour of mixed features, maximum diameter 20 cm) and disclosed the existence of moderate volume of ascetic fluid (Figure 1). Serum CA-125 level was 381U/ml (normal, 0-35 U/ml) and serum CA-15-3 was 326 U/ml (normal, 0-32 U/ml), whereas CA-19-9, CEA and AFP were normal. Six months earlier, at a regular follow up of the patient, all CA biomarkers were normal. One month later just before the surgery, CA-125 increased to 552 U/ml.

On January 2006 the patient underwent exploratory laparotomy, via vertical midline incision. A gross ovar-
ian mass (Figure 2) and moderate quantity of ascites were found. Peritoneal cytology was obtained, the ovarian tumor was removed and was sent for a frozen section biopsy in which the diagnosis of epithelial ovarian carcinoma was established. Thereafter, the surgical procedure was completed by total abdominal hysterectomy, bilateral salpingo-oophorectomy, infra-colic omentectomy, pelvic and para-aortic lymphadenectomy. Definitive histopathologic examination according to the International Federation of Gynecology and Obstetrics (FIGO) revealed a clear cell (Figure 3), stage IIIC ovarian carcinoma (1/34 involved pelvic node), while peritoneal cytology was positive for malignancy. Postoperatively the patient received eight cycles of cytotoxic chemotherapy every three weeks from March to August 2006, four with carboplatin (6 AUC) and paclitaxel (175 mg/m²) and four only with carboplatin (6 AUC). Eighteen months after the diagnosis of malignancy the patient is still alive without evidence of recurrent disease, since pelvic examination and transvaginal ultrasonography, as well as MRI of the abdomen and CA biomarkers (CA-125: 12 U/ml) are all normal.

Discussion

The present case report refers to a patient with clear cell ovarian carcinoma on a previously established diagnosis of PM. To the best of our knowledge, such combination concerning the subtype of the epithelial ovarian cancer has never been mentioned before. A review of the relative literature is also presented.

Polymyositis and dermatomyositis are idiopathic inflammatory myopathies of undetermined etiology. Connective tissue diseases present with similar clinical symptoms and signs like the myopathies and are usually classified together. Diagnostic criteria for the PM and DM was first suggested by Bohan and Peter. According to their definition five major criteria are used for the diagnosis of PM and DM: symmetrical proximal muscle weakness, elevated serum levels of muscle enzymes, abnormal electromyogram, muscle-biopsy and dermatologic signs (Table 1). Four out of the five diagnostic criteria relate to the muscle disease, while the fifth to cutaneous disease. The weakness of the muscles is progressing over weeks to months (with or without dysphagia or involvement of the respiratory muscle). The diagnosis of the PM is considered definite in case of four criteria without the dermatologic rash, while three criteria out of five, or four criteria including the rash for the DM diagnosis. The diagnosis of PM is probable when there are three criteria (without the rash) and two criteria (with the rash) for the DM, while possible diagnosis of the PM includes two criteria without the rash and one criterion plus the rash for the DM. Since then, diagnostic criteria with small variations for both PM and DM have been proposed by others. Our patient is in accordance with the previous diagnostic PM criteria. However, diagnosis of the idiopathic inflammatory myopathy sometimes is unclear because of the overlapping signs between myopathies and other collagen-vascular diseases (lupus erythematosus
and scleroderma). It is not always easy to classify idiopathic inflammatory myopathies because they represent a heterogeneous group of disorders with overlapping symptoms and signs. Many classifications have been proposed but the most popular is that of Pearson’s. According to this, PM is included in the group I, while DM in group II, group III is defined as PM and DM in association with neoplasia, group IV is childhood PM or DM and in group V are included the PM and DM with associated collagen-vascular disease (Table 2).

The relationship between malignant disease and myositis was first described in 1916. Since then, several authors confirmed the association between malignancy and idiopathic inflammatory myopathies with a frequency ranging 6-40%. However clinical outcomes of the studies are limited by referral bias, lack of controls and inclusion criteria for myositis. Two Scandinavian reports (Sweden & Finland) in a population-based study with PM and DM showed an overall incidence of associated malignancy 13% (103/788) and 13.8% (34/246) respectively. The same figures in the DM group of patients were 15% with RR for male and female patients, 4.4 (95% CI, 3.0-6.6) of the DM patients involved with malignancy, while in the PM group the RR was 2.1 (95% CI, 1.4-3.3). In the same study an increased risk of malignancy was noted four years before (OR: 3.6; 95% CI, 2.7-6.7) and four years after the diagnosis of DM (OR: 2.3; 95% CI, 1.2-4.2), which strongly supports the paraneoplasmatic nature of DM, while in the PM group an increased risk of cancer was noted only in a five years period following the myositis diagnosis (OR: 2.2; 95% CI, 1.1-4.5).

Ovarian cancer is the most common malignancy of the female genital tract of women diagnosed with myositis. Although it appears to be an increased risk for ovarian cancer among patients with DM, data relating PM and ovarian cancer is limited. The Scandinavian groups (Sweden & Finland) demonstrated a relative risk (RR) of ovarian cancer in DM population 16.7 (95% CI, 5.4-38.9) and 32 (95% CI, 8.7-82) respectively, while no case of ovarian cancer was presented in the PM group of patients. Cherin and co-authors, found a much higher incidence of ovarian cancer (13.3%) in a DM female population compared with general female population (1%).

Table 2: Classification of polymyositis (PM) and dermatomyositis (DM)

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<thead>
<tr>
<th>Groups</th>
<th>Classification</th>
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<tbody>
<tr>
<td>I</td>
<td>Typical PM</td>
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<tr>
<td>II</td>
<td>Typical DM or DM sine myositis</td>
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<tr>
<td>III</td>
<td>Typical DM or DM sine myositis, or PM associated with malignancy</td>
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<td>IV</td>
<td>Childhood DM</td>
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<td>V</td>
<td>PM or DM connective tissue disease overlap syndrome</td>
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while no case of ovarian carcinoma was observed in the PM group. These results have also been supported by others. However, in a retrospective review of 1891 women with DM and PM, two out of 14 patients with ovarian cancer were identified in the PM group of patients, with advanced FIGO stage (stage III-IV) and with high histological grade in both cases. Additionally, another two case reports of malignancy of female genital tract (ovary and vagina) in patients with concurrent diagnosis of PM were reported in the literature.

Malignancies may follow or precede the diagnosis of the inflammatory myopathies, although predominantly PM and DM diagnosis precedes the diagnosis of cancer. A previous report analyzing ten patients with gynecologic malignancies, (five cases of ovarian cancer), in a setting of patients with a previous diagnosis of dermatomyositis-polymyositis, showed a time interval between myositis and gynecologic malignancy ranging from three months to six years. The mean patients’ age was 53 years (range 40-66 years) at the time of malignancy diagnosis. Similarly in our case, PM diagnosis preceded the diagnosis of the epithelial ovarian cancer almost four years, while the patient’s age at the time malignancy diagnosed was 53 years. Paraneoplastic nature of the DM in the patients with previous diagnosis of malignant disease was strongly supported. On the other hand, there is no clear explanation whether the inflammatory nature of the myopathies or the immunosuppressive treatment are correlated with the malignancies, which are following the diagnosis of PM and DM. However, the RR of cancer among patients with previous PM and DM diagnosis decreases with time, as well as the risk for cancer was lower in the patients who had previously received cytotoxic treatment for inflammatory myopathies.

Early detection of ovarian cancer in patients with a previous diagnosis of myositis is critical, since 5-year survival rate of patients with disease limited to the ovaries (stage I) reaches almost 90%, while in cases with peritoneal spread it falls to less than 35%. Unfortunately, 2/3 of patients with ovarian malignancy are diagnosed when the disease has already spread beyond to the ovaries. Carlson and co-authors summarizing the literature, demonstrated 78% sensitivity and 98.9% specificity for detection of ovarian carcinoma using serum CA-125. The same figures concerning the use of transabdominal or transvaginal ultrasonography were 85% and 93.8% respectively. However, further analysis in a subgroup of patients with early stage ovarian cancer (stage I), the sensitivity of serum CA-125 for detection of ovarian malignancy was less than 50%. In another study of a small group of patients with dermatomyositis (n: 14), including four cases of ovarian malignancy, the sensitivity and specificity of CA-125 antigen (≥35 U/ml) for detection of ovarian cancer was 50% and 100% respectively. Elevated serum levels of CA-125 were detected in two patients that increased at least five and 13 months before the definitive diagnosis of ovarian cancer. The authors concluded that serum CA-125 may be a useful tool for the detection of ovarian malignancy in patients with a previous diagnosis of dermatomyositis. Similarly, another study concluded that cancer antigens CA-125 and CA-19-9 could be useful screening markers for the developing tumors in patients with inflammatory myopathies. In our case, pelvic examination, transvaginal ultrasonography and serum CA-125 contributed to ovarian cancer detection, although CA-125 six months before the diagnosis of the pelvic tumor was normal.

In conclusion, after confirmed diagnosis of inflammatory PM, the patient should have a thorough assessment of the disease severity, to predict prognosis and to identify the associated disorders. Physician must consider the possibility of occult malignancy in this setting of patients. In a female population, because of the fact that early detection of ovarian cancer is crucial for the patient’s survival, regular follow up of patients with previous diagnosis of PM including pelvic examinations, transvaginal ultrasonography, serum CA-125 levels may be useful screening and diagnostic tools, although the early detection is not always feasible.

References


