

## Carcinoma of unknown primary and paraneoplastic dermatomyositis

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### Abstract

Dermatomyositis is known to be associated with neoplastic disorders, however the presentation of carcinoma of unknown primary as dermatomyositis is rare. We describe a case index of 50-year-old female who presented with enlarged inguinal lymph nodes accompanied with symmetric proximal muscle

weakness and erythematous plaques. Conventional basic work-up did not reveal the diagnosis, however, positron emission tomography-computed tomography and re-staining of the pathology specimen suggested the ovaries as the primary site. Chemotherapy including carboplatin paclitaxel and bevacizumab led to complete response of disease and improvement in the dermatomyositis. The present case emphasizes the importance of a thorough directed evaluation for the underlying cancer in patients with carcinoma of unknown primary presenting as dermatomyositis. We further provide an up-to-date detailed review of published data describing these clinical entities.

**Key words:** Paraneoplastic; Dermatomyositis; Cancers of unknown primary; Positron emission tomography

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**Core tip:** The presentation of carcinoma of unknown primary as dermatomyositis is rare. Positron emission tomography-computed tomography and pathology case oriented evaluation may identify the site of origin. We provide an up-to-date detailed review of published data describing these clinical entities.

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### INTRODUCTION

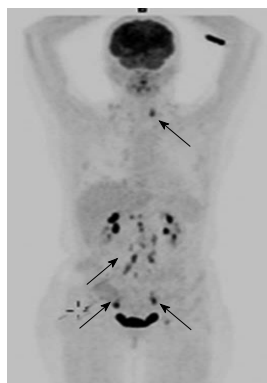
Cancer of unknown primary origin (CUP) is a group of metastatic tumors for which the site of origin cannot be detected at the time of diagnosis. In most of the cases, the source of the cancer will never be determined.

According to the European society of medical oncology, CUPs account for up to 5% of all malignancies<sup>[1]</sup>. The biology of these tumors is not fully elucidated although mechanism of metastatic spread in the absence of growth of the primary tumor can occur through site-specific transformation of disseminated cells, or oncogene induction at metastatic stroma.

Dermatomyositis is a connective-tissue disease characterized by progressive, proximal muscle weakness and pathognomonic cutaneous findings. Malignancy is associated with dermatomyositis in up to 40% of patients, representing a paraneoplastic phenomenon<sup>[2,3]</sup>. We describe here a rare case of a female who presented with carcinoma of unknown origin accompanied with symmetric proximal muscle weakness and erythematous plaques.

## CASE DESCRIPTION

A 50-year-old woman with carcinoma of unknown origin was admitted to the E.R because of intense weakness. She was evaluated one month earlier when she underwent biopsy from enlarged left inguinal lymph node. The biopsy revealed poorly differentiated carcinoma of unknown origin (performed out of our institute). On arrival, her physical examination revealed proximal weakness, which was profound in all extremities. Skin manifestations included peri-orbital edema and erythematous plaques on the extremities. She had enlarged left inguinal lymph node and signs of biopsy from the right lymph node. Biochemical analysis demonstrated elevated creatine kinase 5600 u/L (normal range 26-192), elevated AST 147(normal range 0-40) and ALT 130 (normal range 0-35). A computed tomography (CT) scan was unremarkable except enlarged left inguinal lymph node. Indirect immunofluorescence for anti-Jo-1 and ANA were negative. Tumor markers showed CEA-4.16 (0-4) CA15-3 -60 (0-30) CA125 80 (0-30). The patient underwent another biopsy from the left lymph node for re-pathology evaluation and staining which showed poorly differentiated Carcinoma. Staining for keratins: CK7 - positive strong, CK20 - weak, CK5/6 - negative, WT1 - positive and TTF - negative. Gynecological evaluation, colonoscopy and endoscopy were unremarkable. Since dermatomyositis is associated with gynecological - ovarian cancer there was a clinical decision to look for findings at the urogenital system. Gynecologist examination and vaginal US were unremarkable. It was then decided to perform positron emission tomography (PET)-CT scan which demonstrated increased standardized uptake values uptake in the left pelvis in an ovarian cyst and there was also high standardized uptake values uptake in paraaortic and cervical lymph node (Figure 1). These observations have led us to re-staining the specimen for CA125 and p53 which were both positive suggestive



**Figure 1** Positron emission tomography-computed tomography scan which demonstrated increased standardized uptake values uptake in the pelvis in an ovarian cyst and uptake in para-aortic and cervical lymph node (arrows).

of ovarian origin. The patient begun chemotherapy treatment with protocol directed to ovarian cancer including carboplatin [Area under the curve (AUC) 6] paclitaxel 175 mg/m<sup>2</sup> and bevacizumab 15 mg/kg every three weeks. After 2 cycles dose reductions in both carboplatin (to AUC 4-5) and paclitaxel (to 80 mg/m<sup>2</sup> weekly) were needed due to neuropathy and neutropenia. She also received steroids (prednisone 60 mg which was gradually tapered off and replaced with methotrexate) for dermatomyositis. This treatment (chemotherapy and/or the steroids) led to complete response in the disease and improvement in the dermatomyositis.

## LITERATURE REVIEW

Few studies demonstrated that dermatomyositis and polymyositis are association with different cancers<sup>[4-6]</sup>. A pooled analysis from Scandinavian repositories, confirmed that both dermatomyositis and polymyositis are associated with malignancy (dermatomyositis more than polymyositis)<sup>[3]</sup>. This study confirmed that ovarian, lung, gastric, colorectal, and pancreatic cancers were the cancers most strongly associated with dermatomyositis but other cancers were associated with dermatomyositis as well. Cancer treatment, local (surgery) or systemic (chemotherapy) usually results in remission of the dermatomyositis, and recurrence of symptoms can represent relapse of the malignant disease, further supporting its paraneoplastic origin<sup>[7,8]</sup>. Due to the increased risk of some cancers in patients with dermatomyositis, further examinations which may include whole body imaging, mammography and gynaecological evaluation are justified.

CUPs diagnosis requires pathology evaluation<sup>[1]</sup>. CUPs are categorized by pathological evaluation into: Differentiated carcinomas (well, moderately, or poorly); undifferentiated neoplasms; squamous cell carcinomas and carcinomas with neuroendocrine differentiation. In

the past CUP was characterized as an individual entity with dismal prognosis, while as our understanding of cancer biology evolved it became clear that CUP may retain the underpinnings of the primary origin<sup>[9]</sup>. Staining for keratins, may mislead the clinicians if interpreted incorrectly. For example our patients was CK7 positive and CK20 - weak - if weak is interpreted as negative, lung breast and thyroid cancers are more suspected. If CK20 - weak staining is interpreted as positive ovarian and pancreas cancers are suspected and WT-1, p53 and CA125 may add information as shown in our case. Full physical examination, blood and biochemistry analysis, and CT scans of thorax, abdomen and pelvis constitute the basic work-up in CUPs. Other evaluation should be only clinically guided. The minority of patients with CUP (less than 20%) belong to subsets with more favorable outcomes and treatment response and it is therefore crucial to identify this patients during the work-up<sup>[1,10,11]</sup>. Peritoneal carcinomatosis in females represent one example of this favorable risk CUP. Our patient pathology did not reveal serous papillary but rather poorly differentiated carcinoma. Moreover the disease distribution according the PET-CT was not classic for ovarian cancer except uptake in the left ovary. However the decision to treat her with chemotherapy used for ovarian cancers seems rational.

PET-CT is one of the most sensitive imaging techniques to detect malignant lesions and has been used in different cancer conditions with quite success<sup>[12-15]</sup>. Selva-O'Callaghan *et al*<sup>[16]</sup> prospectively evaluated the role of PET-CT in the diagnosis of occult tumors in patients with dermatomyositis/polymyositis. Using PET-CT they evaluated prospectively 55 patients with myositis. 9 out of the 55 patients were diagnosed with cancer. PET-CT identified 6 out of the 9 patients. The authors concluded that PET-CT for diagnosing CUP in patients with myositis was an option comparable to other multi diagnostic tests.

As the radiotracer doses administered using PET-CT are relatively small, the risk is very low compared with the potential benefits. There are no known long-term adverse effects from such low-dose exposure and the potential benefits from PET-CT outweighs the risks which may include allergic reactions (rare and mild), and exposure to low amount of radiation<sup>[17]</sup>.

## CONCLUSION

In conclusion this rare case of patient with carcinoma of unknown primary emphasizes the importance of a thorough directed evaluation and the usage of PET-CT for the underlying cancer in patients with carcinoma of unknown primary presenting with dermatomyositis.

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