

Palmar fasciitis with polyarthrititis-associated ovarian cancer: Case report and literature review

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Abstract. Palmar fasciitis and polyarthrititis (PFPA) is an uncommon disorder clinically characterized by rapidly developing bilateral arthritis of the hands and fasciitis of the palms. This cancer-associated syndrome, primarily linked to ovarian cancer, has also been associated with multiple different malignancies. PFPA symptoms usually precede the detection of ovarian cancer. In all patients from case series and single case reports described, ovarian cancer is already present at an advanced stage. Therefore, the authors aimed to present a case and systematically review available evidence on the association between PFPA and ovarian cancer, as gynecological oncologists. Awareness and recognition of PFPA may allow for earlier diagnosis and treatment of an occult ovarian cancer. The commitment of the attending gynecologists to become familiar with and identify rare diseases may lead to the detection at an early and curative stage and potentially life-saving therapeutic interventions.

of the hands and fasciitis of the palms (1,2). This results in pain, swelling and progressive contractures of the hands. These symptoms can co-occur with less severe synovitis of distant articulations. The palmar skin generally shows nodular erythema, and nodularity of the flexor tendons is often noted. This is a rare disease, while it is important for physicians to be able to recognize the disease in the patients with these characteristic clinical symptoms and screen for malignancy (3-5). Extensive review of underlying malignancies associated with PFPA showed ovarian cancer accounting for the majority (37%) of the cases (6).

In the all patients from case series and single case reports described, the ovarian cancer is already present in an advanced stage. We attempted to present our case and systematically review available evidence on the association between PFPA and ovarian cancer, as gynecological oncologists.

2. Case report

A 61-year-old woman presented with a 1-year history of bilateral progressive painful swelling of the hands (Fig. 1) with stiffness and diffuse arthralgia in the elbows and knees. In addition, a half-year after the onset, she suffered from fatigue and reported a weight loss of 2 kg within the last 1-month. There was no improvement with prednisone (15 mg/day). Laboratory tests revealed a normal complete blood count, sedimentation rate, and routine chemistry results. Antinuclear antibody, extractable nuclear antigen antibodies, anti-citrullinated peptide antibodies and rheumatoid factor testing were normal. Magnetic resonance imaging (MRI) showed high-intensity nodules above the flexor tendons. However, there was no evidence of MRI findings suggestive of the existence of arthritis.

Consideration of the unusual clinical findings and the progressive palmar contracture led to possible diagnosis of palmar fasciitis. The cancer-associated disease (6-8) prompted us to screen the most frequent underlying malignancy including ovarian cancer. Abdominal MRI showed a mass of the bilateral ovary with signs of peritoneal and omental metastases (Fig. 2).

The patient was submitted to exploratory laparotomy. There was a solid, gray and brown mixed mass (5 cm) in the left ovary, widespread malignant deposits (<2 cm) within the pelvis, and omental fullness due to metastatic tumor. The right

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1. Introduction

Palmar fasciitis with polyarthrititis (PFPA) has a characteristics clinical course that involves rapidly bilateral arthritis

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ovary was involved. A complete staging with hysterectomy, bilateral salpingo-oophorectomy, omentectomy was performed. Histological examination of the tissue revealed a poorly differentiated serous adenocarcinoma originated from left ovary with omental involvement and peritoneal dissemination. Cytology of ascites yielded poorly differentiated adenocarcinoma. The stage was IIIB (pT3BNxM0). The patient was expected to receive postoperative chemotherapy with carboplatin and paclitaxel. Although the patient is still under intensive chemotherapy, the dismal prognosis of this condition prompted us to review our experience with PFPA associated ovarian cancer and previous literatures. The patient provided written informed consent to study publication.

3. Literature review of PFPA-associated ovarian cancer

In a literature review we found 17 case series and single case reports of PFPA associated ovarian and fallopian cancers (Table I). The association between the malignancies and a PFPA condition has been dominantly in the elderly. Their age of previously reported patients was postmenopausal women, except younger 2 cases (25 and 42 years).

In over 60% of all cases, by far the most frequently occurring histological type was serous (papillary) adenocarcinoma. The poorly differentiated or undifferentiated adenocarcinoma accounted for 25%, and the characterized as endometrioid only in one report (6 cases). All patients were diagnosed already in advanced stage of metastatic spreading.

PFPA symptoms preceded the diagnosis of ovarian cancer, or PFPA symptoms led to immediate detection of an underlying these cancers. Interestingly in 2 cases of 3 fallopian tube cancers, the diagnosis of underlying malignancies by laparotomy preceded the onset of PFPA symptoms by 1 year (9,10). In another case of fallopian tube cancer, the diagnosis of PFPA led to the immediate detection of an underlying malignancy (11). There are many similarities between fallopian tube cancer and ovarian cancer, and ovarian cancer is believed to originate in the distal and proximal fallopian tube (12-15). Research published over the past 10 years has suggested that the most 'ovarian cancer', and specifically the high-grade serous carcinoma subtype of ovarian cancer, actually originates in the fallopian tube (13,15). PFPA-associated fallopian tube cancer may be the precursor of at least ovarian serous adenocarcinoma of the ovary.

The pathophysiology of PFPA is unclear. One hypothesis involves abnormalities in humoral and immune responses associated with the malignancy and responsible for overproduction of certain cytokines (16,17). Considering all reported cancer-associated syndromes and associated cancer, the majority of affected patients have been elderly women, which suggests the female hormone state may predispose to this syndrome as is the case in most autoimmune disease. The cytokines [e.g., vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), transforming growth factor β (TGF- β)] play an important role in ovarian stromal proliferation and emergence of ovarian cancer (18-20). Ovarian cancer and fallopian tube cancer release many types of cytokines such as VEGF, IGF, TGF- β (20). A higher level of TGF- β and VEGF may be a candidate to facilitate the rapid progression in the patients with PFPA associated with malignancies.

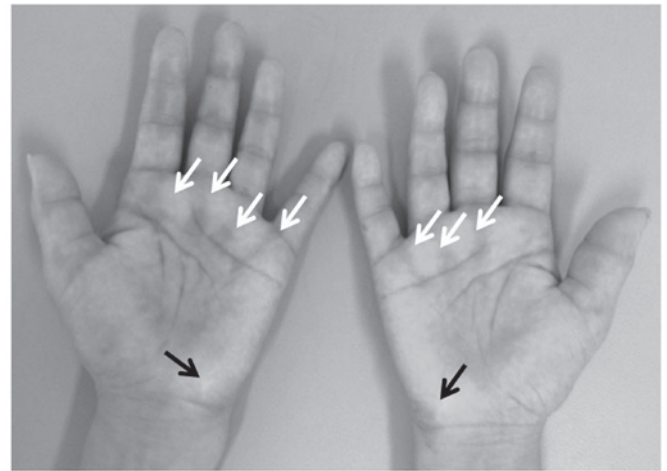


Figure 1. Palmar aspects of edema surrounding the elastic hard nodule (white arrows) and redness of the elastic hard nodules (black arrows).

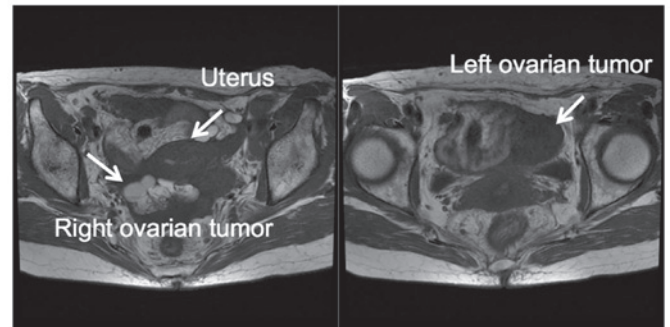


Figure 2. Abdominal T2-weighted MRI, showing evidence of bilateral ovarian tumors, peritoneal implantation and significant amount of ascites.

Treatment of the underlying cancer is paramount to the management of PFPA symptoms. Almost half of the patients reported describe a decrease in the symptoms after surgery, chemotherapy and/or radiotherapy (6,21). The role of new biological agents, such as TGF inhibitors and VEGF inhibitors, in this indication remains unclear, but their immunosuppressive and anti-angiogenic properties could theoretically be detrimental and trigger cancer progression.

4. Ovarian benign tumors

PFPA has been implicated also with ovarian non-malignant tumors including endometrial cyst (1) and paraovarian cyst (22). As PFPA was suspected, a more complete investigation was performed in these 2 cases. Abdominal imaging demonstrated a pelvic cystic mass rising from adnexa. Currently there are no effective screening methods for ovarian cancer and the malignancies frequently remains undiagnosed until metastasis has occurred. When found in PFPA patients, the ovarian tumor highly suspected as benign should be removed and submitted to pathological examination.

5. Comments

Learning PFPA and its presentations in particular by gynecologic oncologist can rise the suspicion of underlying

Table I. Fallopian tube and ovarian cancers related palmar fasciitis with polyarthritis.

First author, year	Age (years)	Histology	Stage	(Refs.)
A, Fallopian tube				
Fukui, 2015	64 ^a	Serous adenocarcinoma	pT3cNxM0	(11)
Taggart, 1984	58	Well differentiated adenocarcinoma	Not described (peritoneal spread)	(10)
Denschlag, 2004	73	Serous papillary adenocarcinoma	Not described (complete staging surgery performed) with partial rejection of colon due to tumor infiltration	(9)
B, Ovary				
Medsker, 1982	6 postmenopausal (50 to 65)	Endometrial carcinoma, G2 or G3	Non-resectable tumor and peritoneal seeding in all patients.	(23)
Martorell, 2004	4 postmenopausal (51 to 73)	Serous papillary adenocarcinoma	2 of pT4NxM1, 1 of pT3CN0M0 and 1 of pT3BN0M0	(24)
Taggart, 1984	42	Poorly differentiated adenocarcinoma	Not described (peritoneal spread)	(10)
Yogarajah, 2008	74	Poorly differentiated adenocarcinoma	Not described (peritoneal spread)	(25)
Preda, 2009	62	Poorly differentiated adenocarcinoma	Inoperable	(16)
Strobel, 1992	59	Serous adenocarcinoma	pT3CN1M0	(26)
Salmon, 2013	2 postmenopausal (58 and 69)	Serous adenocarcinoma and adenocarcinoma	pT3BN0M0 and T3CNxM0 (not operated)	(27)
Pfinsgraff, 1986	57	Adenocarcinoma	T4NxM1	(28)
Bremer, 1967	50	Not identified	T4NxM1	(29)
Van Marcke, 2017	70	Serous adenocarcinoma	pT3CN1M0	(21)
Qureshi, 2011	73	Serous adenocarcinoma	pT3CNxM0	(7)
Manger, 2014	73	Serous adenocarcinoma	pT3CNxM0	(6)
Vinker, 1996	25	Serous papillary adenocarcinoma	Stage IV	(30)
Shiel, 1985	75	Serous adenocarcinoma	Stage IV	(31)
	61	Serous adenocarcinoma	pT3BNxM0	Present case
^a This case is without polyarthritis.				

ovarian/fallopian cancer. The commitment of the attending physicians to become familiar with and identify rare disease may lead to the detection at an early and curative stage. As the symptoms of PFPA can usually precede cancer detection, and are unrelated to tumor stage, rapid diagnosis of PFPA can expedite effective management of the malignancy. Currently there are no effective screening methods for ovarian cancer and the malignancies frequently remains undiagnosed until advance stage. We recommend a thorough malignancy work-up by gynecological oncologist for any women presenting

with the sudden onset of unexplained hand pain, inflammatory fasciitis, or palmar fibromatosis.

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