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Paraneoplastic Palmar Fasciitis and Polyarthrititis Syndrome in a Patient With Advanced Prostate Cancer

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Keywords

Anti-TNF therapy; Palmar fasciitis and polyarthrititis syndrome; Paraneoplastic syndrome; Prostate cancer

Introduction

The term “palmar fasciitis and polyarthrititis syndrome” (PPFAS) was first described by Medsger et al.¹ in 1982 for a disorder characterized by a symmetric arthritis with flexion contractures and thickening of the palmar fascia coexisting with ovarian carcinoma. Since that seminal report published 30 years ago, only 48 additional cases of PPFAS have been described in the literature, and these have been associated with a number of different neoplasms, including gynecologic malignancies (ovarian and fallopian tube cancers),^{2–16} pancreatic adenocarcinoma,^{17–20} non—small cell and small cell lung carcinoma,^{3,20–22} breast carcinoma,^{23–26} prostate carcinoma,²⁷ gastric cancer,²⁸ colon cancer,²⁰ transitional cell carcinomas of the urinary tract,^{6,20,29} carcinoma of unknown origin,¹⁷ and hematologic malignancies^{17,30} (Appendix Table 1).

In this case report, we describe a patient with advanced prostate cancer who developed PPFAS during the course of his disease progression, and we summarize and review the clinical characteristics, associated malignancies, and potential therapies for PPFAS.

Case Report

A 60-year-old man presented to the urology clinic with hematospermia and microscopic hematuria. A test for prostate-specific antigen (PSA) showed a level of 34 ng/mL in January of 2011. Ultrasound-guided needle biopsies of the prostate gland were performed, revealing prostate adenocarcinoma in 7 of 12 cores, with a maximum Gleason score of 5 + 5 = 10. Staging tests showed enlarged pelvic and retroperitoneal lymph nodes on computed

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Disclosure

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tomography (CT) scan consistent with metastatic prostate cancer, and bone scan results were unremarkable. Treatment with a luteinizing hormone-releasing hormone (LHRH) agonist (leuprolide) was initiated, resulting in a PSA nadir of 0.8 ng/mL achieved after approximately 3 months. Seven months later, the patient noticed rectal bleeding and the PSA level increased to 13.6 ng/mL. He underwent a proctoscopy that revealed locally recurrent prostate cancer invading into his rectal wall, which was treated with a course of external-beam radiation therapy in January 2012. Bicalutamide 50 mg/d was added to his treatment regimen with continuation of his LHRH agonist at that time. However, neither a PSA decline nor a radiographic response was achieved with the addition of bicalutamide.

Two months later, the patient began to experience symptoms of polyarthrititis with bilateral pain and swelling and stiffness in his hands, wrists, knees, ankles, and feet. He also noticed thickening and erythema of his palmar skin followed by rapid progression to flexion contractures in both hands. Physical examination revealed synovitis of the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints with marked restriction of movement, and the skin of the palms was leathery and rock-hard to palpation consistent with palmar fasciitis (Fig. 1). The patient had pain and decreased range of motion in his cervical spine, elbows, knees, ankles, and feet. The patient showed no signs of Raynaud's phenomenon. At an initial rheumatologic consultation, the results of laboratory tests, including full blood count, antinuclear antibody (ANA), uric acid, erythrocyte sedimentation rate (ESR), and an antibody screen (anti—double-stranded DNA, anti-centromeric protein, anti—extractable nuclear antigen, anti-topoisomerase I, anti-cyclin citrullinated protein) were all unremarkable. Plain-film x-rays of the hands showed no findings of acute bony, soft tissue, or joint space abnormalities. A bone scan was consistent with an inflammatory polyarthropathy, without evidence of osseous metastasis. A diagnosis of PFPAS was made. Although this syndrome is often resistant to anti-inflammatory and anti-rheumatic therapies, prednisone 10 mg/d was initiated in combination with methotrexate (MTX) 15 mg weekly (plus folic acid 1 mg/d), on the basis of the belief that rheumatologic paraneoplastic syndromes are immune-mediated. The patient did not experience significant improvement in his symptomatology with this regimen.

Five months later, in July 2012, after a further elevation in PSA (to 76 ng/mL) and new evidence of bone metastases in the pelvis and spine, a diagnosis of metastatic castration-resistant prostate cancer was made and abiraterone 1000 mg/d was added to his treatment regimen (and bicalutamide was discontinued). The introduction of abiraterone resulted in a brief stabilization of PSA and radiographic disease lasting approximately 6 months. However, because the patient had not noticed significant symptomatic or functional improvement in his rheumatologic symptoms, adalimumab (anti-TNF therapy) was added to MTX and prednisone after the patient was counseled about the theoretic risk of accelerated cancer progression using this agent. During the next several weeks, joint mobility, pain, and swelling modestly improved; however, the palmar fasciitis and flexion contractures persisted.

In January of 2013, despite the use of abiraterone together with LHRH agonist therapy, the patient experienced further radiographic disease progression with new metastatic lesions in the liver, lungs, adrenal gland, multiple lymph node areas, and bones. Because of the

uncertain safety profile of tumor necrosis factor (TNF) inhibitors in the setting of active metastatic cancers and the limited benefit achieved in his rheumatologic symptoms, adalimumab and MTX were both discontinued at that time. The patient quickly initiated cytotoxic chemotherapy with docetaxel, and the abiraterone was discontinued. At the time of writing, the patient has received 4 cycles of docetaxel with a significant clinical response: The PSA level has decreased to 2.4 ng/mL, and this was accompanied by a partial radiographic response in soft tissue target lesions on CT scan. Rheumatologic symptoms are largely unchanged, but have not continued to worsen.

Discussion

PFPAS is a paraneoplastic condition that traditionally occurs in women (85% of all reported cases) and is usually seen in association with ovarian cancer or other gynecologic malignancies. This is only the second description of this syndrome occurring in the context of prostate adenocarcinoma. Genitourinary malignancies, including transitional cell carcinoma of the urinary tract and prostate adenocarcinoma, represent approximately 10% of all reported cases of PFPAS (5/49). By taking into account the relative infrequency of this syndrome in men, the underlying malignancy has been found to be prostate cancer in 2 of the 7 male patients with PFPAS reported thus far (Table 1). Although the number of cases of PFPAS associated with genitourinary malignancies is small, the clinical constellation of signs and symptoms of this syndrome in these patients seems similar to that observed in the context of other malignancies, such as the gynecologic cancers. In other words, there do not seem to be any genitourinary cancer-specific distinguishing features of this syndrome.

The underlying mechanism for paraneoplastic PFPAS is currently unknown. However, it is likely that fibrogenic and connective tissue growth factors and autoimmune mechanisms produced by the neoplasm are responsible for the development of PFPAS, because complement and immunoglobulin deposits have been found in some of the fascial tissues.^{3,5,23} There has been no direct or consistent link with any particular autoantibodies. However, the ESR is usually elevated, ANA is often weakly positive, and rheumatoid factor (RF) is almost always negative.

Traditionally, the severity of paraneoplastic syndromes is unrelated to the size of the primary tumor or the extent of metastatic disease. In most cases of PFPAS, the rheumatologic symptoms preceded the detection of the underlying malignancy,^{1,3,5–11,15–18,20,21,23,26,28} whereas in some cases the PFPAS occurred simultaneously with^{14,17,24} or after the initial cancer diagnosis.^{2,4,6,19,22,29} It may also develop as the first symptom of cancer recurrence or progression (as was the case in our patient).^{2,8,12,25,27,30,31} Indeed, in both cases of prostate cancer-related PFPAS, the rheumatologic symptoms appeared at the time of progression to the castration-resistant state. Exacerbation of inflammatory joint symptoms during subsequent relapse/progression of the underlying malignancy may also occur.¹⁴

Clinical features of PFPAS include pain and diffuse synovitis of the hands (usually at the MCP and PIP joints) and a symmetric polyarthritis with rapid progression of palmar fasciitis with flexion contractures of the hands. Unlike the scleroderma-related syndromes (which

this condition may mimic), patients with PFPAS universally lack evidence of sclerodactyly. Although arthritic symptoms may involve multiple additional joints (as was the case in our patient, thus the term “polyarthritis”), plantar fasciitis is less common and has been reported in only 5 patients.^{1,2,17,22,27} The development of symptoms (especially in the palms and hands) is usually rapid, leaving the patient severely disabled in the span of several days or weeks.

Laboratory tests, such as acute-phase reactants and the presence of antibodies, generally provide unremarkable results.^{1–9,12,14–20,22,24,25,29} ANA and rarely RF are the most common antibodies detected in PFPAS cases, suggesting a potential role for autoimmunity; however, these antibodies are not specific, are often present at low titers,^{3,17,28} and may be found commonly in patients with cancer who do not show any signs or symptoms of rheumatologic disease. Therefore, the prototype of PFPAS seems to be a seronegative disorder. However, to further differentiate true paraneoplastic rheumatic syndromes from the coincidental co-occurrence of rheumatologic symptoms with cancer, autoantibodies may contribute to differentiate the 2 entities. The main differential diagnosis for PFPAS includes systemic sclerosis (scleroderma syndromes), which can be ruled out through specific autoantibody screens, the absence of Raynaud’s phenomenon, and the presence of normal nail-fold capillaries. In addition, the presence of synovitis and the rapid progression of contractures of the hands make Dupuytren’s disease an unlikely diagnosis.

PFPAS is generally a nonerosive form of arthropathy producing radiologic findings of periarticular demineralization and narrowing of joint compartments without erosions.^{1,7,23,25,28} However, in most cases, x-rays of the joints show no abnormalities (as was the case in our patient).^{2,6,9,11,16,17,19,21,29} As the disease progresses, contractures develop and x-ray films of the hands may show flexion deformities of the MCP and PIP joints.^{3,8,15} In some instances, PIP joints may be affected preferentially with relative sparing of MCP joints, although this is uncommon.¹⁴

The histopathologic abnormalities in PFPAS are nonspecific and have unclear diagnostic value. Biopsies may demonstrate features of nodular fasciitis,⁸ mononuclear or lymphocytic infiltrates,^{3,5,8,12,17,21,24} fibroblastic proliferation,^{6,8} and perivascular²⁷ or diffuse fibrosis.^{3,5,8,12,17} Biopsy is not generally recommended to confirm the diagnosis, which is usually performed on clinical grounds.

Corticosteroids are often used as a first-line therapy. The efficacy of systemic steroids in patients with PFPAS is somewhat disappointing, with infrequent improvement of the polyarthritis and no effect on the joint contractures.^{1–4,6–9,12,14,16–23,25,30,31} Results have been largely disappointing with the use of conventional disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate,^{12,19,21,29} hydroxychloroquine,^{6,14} D-penicillamine,^{17,27} and sulfasalazine.¹⁴ More recently, TNF inhibitors¹² have been attempted as a second-line treatment or in combination with corticosteroids.^{14,29} Although there is no clear demonstration of symptom improvement with TNF inhibitors such as adalimumab (as used in our patient) for this indication, the lack of effective therapy for this disabling syndrome and the belief that it is an immune-mediated disorder have led to its use as a second-line therapy in some patients. However, of particular concern for patients with

cancer are the immunosuppressive effects of anti-TNF antibody therapies and their potential effect on accelerating cancer progression. Although it is hard to prove, the rapid acceleration of the disease in our patient and the development of widespread soft tissue metastases occurring during the course of treatment with adalimumab make us wonder whether this therapy may have accelerated his cancer progression. Surgery, chemotherapy, and radiotherapy for specific underlying oncologic disorders seem to be the only treatment with a positive effect on the inflammatory component of PFPAS.^{1,5,8,10–12,16,22–24,26,28,30} However, contractures are often irreversible and usually persist despite anti-inflammatory, DMARD, and anti-cancer therapies.^{1,2,4–9,12,14,16–19,23,25,27,30,31} In a few cases, flexion contractures modestly improved with effective anti-neoplastic therapy.^{11,15,28}

Conclusion

PFPAS is a rare paraneoplastic syndrome that usually occurs in women and that is characterized by a nonerosive polyarthritis and fibrosis of the palmar fascia, resulting in contractures of the hands. We presented the second case of PFPAS associated with advanced prostate cancer and described an apparent acceleration of cancer progression during anti-TNF antibody therapy. The fact that PFPAS is generally resistant to anti-inflammatory and anti-rheumatic therapies emphasizes the importance of early diagnosis and treatment of the underlying malignancy to prevent development of permanent flexion contractures. In addition, clinicians should consider prostate cancer and other malignancies as the underlying diagnosis in a male patient presenting with PFPAS and no known history of cancer.

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Clinical Practice Points

- Palmar fasciitis and polyarthritis is an uncommon paraneoplastic syndrome associated with a variety of malignancies, including transitional cell carcinoma of the urinary tract and prostate adenocarcinoma.
- Clinically, patients present with pain and diffuse synovitis of the hands characterized by symmetric, rapidly progressing palmar fasciitis with eventual development of flexion contractures in the hands. Symptoms also may involve multiple additional joints, potentially resulting in major disability and limitation in patients' activities of daily living.
- Laboratory tests usually prove unremarkable, and radiographic findings are often nonspecific but may show a nonerosive arthropathy.
- Corticosteroids are the most widely used treatment for this syndrome, but outcomes are generally poor and flexion contractures are usually irreversible. Conventional anti-rheumatic drugs and anti—tumor necrosis factor inhibitors have not proven effective.
- Successful treatment of the underlying neoplasm may result in gradual improvement of rheumatologic symptoms, especially those related to synovitis. Residual disabling flexion contractures often remain unchanged.

Figure 1.

Clinical Appearance of the Hands in a Patient With PFPAS. A and C, Palmar Surfaces of Both Hands, Demonstrating Palmar Fasciitis With Flexion Contractures at the MCP and PIP Joints. B and D, Dorsal Surface of Both Hands, Demonstrating Bilateral "Claw Hands"

Table 1

Summary of all Published Male Patients With Paraneoplastic PFPAS, Excluding the Present Case

Patient No.	Type of Malignancy	Timing in Relation to Cancer	Joint Involvement	Fasciitis (Location)	Serology	Treatment	Improvement?	Reference
1	Squamous cell carcinoma of unknown primary site	Preceded malignancy by 10 mo	Hands, wrists, shoulders, hips, ankles, feet	Palmar and plantar	ESR 110 mm/h ANA — RF —	Chemotherapy	No	Pfingsgraff et al. ¹⁷
2	Hodgkin's disease	Preceded malignancy by 5 mo	Hands, shoulders, feet	Palmar and plantar	ANA titer, 1:40	Corticosteroids, chemotherapy	Yes, partial Yes, partial	Pfingsgraff et al. ¹⁷
3	Prostate adenocarcinoma	Occurred at the time of recurrent disease	Hands, shoulders, knees, feet	Palmar and plantar	ESR — ANA — RF — ASMA +	Estramustine, D-penicillamine, colchicine	Yes, partial Yes, partial Yes, partial	Van den Bergh et al. ²⁷
4	Chronic lymphocytic leukemia	Occurred at the time of recurrent disease	Hands, wrists, shoulders, hips, knees	Palmar only	ESR 86 mm/h	Systemic corticosteroids, local injection of corticosteroids, chemotherapy	Yes, partial Yes, partial Yes, partial	Mathieu ³⁰
5	Gastric adenocarcinoma	Preceded malignancy by 5 mo	Hands, wrists, elbows, shoulders, hips, knees, ankles	Palmar only	ANA titer, 1:80 RF + Soluble IL-2 receptor high	Curative surgery	Yes, total	Enomoto et al. ²⁸
6	Non—small cell lung carcinoma	Preceded malignancy by 2.5 years	Hands, wrists, shoulders, hips	Palmar only	ESR 42 mm/h ANA — RF titer, 1:80 AMA titer, 1:320 ENAs — ANCA —	Corticosteroids, MTX, adalimumab, cyclophosphamide	Yes, partial No No No	Sheehy et al. ²¹

Abbreviations: Ab = antibody; AMA = anti-mitochondrial antibody; ANA = antinuclear antibody; ANCA = anti-neutrophil cytoplasmic antibody; ASMA = anti-smooth muscle antibody; ENA = extractable nuclear antigen antibody; ESR = erythrocyte sedimentation rate; MTX = methotrexate; PFPAS = palmar fasciitis and polyarthritits syndrome; RF = rheumatoid factor.

Appendix Table 1

Summary of all Published Reports of Paraneoplastic PFPAS

Patient No.	Malignancy	Timing	Joint Involvement	Fasciitis	Serology	Treatment	Improvement	Reference
1	Ovarian adenocarcinoma	Preceded malignancy by 6 mo	Hands, shoulders, elbows, knees and wrists	Palmar	ESR elevated ANA +	Corticosteroids Intraperitoneal chemotherapy	No No	Medsger et al. ¹
2	Ovarian adenocarcinoma	During chemotherapy for advanced disease	Hands, wrists, shoulders, feet	Palmar and plantar	ESR elevated ANA –	Intra-articular corticosteroids Stellate ganglion block Systemic corticosteroids Chemotherapy	No No No No	Medsger et al. ¹
3	Ovarian adenocarcinoma	Preceded malignancy by 4 mo	Hands, knees, shoulders	Palmar	ESR elevated ANA –	Carpal tunnel release Chemotherapy	Yes Yes	Medsger et al. ¹
4	Ovarian adenocarcinoma	Preceded malignancy by 4 mo	Shoulders, hands, wrist, ankle, feet	Palmar	ESR elevated ANA –	Chemotherapy	No	Medsger et al. ¹
5	Ovarian adenocarcinoma	Preceded malignancy by 7 mo	Hip, shoulder, knees, ankles, hands	Palmar	ESR elevated ANA –	Corticosteroids Physical therapy Chemotherapy	Yes Yes Yes	Medsger et al. ¹
6	Ovarian adenocarcinoma	Preceded malignancy by 23 mo	Shoulders, hands, knees, ankles	Palmar	ESR elevated ANA –	NSAIDs Chemotherapy and radiotherapy	Yes Yes	Medsger et al. ¹
7	Small cell carcinoma of the lung, grade 1 transitional cell carcinoma of bladder Adenocarcinoma of colon	After the diagnosis of transitional cell carcinoma of bladder Preceded diagnosis of small cell carcinoma and adenocarcinoma of colon	Hand, wrists, shoulders, ankles	Palmar	ESR 55 mm/h ANA – RF –	Corticosteroids	Yes	Baron ²⁰
8	Pancreatic adenocarcinoma	Preceded recurrent disease	Hands, wrists, shoulders	Palmar	—	Corticosteroids	No	Baer and Phillips ³¹
9	Adenocarcinoma of the fallopian tube	Preceded recurrent disease	Hands, knees, elbows, ankles, shoulders	Palmar	ANA – RF –	Corticosteroids Radiotherapy	No No	Taggart et al. ²
10	Ovarian adenocarcinoma	During adjuvant chemotherapy	Hands, shoulders, hips, knees, feet	Palmar and plantar	ESR 20 mm/h RAHA – ANF –	Physical therapy Corticosteroids Chemotherapy	No No No	Taggart et al. ²
11	Pancreatic adenocarcinoma	Preceded malignancy by 4 mo	Hands, shoulders	Palmar	ESR 11 mm/h ANA – RF –	Corticosteroids Stellate ganglion block Physical therapy Chemotherapy	No No No No	Michaels and Sorber ¹⁸
12	Small cell lung carcinoma	Preceded malignancy by 3 mo	Hands	Palmar	WSR 41 mm/h RF –	NSAIDs (declined chemotherapy)	No	Shiel et al. ³
13	Ovarian adenocarcinoma	Preceded malignancy by 1 mo	Hands, wrists,	Palmar	WSR 42 mm/h ANA titer 1:40	NSAIDs Corticosteroids Chemotherapy	No Yes Yes	Shiel et al. ³
14	Chronic myelogenous leukemia	Preceded malignancy by 6 mo	Hands, wrists, shoulders	Palmar	ANA – RF –	NSAIDs Corticosteroids Chemotherapy	No No Yes	Pfingraff et al. ¹⁷

Patient No.	Malignancy	Timing	Joint Involvement	Fasciitis	Serology	Treatment	Improvement	Reference
15	Pancreatic adenocarcinoma Parathyroid adenoma	Preceded malignancy by 3 mo	Hands, shoulders, wrists, knees, feet	Palmar and plantar	—	NSAIDs Stellate ganglion block Corticosteroids D-penicillamine Chemotherapy	No No No No Yes	Pfingsraff et al. ¹⁷
16	Squamous cell carcinoma unknown primary	Preceded malignancy by 10 mo	Hands, wrists, shoulder, hips, knees	Palmar and plantar	WSR 110 mm/h RF – ANA –	Chemotherapy	No	Pfingsraff et al. ¹⁷
17	Adenocarcinoma unknown primary	Concurrent	Hands, wrists, shoulders	Palmar	WSR 9 mm/h	NSAIDs Physical therapy (declined chemotherapy)	No No	Pfingsraff et al. ¹⁷
18	Hodgkin disease	Preceded malignancy by 5 mo	Hands, shoulder, feet	Palmar and plantar	ANA titer 1:40	Corticosteroids Chemotherapy	Yes Yes	Pfingsraff et al. ¹⁷
19	Breast cancer	Preceded malignancy by 1 years	Hands, wrists, shoulders, hips, knees, ankles, cervical spine	Palmar	ANA – Anti-dsDNA – Complement and cryoglobulins normal	Corticosteroids Chemotherapy	Yes Yes	Valverde-Garcia et al. ²³
20	Adenocarcinoma of the coelomic epithelium	During adjuvant chemotherapy	Hands, elbows, shoulders	Palmar	ESR normal ANA – RF – APF – CRP –	NSAIDS Corticosteroids	No Yes	Willemse et al. ⁴
21	Adenocarcinoma of prostate Prolactinoma	Preceded recurrence of malignancy	Hands, shoulders, knees, feet	Palmar and plantar	ESR – ANA – RF – ASMA + Complement normal	Estramustine D-penicillamine Colchicine	Yes Yes Yes	Van den Bergh et al. ²⁷
22	Chronic lymphoid leukemia	Preceded recurrence of malignancy	Hands, wrists, shoulders, hips, knees	Palmar	ESR 86 mm/h	Systemic corticosteroids Local injection of corticosteroids Chemotherapy	Yes Yes Yes	Mathieu ³⁰
23	Ovarian adenocarcinoma	Preceded malignancy by 6 mo	Hands, shoulders, knees	Palmar	ANA – VDRL – Complement normal Cryoglobulins normal	ACTH therapy Physical therapy Chemotherapy	Yes Yes Yes	Vinker et al. ⁵
24	Breast carcinoma	Simultaneous with initial diagnosis	Hands, feet	Palmar	ANA – RF –	Chemotherapy	Yes	Saxman and Seitz ²⁴
25	Transitional cell carcinoma of the renal pelvis	Preceded malignancy by 8 mo	Hands	Palmar	ESR 45 mm/h CRP 25 mg/L ANA – RF – Anti-dsDNA Ab – Anti-topoisomerase I Ab – Complement normal	NSAIDs Hydroxychloroquine Corticosteroids	No No No	Grados et al. ⁶

Patient No.	Malignancy	Timing	Joint Involvement	Fasciitis	Serology	Treatment	Improvement	Reference
26	Adenocarcinoma of the uterus	1 years after diagnosis of malignancy	Hands, elbows, shoulders, knees, ankles	Palmar	ESR 33 mm/h ANA – RF – Complement normal	Surgery to release median nerve	Yes	Grados et al. ⁶
27	Early-stage gastric carcinoma	Preceded malignancy by 5 mo	Hands, wrists, elbows, shoulders, hips, knees, ankles	Palmar	ANA titer 1:80 speckled pattern RF + Soluble IL-2 receptor 4440 µ/mL (ref <530)	Curative surgery	Yes	Enomoto et al. ²⁸
28	Endometrial adenocarcinoma	Preceded malignancy by 2 mo	Hands	Palmar	ESR – ANA – RF – CRP –	Local injection of corticosteroids Hormonal therapy Corticosteroids Physical therapy Chemotherapy	No Yes Yes Yes Yes	Docquier et al. ⁷
29	Ovarian adenocarcinoma	Preceded malignancy by 4 mo	Hands, wrists, shoulders	Palmar	ESR normal ANA – RF –	Corticosteroids Physical therapy Chemotherapy Tamoxifen	No Yes Yes Yes	Martorell et al. ⁸
30	Ovarian adenocarcinoma	Preceded malignancy by 3 mo	Hands, wrists, elbows, knees, ankles, feet	Palmar	—	NSAIDs Corticosteroids Surgery Chemotherapy Tamoxifen	No Yes No No No	Martorell et al. ⁸
31	Ovarian adenocarcinoma	During first-line palliative chemotherapy	Hands	Palmar	ANA titer 1:10,000 RF –	Corticosteroids Chemotherapy	No No	Martorell et al. ⁸
32	Ovarian adenocarcinoma	Preceded malignancy by 9 mo	Hands	Palmar	ANA – RF – ENAs – (SS-A/Ro and SS-B/La)	Chemotherapy	Yes	Martorell et al. ⁸
33	Fallopian tube carcinoma	Preceded malignancy 1 years	Hands	Palmar	ANA – RF – PR3/MPO – Complement normal	Corticosteroids COX-2 inhibitor Topical diclofenac Chemotherapy	No No No Yes	Denschlag et al. ⁹
34	Ovarian adenocarcinoma	Preceded malignancy by 1 years	Hands	Palmar	ANA– RF – ENA –	NSAIDs Corticosteroids Surgery Chemotherapy	No No Yes Yes	Giannakopoulos et al. ¹⁵
35	Non—small cell lung carcinoma	Preceded malignancy by 2.5 years	Hands, wrist, shoulders, hips	Palmar	ESR 42 mm/h ANA – RF titer 1:80 ASMA 1:320 ENA – PR3/MPO –	Corticosteroids MTX Adalimumab Cyclophosphamide	Yes No No No	Sheehy et al. ²¹
36	Pancreatic adenocarcinoma	1 y after diagnosis	Hands, wrists, elbows, knees	Palmar, wrists, elbows, knees	ANA – RF –	Corticosteroids MTX	Yes Yes	Haroon and Phelan ¹⁹

Patient No.	Malignancy	Timing	Joint Involvement	Fasciitis	Serology	Treatment	Improvement	Reference
					ESR – ENA –			
37	Ovarian adenocarcinoma	Preceded malignancy 4 mo	Hands	Palmar	—	Chemotherapy	Yes	Yogarajah et al. ¹⁰
38	Ovarian adenocarcinoma	Preceded malignancy by 4 mo	Hands, shoulders, and knees	Palmar	ANA – RF – PR3/MPO – Complement normal	NSAIDs Local ointments Surgery Physical therapy	No No Yes Yes	Bolibar et al. ¹⁶
39	Ovarian adenocarcinoma	Preceded malignancy by 6 mo	Hands, shoulders, knees, hips, feet	Palmar	—	NSAIDs Glucosamine sulfate Surgery for underlying malignancy	No No Yes	Preda et al. ¹¹
40	Breast cancer	At progression of malignancy	Hands, wrists, elbows, knees	Palmar	ESR 52 mm/h ANA – RF –	Corticosteroids NSAIDs	Yes No	Krishna et al. ²⁵
41	Ovarian adenocarcinoma	Preceded malignancy by 4 mo	Hands, wrist, shoulder	Palmar, wrist, shoulder	ANA – RF –	Corticosteroids Surgery Chemotherapy	No Yes Yes	Qureshi et al. ¹²
42	Transitional cell carcinoma of the bladder	After diagnosis	Hands	Palmar	CRP 3.7 mg/dL RF – Complement normal	Corticosteroids plus MTX Physical therapy	Yes Yes	Clarke et al. ²⁹
43	Ovarian adenocarcinoma	Preceded malignancy by 6 mo	Hands	Palmar	CRP – ANA – RF –	Surgery Chemotherapy	Yes Yes	Nahar and Al-Rajhi ¹³
44	Breast carcinoma	Preceded malignancy by 6 mo	Hands	Palmar	—	Chemotherapy	Yes	Sandhya and Danda ²⁶
45	Non—small cell lung cancer	18 mo after diagnosis of malignancy	Hands and feet	Palmar and plantar	CRP normal ESR normal	Radiotherapy Corticosteroids	Yes Yes	McGivern and McAleese ²²
46	Ovarian adenocarcinoma	Simultaneous; flair with malignancy relapse	Hands, knees, feet	Palmar	ESR 100 mm/h CRP 25 mg/L RF – ACPAs –	Surgery plus chemotherapy Corticosteroids plus hydroxychloroquine Sulfasalazine	Yes No Yes No	Salmon et al. ¹⁴
47	Ovarian adenocarcinoma	Simultaneous with malignancy	Hands, knees, feet	Palmar	ESR 35 mm/h CRP 31 mg/L ANA titer 1:8000 RF – ACPAs – ACAs – Anti-topoisomerase I Ab –	Corticosteroids	Yes	Salmon et al. ¹⁴
48	Uterine cancer	Preceded malignancy by 2 years	Hands, shoulders, elbows	Palmar	ANA –	Corticosteroids Hydroxychloroquine	Yes Yes	Salmon et al. ¹⁴

Abbreviations: Ab = antibody; ACA = anti-centromere antibody; ACPA = anti-citrullinated peptic antibodies; ACTH = adrenocorticotrophic hormone; ANA = antinuclear antibody; ANF = antinuclear factor; APF = anti-perinuclear factor; ASMA = anti smooth muscle antibody; COX-2 = cyclooxygenase 2; CRP = C-reactive protein; dsDNA = double-stranded DNA; ENA = extractable nuclear antigen; ESR = erythrocyte sedimentation rate; IL = interleukin; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; PFPAS = palmar fasciitis and polyarthritits syndrome; PR3/MPO = anti-neutrophil cytoplasmic antibody; RAHA = rheumatoid arthritis hemagglutination titer; RF = rheumatoid factor; VDRL = venereal disease research laboratory; WSR = Westergren sedimentation rate.