Palmar Fasciitis and Polyarthritis Syndrome in Pancreatic Carcinoma

David Veitch, MBCHB, BSc(Imm), Ted Tsai, MBBS/BSci(Med)/BArts, and Fredrick Joshua, PhD, MBBS, FRACP

Abstract: Palmar fasciitis and polyarthritis syndrome is a rare paraneoplastic condition that may portend a diagnosis of malignancy. We describe the case of a 73-year-old man who presented with progressive palmar swelling, erythema, pain, and contractures of both hands, This presentation and associated weight loss eventually led to the diagnosis of metastatic pancreatic adenocarcinoma. This case highlights the often delayed, but important diagnosis of this unusual paraneoplastic phenomenon which can mimic arthropathy, Dupuytren contracture, and scleroderma. Our case is also the first documentation of the extensive inflammatory magnetic resonance imaging changes in palmar fasciitis and polyarthritis syndrome, which affects all tissue planes including the synovium and explains its confusing clinical manifestations.

Key Words: palmar fasciitis, paraneoplastic, polyarthritis, MRI, pancreatic cancer

(*J Clin Rheumatol* 2013;19: 203–205)

CASE REPORT

A 73-year-old man was admitted in December 2011 with a 2-week history of progressive pain, erythema, and swelling over the right thenar eminence and thumb. These symptoms developed 1 month after the right thumb pad was pricked by a thorn while gardening. He was systemically well with no fevers, night sweats, or rigors. There was no foreign body in the thumb.

The patient had a history of alcohol excess, consuming around 500 mL of sherry per day. He had a 1-year history of a progressive right little-finger Dupuytren contracture, without other features of chronic liver disease. There was no history of Raynaud phenomenon, acid reflux, skin mottling, hyperhidrosis, or skin hypersensitivity. He was previously healthy with the exception of bilateral hearing loss post–bilateral stapedectomy in his teenage years. He had no regular medications.

Examination showed mild general swelling of the right hand, particularly over the thumb base. He had a fixed flexion deformity of the little-finger proximal interphalangeal joint and multiple firm, nontender, subcutaneous nodular swellings over the index- and little-finger metacarpophalangeal joints on the palmar aspect, with overlying cutaneous erythema and no joint tenderness. The skin temperature was normal, and there was appropriate sweating of the hand. The rest of his physical examination was normal with no abnormalities of the left hand and shoulders and no palpable abdominal organomegaly, lymphadenopathy, or skin findings.

From the Department of Rheumatology, Prince of Wales Hospital, Barker Street, Randwick, Sydney, New South Wales, Australia.

The authors declare no conflict of interest.

Correspondence: Fredrick Joshua, PhD, MBBS, FRACP, Combined Rheumatology Practice, 19 Kensington St, Kogarah, Sydney, New South Wales, 2217, Australia. E-mail: fredjoshua@unsw.edu.au.

ISSN: 1076-1608/13/1904–0203
DOI: 10.1097/RHU.0b013e3182937abb

Full blood count and calcium/magnesium/phosphate, renal, liver, and thyroid function tests were normal. His C-reactive protein was 5 mg/L (<3 mg/L), erythrocyte sedimentation rate was 2 mm/h (0–14 mm/h), and urate was 0.34 mmol/L (0.29–0.52 mmol/L). Autoimmune serology including rheumatoid factor, cyclic citrullinated peptide, and antineutrophil cytoplasmic antibodies were negative. Antinuclear antibody was positive at a titer of 1:320, with both speckled and cytoplasmic patterns; but extractable nuclear antigens were negative. He was negative for HLA-B27. Hepatitis B and C serologies were unremarkable.

Radiograph of the right hand showed only chondrocalcinosis of the triangular cartilage and degenerative changes, with no evidence of foreign bodies. Ultrasound showed hypoechoic nodules of the palmar fascia at the index (25 × 18 mm) and little (8 × 7 mm) fingers, suggestive of palmar fibromas.

He was empirically treated for atypical hand cellulitis with 3 days of intravenous cephazolin and metronidazole, followed by oral flucloxacillin. The hand was elevated in a splint for analgesia. Biopsy to exclude atypical mycobacterial or nocardia infection was considered but not performed, as his pain had subjectively alleviated. Differential diagnoses of gout or psoriatic arthropathy were made following rheumatology review, and a 1-week course of oral colchicine 0.5 mg twice a day in combination with indomethacin 50 mg three times daily as required was commenced.

An outpatient magnetic resonance imaging (MRI) with gadolinium of the right thumb 6 weeks later showed mild synovitis in the metacarpophalangeal joint only.

Following completion of the 1-week indomethacin, colchicine, and flucloxacillin course, his right thumb was persistently painful and swollen. He was then commenced on a 3-week weaning course of prednisolone starting at 10 mg daily with minimal response. Two weeks after the prednisolone wean, he developed worsening pain, swelling, and erythema, which had spread across his entire right hand and, to a lesser extent, his left hand (Fig. 1). The pain, swelling, and increasing flexion contractures of his fingers impaired his daily function. In addition, he developed bilateral base of metatarsophalangeal pain, with mild swelling and plantar fascial thickening on examination. He had 7-kg weight loss over the last 3 months but no other systemic symptoms. He was readmitted and commenced on prednisone 25 mg daily and regular naproxen 500 mg twice a day with some symptomatic benefit.

Further investigations showed negative angiotensin-converting enzyme, raised β2 microglobulin of 3.8 mg/L (0.8–1.7 mg/L), and lactate dehydrogenase of 328 U/L (<250 U/L). Repeat inflammatory markers were normal.

Despite a normal computed tomography (CT) of the right hand, MRI of the right hand showed an unusually diffuse distribution of inflammation affecting the subcutaneous and deep extra-articular soft-tissue planes, tenosynovial compartments, and flexor and extensor tendons (Fig. 2).

A contrast CT of the chest/abdomen/pelvis to investigate the weight loss revealed bulky para-aortic and paracaval

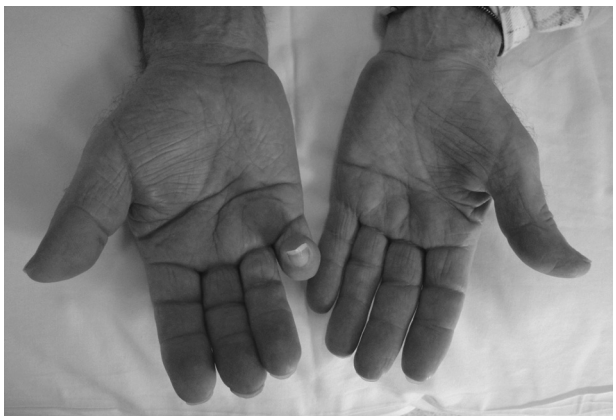

FIGURE 1. Right fifth-finger Dupuytren contracture. Widespread swelling of the right hand and lateral aspect of the left hand. Associated cutaneous erythema. Available in color online at www.jclinrheum.com

lymphadenopathy in the upper abdomen and several smaller retrocrural lymph nodes. No primary neoplasm or infection was identified. The chest CT showed no evidence of pulmonary fibrosis. Lymphoma was suspected. Positron emission tomography scan showed avid glucose uptake in the above nodes only, with no primary tumor site identified.

Computed tomography–guided core biopsy of the para-aortic lymph nodes showed cytological features consistent with metastatic large cell carcinoma. The histopathology showed a poorly differentiated metastatic adenocarcinoma, with strongly positive CK7 and MNF-116 (pan-cytokeratin) staining suggesting a primary carcinoma from the upper gastrointestinal tract, biliary tract, or pancreas. The tumor cells had high-grade nuclei arranged within desmoplastic stroma. Gastroscopy and colonoscopy with multiple biopsies were normal.

Tumor markers including α-fetoprotein, carcinoembryonic antigen, and prostate-specific antigen were negative. However,

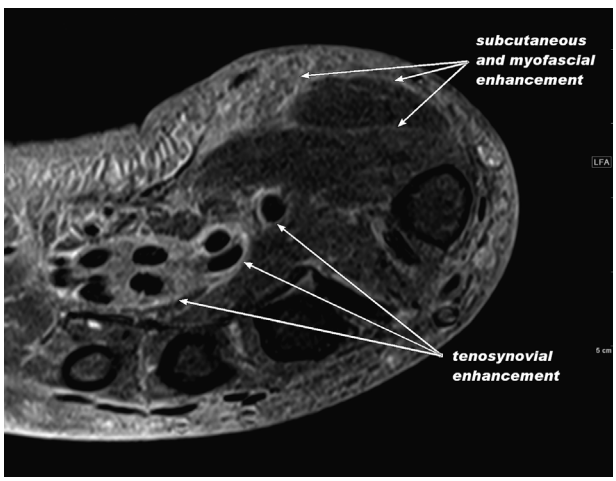

FIGURE 2. Axial T2 MRI of the right hand demonstrating diffuse subcutaneous and deep fascial edema and enhancement. Mild diffuse tenosynovial enhancement involving both the long flexor and the extensor tendon compartments.

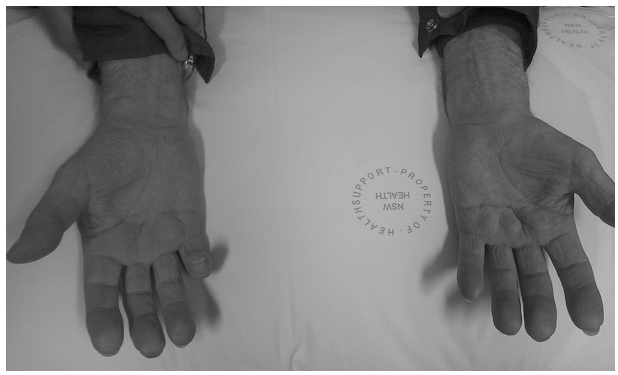

FIGURE 3. Clinical improvement seen after 2 months of treatment with gemcitabine chemotherapy. Available in color online at www.jclinrheum.com

CA-19–9 antigen was raised at 157 kU/L (<40 kU/L). An endoscopic ultrasound showed a 2.8-cm heterogeneous mass in the inferior margin of the uncinate process of the pancreas, with extensive para-aortic lymphadenopathy consistent with metastatic pancreatic carcinoma. Paraneoplastic palmar fasciitis due to pancreatic carcinoma was diagnosed. He was commenced on gemcitabine chemotherapy, and after 2 months of treatment, there was clinical improvement of his palmar fasciitis with a reduction in both the swelling and the functional contractures (Fig. 3). Further clinical follow-up 12 months later showed continued improvement with chemotherapy in the swelling, although there was incomplete resolution in the functional contractures and ongoing pain. Because of progression of his cancer, he was being treated palliatively, so no further imaging was performed.

DISCUSSION

Palmar fasciitis and polyarthritis syndrome (PFPAS) is a rare paraneoplastic syndrome most commonly, but not exclusively, described with ovarian cancer. Palmar fasciitis and polyarthritis syndrome was first described in 1982 by Medsger et al.,[1] who reported 6 ovarian malignancies associated with mainly hand and shoulder arthritis and palmar fasciitis. Since then, approximately 50 PFPAS cases associated with various gastrointestinal, reproductive, and urogenital tracts malignancies have been reported. Other less reported malignancies include thyroid cancers and hematologic malignancies such as multiple myeloma and chronic myeloid leukemia with more curable conditions such as benign endometrial cyst of the ovary and Hodgkin disease reported in isolated cases.[2] Early recognition of this condition is important as it can precede the diagnosis of malignancy.[3]

The clinical manifestations of PFPAS are variable. In the majority of cases, polyarthritis affects the small joints of the hand. Involvement of larger joints is less common and often less severe. In addition, patients usually develop widespread, painful swelling of the hands associated with nodular thickening of the palmar fascia. Skin changes include erythema and induration of the palms.[4] A recent report of paraneoplastic palmar fasciitis in carcinoma of the breast highlights the heterogeneity of the clinical presentation with diffuse thickening of the palmar fascia seen without nodules or skin changes and no evidence of joints affected by polyarthritis.[5]

The 5 cases of PFPAS associated with pancreatic adenocarcinoma have occurred exclusively in female patients.[6–10] Baer and

Phillips[6] described a woman with PFPAS who had diffuse flexion contractures 1 year after the diagnosis of metastatic pancreatic adenocarcinoma, with no response to prednisolone 20 mg daily. Michaels and Sorber[7] described a patient presenting concomitantly with symptoms of metastatic malignancy and PFPAS who was unresponsive to nonsteroidal anti-inflammatory agents (NSAIDs), methylprednisolone, and chemotherapy. Giannakopoulos et al.[8] reported a patient diagnosed synchronously with ovarian and pancreatic carcinoma 12 months after the onset of PFPAS that was again unresponsive to NSAIDs and prednisone. Symptoms alleviated after hysterectomy with bilateral salpingo-oophorectomy and chemotherapy. Pfinsgraff et al.[9] reported a 59-year-old woman who presented with PFPAS 7 months before the diagnosis of pancreatic adenocarcinoma who, unusually, developed plantar fasciitis, as was seen in our patient. Her symptoms were unresponsive to both prednisone and D-penicillamine, but alleviated dramatically with chemotherapy.[9] Finally, Haroon and Phelan[10] described a woman with atypical PFPAS causing disabling flexion contractures of the knees, elbows, and wrists in addition to the hands, rendering her wheelchair-bound. These symptoms developed 1 year after curative surgery for pancreatic adenocarcinoma. No residual tumor was detected after the diagnosis of PFPAS, and although the symptoms gradually alleviated with corticosteroids and methotrexate, the disabling contractures remained.[10]

Comparing the above reports with our case, we describe the first male patient with pancreatic cancer–associated PFPAS. Only 20% of all reported PFPAS cases occur in male patients. In addition, antinuclear antibody was positive at 1:320 titer in our patient. Of the 5 cases described above, only Haroon and Phelan,[10] Michaels and Sorber,[7] and Giannakopoulos et al.[8] comment on antinuclear antibody, which was negative in all 3 cases.

Our case is also the first documentation of the extensive inflammatory MRI changes in PFPAS, which affects all tissue planes including the synovium. The new MRI findings include the constellation of abnormalities that can mimic other inflammatory arthropathies, in particular psoriatic arthritis, with soft-tissue edema, tenosynovitis, and a mild articular synovitis, although there is also an element of fibrosis that is not seen in other inflammatory arthritides. This explains its clinical manifestation as an atypical inflammatory arthropathy, with significant dermatosis and fibrosis, which was initially attributed to Dupuytren contracture, given our patient's significant alcohol intake. However, his presentation of progressive, atypical inflammatory arthropathy, weight loss, and poor response to NSAIDs and prednisone raised the suspicion of a paraneoplastic syndrome.

Interestingly, our patient's pain and swelling responded partially only to the higher doses of corticosteroid, which was not a consistent feature among the other case reports.[11] Indeed, corticosteroid therapy for PFPAS in general gave only modest benefit at best. The best relief from PFPAS appears to be treatment of the underlying malignancy, either surgically or with chemotherapy, as seen in our case.[12–14]

KEY POINTS

- Palmar fasciitis and polyarthritis syndrome has been associated primarily with ovarian cancer but may occur in any gastrointestinal, urogenital, and reproductive tract organs, as well as thyroid and hematologic malignancies.
- Magnetic resonance imaging findings may show mild but widespread inflammatory changes across all tissue planes of the hand.
- Treatment options are limited, but patients may at least partially respond to glucocorticoid therapy and treatment of the underlying malignancy.

REFERENCES

1. Medsger TA, Dixon JA, Garwood VF, et al. Palmar fasciitis and polyarthritis associated with ovarian carcinoma. *Ann Intern Med*. 1982;96:424–431.
2. Clarke LL, Kennedy CT, Hollingworth P, et al. Palmar fasciitis and polyarthritis syndrome associated with transitional cell carcinoma of the bladder. *J Am Acad Dermatol*. 2011;64:1159–1163.
3. Marengo MF, Suarez-Almazor ME, Lu H, et al. Neoplastic and paraneoplastic synovitis. *Rheum Dis Clin North Am*. 2011;37:551–572.
4. Shah A, Jack A, Liu H, et al. Neoplastic/paraneoplastic dermatitis, fasciitis, and panniculitis. *Rheum Dis Clin North Am*. 2011;37:573–592.
5. Sandhya P, Danda D. Paraneoplastic palmar fasciitis in carcinoma breast. *J Clin Rheumatol*. 2012;18:112.
6. Baer AN, Phillips RM Jr. Pancreatic carcinoma and palmar fasciitis. *Ann Intern Med*. 1983;99:411–412.
7. Michaels RM, Sorber JA. Reflex sympathetic dystrophy as a probable paraneoplastic syndrome: case report and literature review. *Arthritis Rheum*. 1984;27:1183–1185.
8. Giannakopoulos ChK, Kyriakidou GK, Toufexi GE. Palmar fasciitis and polyarthritis associated with secondary ovarian carcinoma. Case report. *Eur J Gynaecol Oncol*. 2005;26:339–341.
9. Pfinsgraff J, Buckingham RB, Killian PJ, et al. Palmar fasciitis and arthritis with malignant neoplasms: a paraneoplastic syndrome. *Semin Arthritis Rheum*. 1986;16:118–125.
10. Haroon M, Phelan M. A paraneoplastic case of palmar fasciitis and polyarthritis syndrome. *Nat Clin Pract Rheumatol*. 2008;4:274–277.
11. Martorell EA, Murray PM, Peterson JJ, et al. Palmar fasciitis and arthritis syndrome associated with metastatic ovarian carcinoma: a report of four cases. *J Hand Surg Am*. 2004;29:654–660.
12. Alexandroff AB, Hazleman BL, Matthewson M, et al. Woody hands. *Lancet*. 2003;361:1344.
13. Enomoto M, Takemura H, Suzuki M, et al. Palmar fasciitis and polyarthritis associated with gastric carcinoma: complete resolution after total gastrectomy. *Intern Med*. 2000;39:754–757
14. Denschlag D, Riener E, Vaith P, et al. Palmar fasciitis and polyarthritis as a paraneoplastic syndrome associated with tubal carcinoma: a case report. *Ann Rheum Dis*. 2004;63:1177–1178.