www.nature.com/clinicalpractice/rheum

A paraneoplastic case of palmar fasciitis and polyarthritis syndrome

Muhammad Haroon* and Mark Phelan

SUMMARY

Background A 58-year-old woman presented with arthritis of the small joints of her hands and rapidly progressive joint contractures. She was wheelchair bound within 2 months of the onset of her symptoms. Physical examination revealed synovitis of the small joints of her hands and palmar fasciitis. The patient had been diagnosed with pancreatic carcinoma approximately 1 year before the presentation of her rheumatic symptoms, and had undergone radical pancreatico-duodenectomy.

Investigations Physical examination; routine laboratory work, including full blood count and measurement of erythrocyte sedimentation rate and C-reactive protein; serological tests for rheumatoid factor, antinuclear antibodies and extractable nuclear antibodies; measurement of serum tumor markers; radiological investigations, including X-rays of her hands and feet, whole-body CT-scans and radioisotope bone scan.

Diagnosis The patient's rheumatic presentation was diagnosed as a paraneoplastic syndrome associated with pancreatic carcinoma.

Management The patient's condition was managed with corticosteroids and methotrexate. No residual tumor or evidence of metastatic disease have been detected in the 1.5 years since the initial presentation of her rheumatic symptoms.

KEYWORDS joint flexures, malignancy, palmar fasciitis and polyarthritis syndrome, paraneoplastic, synovitis

CME

M Haroon is a Rheumatology Specialist Registrar and M Phelan is a Consultant Rheumatologist at the South Infirmary-Victoria University Hospital, Cork, Republic of Ireland.

Correspondence
*Rheumatology Specialist Registrar, South Infirmary-Victoria University Hospital, Cork, Republic of Ireland
mharoon301@hotmail.com

Received 3 June 2007 **Accepted** 9 January 2008 **Published online** 18 March 2008
www.nature.com/clinicalpractice
doi:10.1038/ncprheum0768

Vanderbilt Continuing Medical Education online
This article offers the opportunity to earn one Category 1 credit toward the AMA Physician's Recognition Award.

Competing interests
The authors declared no competing interests.

THE CASE

A 58-year-old woman presented to the Accident and Emergency department with rapidly progressive joint flexures. A rheumatological consultation was sought. The patient's first clinical manifestation was the development of purple erythematous papules over the palmar surface of her hands. She reported a 2-month history of increasing pain and swelling of the small joints of her hands and wrists, and painful and stiff elbows and knees. The patient also experienced profound early morning stiffness, but her clinical presentation was atypical, with left-side joints markedly more affected than those on her right side. Rapid progression of flexion contractures involving her hands, wrists, elbows and knee joints resulted in the patient being wheelchair bound upon presentation to the Accident and Emergency department, less than 2 months after the onset of her symptoms. The patient's baseline level of physical activity, before presentation of her rheumatic symptoms, involved independent mobilization at home and independence in her activities associated with daily living. Physical examination revealed bilateral erythema and palpable thickening of palmar fascia, synovitis of the metacarpal phalangeal (MCP) and proximal interphalangeal (PIP) joints, and flexion contractures of all fingers (~60° at MCP joints and ~30° at PIP joints), wrists (~20° bilaterally), elbows (~45° bilaterally) and knee (~45° bilaterally) joints.

Approximately 1 year before the presentation of her rheumatic symptoms, the patient presented with weight loss and jaundice, and was diagnosed with lymph-node-positive pancreatic carcinoma. She was treated with radical pancreatico-duodenectomy. The patient subsequently underwent gastrojejunostomy for anastomotic stricture and

Table 1 The patient's laboratory measurements at the time of admission.

Investigation	Result
C-reactive protein	<10 mg/l (normal range 1–10 mg/l)
Hemoglobin	10.7 g/dl (normal range 13–17 g/dl
Liver and kidney functions	Normal
Erythrocyte sedimentation rate	23 mm/h (normal range <30 mm/h)
Rheumatoid factor	Negative (<15 IU/ml)
Anti-nuclear antibodies	Negative
Extractable nuclear antibodies	Negative
Serum creatine kinase	56 U/l (normal range 0–195 U/l)
Lactate dehydrogenase	326 U/l (normal range 266–500 U/l)
X-rays of hands, wrists and knees	No erosions, essentially normal
CT of abdomen, pelvis, thorax and brain	No residual tumor or metastasis
Technetium-99 bone scan	Slight increased activity in multiple small joints of hands, otherwise normal
Viral hepatitis serology	Negative
HbA1C	5.2% (normal range 4–6%)
Skin biopsy	Increased fibrosis of the dermis
Tumor markers	
CA-125	17 U/ml (normal range 0–30 U/ml)
CA-19.9	21 U/ml (normal range 0–31 U/ml)
CA-15.3	12 U/ml (normal range 0–32 U/ml)
Alpha-fetoproteins	2 ng/ml (normal range 0–8 ng/ml)
Albumin	28 g/l (normal range 35–50 g/l)
Calcium	2.18 mmol/l (normal range 2.1–2.7 mmol/l)
Ferritin	25 μg/l (normal range 17–360 μg/l)
Vitamin B12	347 μg/l (normal range 160–1000 μg/l)

had a protracted postoperative convalescence, but made a complete recovery. She did not develop diabetes postsurgery, and never required insulin or other hypoglycemia medications. Before the onset of pancreatic carcinoma, the patient had been healthy and had no comorbidities.

At the initial rheumatological consultation, the results of laboratory investigations, including full blood count, erythrocyte sedimentation rate, serum C-reactive protein level and serological tests for rheumatoid factor, antinuclear antibodies and extractable nuclear antibodies, were unremarkable (Table 1). Anti-cyclic citrullinated peptide antibodies were not measured. Radioisotope bone scan and radiological examination of hands, wrists and knees were normal. There was no evidence of residual tumor or metastasis detected on CT of the abdomen, pelvis, thorax and brain, and the patient's tumor marker levels were normal.

A presumptive diagnosis of rheumatoid arthritis with atypical features was initially made, and the patient was administered intravenous steroids and methotrexate; however, the atypical clinical picture against the background of malignancy, the rapid progression of symptoms and the subsequent findings from normal investigations led us to revisit the diagnosis. The patient's inflammatory arthritis responded to low-dose maintenance steroids and methotrexate but, unfortunately, she had residual disabling flexion contractures; these contractures were treated with extensive physiotherapy. The patient was diagnosed as having paraneoplastic palmar fasciitis and polyarthritis syndrome. Although many case reports claim a gradual resolution of rheumatic symptoms with successful management of the associated neoplasm, we could not detect any residual tumor or evidence of metastatic disease in our patient.

Box 1 Differential diagnosis.

- Systemic sclerosis
- Complex regional pain syndrome
- Dupuytren's disease
- Eosinophilic fasciitis
- Clinical rheumatoid arthritis

DISCUSSION OF DIAGNOSIS

Paraneoplastic syndrome can have rheumatic manifestations; such rheumatic symptoms either mimic the features of other rheumatic disorders or produce distinctive features. The association between malignant disease and rheumatic symptoms has been described for some time, and such paraneoplastic syndromes can affect a variety of organ systems. Palmar fasciitis and polyarthritis syndrome is an uncommon paraneoplastic presentation that was first described in 1982 by Medsger and colleagues,[1] who reported the association of palmar fasciitis and polyarthritis syndrome with ovarian carcinoma, and described these symptoms as a variant of reflex sympathetic dystrophy (now known as complex regional pain syndrome). More than 40 cases have since been reported, and the majority of patients are female. Although originally described in association with ovarian carcinoma,[1] some case reports link this form of arthritis with colon,[2] pancreas,[3] lung,[4] cervix[5] and hematolymphatic malignancies.[6,7]

The rheumatic symptoms usually precede the occurrence or detection of a tumor, but can also occur simultaneously with, or follow, the diagnosis of neoplasm. By definition, a paraneoplastic syndrome is not produced by the primary tumor itself, or by its metastases, and it is not caused by compression or treatment of the tumor. The underlying mechanism for palmar fasciitis and polyarthritis syndrome has not yet been defined, but it is likely to have an association with fibrogenic and connective tissue growth factors and autoimmune reactions, since immunoglobulin deposits have been found in the fascial tissues.[4,5]

The literature describes the clinical picture of palmar fasciitis and polyarthritis syndrome as presenting with pain and diffuse synovitis of the hands (usually at the MCP and PIP joints), and rapid progression of palmar fasciitis with flexion contractures in the hands and limbs. Although adhesive capsulitis is also common, and symptoms often involve multiple joints, plantar fasciitis rarely manifests. Laboratory investigations, such as tests for acute phase reactants and the presence of autoantibodies, generally provide unremarkable results. Palmar fasciitis and polyarthritis syndrome is a nonerosive form of arthopathy, and, except for some periarticular demineralization, X-rays of joints usually show no abnormalities.

Palmar fasciitis and polyarthritis syndrome can mimic other conditions, including scleroderma, complex regional pain syndrome (reflex sympathetic dystrophy), Dupuytren's disease and eosinophilic fasciitis, and there are also case reports that contain tentative diagnoses of clinical rheumatoid arthritis (Box 1). The absence of Raynaud's syndrome, the lack of specific autoantibodies and the rapid progression of clinical features help exclude scleroderma; the synovitis and indurated swelling of digits, and the rapid progression of clinical features of the hand, make Dupuytren's disease an unlikely diagnosis. In contrast to complex regional pain syndrome, palmar fasciitis and polyarthritis syndrome almost always presents with bilateral inflammatory arthritis and fasciitis that is not localized to a particular limb, and usually has a more severe presentation.

In the current patient, no evidence of persistent malignant disease has been detected using conventional screening methods (PET scanning was unavailable). The paraneoplastic nature of the patient's disorder is, therefore, hypothetical. The case is regarded as a paraneoplastic presentation, however, since the history of extensive malignancy was diagnosed before presentation of rheumatic symptoms and peripancreatic lymph nodes were positive during tumor resection. Moreover, pancreatic carcinomas tend to develop early subclinical metastases, and parapancreatic lymph node morphology, determined on CT, is not a useful predictor of malignancy.[8]

Most case reports have described the association of the clinical spectrum of palmar fasciitis and polyarthritis syndrome with different malignancies; however, three previous case studies reported palmar fasciitis and polyarthritis syndrome that was not associated with detectable neoplasm. Seaman *et al.*[9] reported seven patients who developed palmar fasciitis while receiving an antituberculosis drug (ethionamide); the palmar fasciitis resolved when the treatment was discontinued. Laszlo *et al.*[10] described a 75-year-old woman who developed palmar fasciitis and

polyarthritis syndrome; this syndrome was described as idiopathic, and the duration of follow-up was only 12 months. Finally, Sung and colleagues[11] reported a case of a 31-year-old Korean woman; her palmar fasciitis and polyarthritis syndrome was not found to be associated with malignancy during the 24-month follow-up period from the onset of her first symptoms.

TREATMENT AND MANAGEMENT

Treatment options for this paraneoplastic arthritis remain limited, since the underlying mechanism for palmar fasciitis and polyarthritis syndrome has not yet been defined. Overall, the prognosis for patients with this form of paraneoplastic syndrome is very poor; however, there are case reports that demonstrate the gradual resolution of rheumatic symptoms with successful management of the neoplasm. Treatment regimens, therefore, should incorporate a patient-focused, symptomatic approach and effective cancer treatment.

CONCLUSIONS

We describe a patient who was known to have pancreatic carcinoma with a typical clinical presentation. The patient's rheumatic complaints are not currently associated with detectable progression of the malignancy or with tumor recurrence; however, rheumatic complaints can precede tumor recurrence by a considerable length of time.

Although most patients with arthritis will be accurately diagnosed by treating physicians, difficulties arise with new-onset inflammatory arthritis in the elderly and in patients with uncommon or rare forms of arthritis. Investigating the possibility of an occult neoplasm is recommended when treating an elderly patient with rheumatic symptoms, or when treating a patient of any age who presents with an atypical arthropathy (especially with palmar fasciitis), particularly if unexplained anemia or constitutional symptoms exist. This would ensure timely management of any existing culprit lesion.

Competing interests
The authors declared no competing interests.

References

1 Medsger TA *et al*. (1982) Palmar fasciitis and polyarthritis associated with ovarian carcinoma. *Ann Intern Med* **96:** 424–431
2 Michaels RM and Sorber JA (1984) Reflex sympathetic dystrophy as a probable paraneoplastic syndrome: case report and literature review. *Arthritis Rheum* **27:** 1183–1185
3 Baer AN and Phillips RM Jr (1983) Pancreatic carcinoma and palmar fasciitis. *Ann Intern Med* **99:** 411–412
4 Shiel WC Jr *et al*. (1985) Palmar fasciitis and arthritis with ovarian and non-ovarian carcinomas. New syndrome. *Am J Med* **79:** 640–644
5 Valverde-Garcia J *et al*. (1987) Paraneoplastic palmar fasciitis-polyarthritis syndrome associated with breast cancer. *J Rheumatol* **14:** 1207–1209
6 Pfinsgraff J *et al*. (1986) Palmar fasciitis and arthritis with malignant neoplasms: a paraneoplastic syndrome. *Semin Arthritis Rheum* **16:** 118–125
7 Mathieu E *et al*. (1991) Palmar fasciitis arthritis syndrome revealing relapse of chronic lymphoid leukaemia [French]. *Presse Med* **20:** 521
8 Roche CJ *et al*. (2003) CT and pathologic assessment of prospective nodal staging in patients with ductal adenocarcinoma of the head of the pancreas. *AJR Am J Roentgenol* **180:** 475–480
9 Seaman JM *et al*. (1985) Fasciitis and polyarthritis during antituberculous therapy. *Arthritis Rheum* **28:** 1179–1184
10 Laszlo KS *et al*. (1995) Idiopathic palmar fasciitis. *Int J Dermatol* **34:** 658–660
11 Sung YK *et al*. (2006) Idiopathic palmar fasciitis with polyarthritis syndrome. *J Korean Med Sci* **21:** 1128–1132