A novel case of polyfibromatosis and interstitial granulomatous dermatitis with arthritis

Daniel Litu Chen, MBBS,[a] Alvin H. Chong, FACD,[a] Jack Green, MBBS,[a] David Orchard, FACD,[d] Richard Williams, FRCPA,[b] and Laurence Clemens, FRACP[c]
Melbourne, Australia

Polyfibromatosis is a rare condition in which several cutaneous fibrotic conditions, such as Dupuytren's contracture, keloid formation, Peyronie's disease and plantar fibromatosis, may coexist. Interstitial granulomatous dermatitis with arthritis is also a rare condition characterized by arthritis and infiltrated rope-like lesions with granulomatous histologic features. We report a case of the simultaneous occurrence of both conditions in the same individual. To our knowledge, this has not been previously described. The clinical course has been slow, progressive, and recalcitrant to treatment. (J Am Acad Dermatol 2006;55:S32-7.)

A 65-year-old male retired cleaner of Italian origin presented with a 20-year history of progressive contractures in multiple joints and multiple polymorphic fibrotic cutaneous cords. The initial presentation in 1985 was of Dupuytren-like contractures, which led to bilateral flexion contractures of the third, fourth and fifth fingers. Over the next 3 years, progressive fibrosis developed over the flexor aspects of the patient's wrists, elbows, knees, and ankles, leading to flexion contractures and limitation of mobility. He also had associated inflammatory pain affecting these joints. The patient was not taking any medication at the time of initial presentation.

In 1987, progressively enlarging linear and annular cords began developing on the patient's chest and back. Findings of the initial biopsy in 1988 were nonspecific, but suggested a scleroderma-like superficial fibromatosis. Over the next 15 years, the cutaneous cords slowly increased in size and number. Physical examination revealed multiple infiltrated cords of different sizes and shapes on the patient's chest and back (Fig 1). A linear fibrotic cord extending vertically on the left side of the patient's back measured approximately 15 cm. There were also several annular indurated and nontender plaques on the upper chest with diameters of 3 to 4 cm. These areas are intermittently pruritic.

Periarticular joint fibrosis was also present in a symmetric distribution. This involved the subcutaneous tissue/fasciae of his palms, soles, popliteal fossae, hips, and antecubital fossae bilaterally. He had marked restriction of movements at both shoulder joints and marked flexion deformities of both hands involving his metacarpophalangeal and proximal interphalangeal joints. Knee extension was limited to 165° with flexion limited to 90° bilaterally.

In the 1990s, some years after the development of the joint fibrosis and cutaneous cords, the patient developed coronary artery disease, hypertension, and hyperlipidemia and was subsequently treated with antihypertensive and lipid-lowering drugs. His current medications are pravastatin, enalapril, aspirin, metoprolol, aledronate, and meloxicam.

This progressive fibrosis of multiple joints has increasingly incapacitated our patient's life, leading to severe limitations of self-care activities, including showering, eating, and dressing. He is currently unable to walk for more than 10 meters at a time, despite years of physiotherapy, and relies on his wife for assistance with most daily activities.

The patient had a positive antinuclear antibody of 1:160. Testing for anti–double-stranded DNA and rheumatoid factor yielded negative findings. The results of complete blood cell count, blood biochemistry, all extractable nuclear antigens, and

STIEFEL® Research in Dermatology Production and distribution supported by an educational grant to the American Academy of Dermatology by Stiefel Laboratories, Inc.

From the Departments of Dermatology,[a] Pathology,[b] and Rheumatology,[c] St Vincent's Hospital; and the Department of Dermatology, Royal Children's Hospital.[d]

Funding sources: None.
Conflicts of interest: None identified.
Previously presented as a poster at the St Vincent's Hospital Melbourne Research Week, August 2005.

Reprint requests: Dr Alvin H. Chong, Department of Dermatology, St Vincent's Hospital Melbourne, 41 Victoria Parade, Fitzroy, Victoria 3065, Australia. E-mail: alvin.chong@svhm.org.au.

0190-9622/$32.00

doi:10.1016/j.jaad.2006.02.038

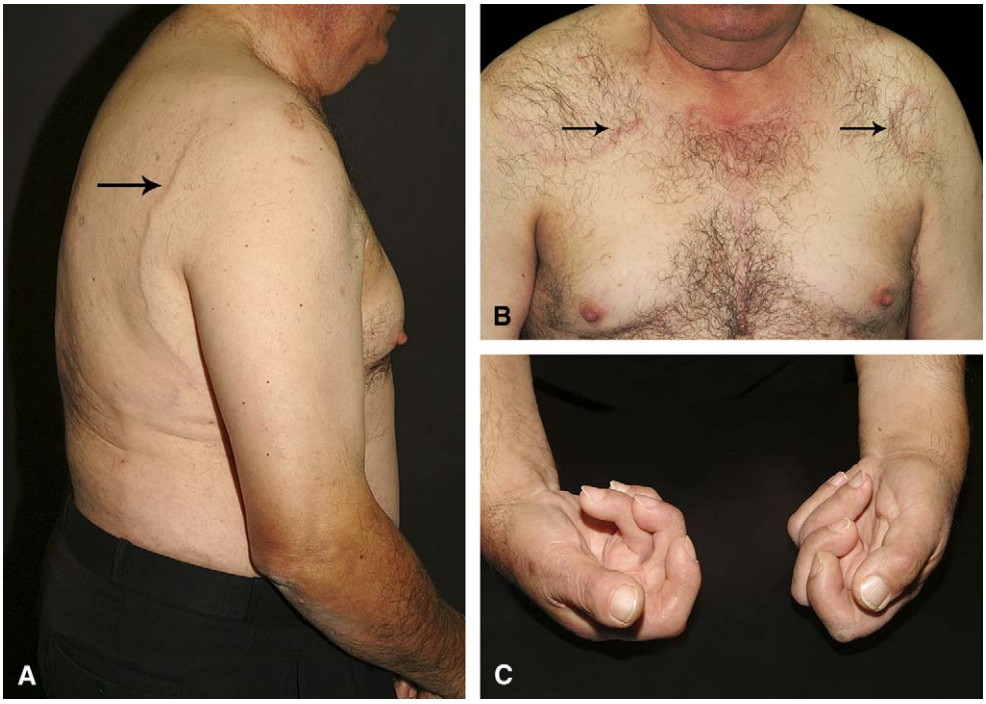

Fig 1. A, Linear, infiltrated cord on back (*arrow*). **B**, Annular lesions on chest (*arrows*). **C**, Severe flexion contractures of both hands.

chest x-ray were within normal limits. X-rays showed widespread erosions and osteoporosis involving hands, feet, wrists, elbows bilaterally and the left shoulder joint.

An incisional biopsy specimen was taken from a fibrotic cord on the patient's back. Hematoxylin-eosin staining revealed thickened dermal collagen, with "busy" cellular dermis more prominent in the reticular dermis (Fig 2, *A*) and characterized by an interstitial infiltrate of histiocytes (Fig 2, *B* and *C*), with some bizarre forms which were occasionally aligned in short palisades along degenerating collagen bundles (Fig 2, *D*).

There was no evidence of a vasculitic process in any of the biopsy material examined. There were no abnormal mitotic figures in the infiltrate. An occasional neutrophil polymorph was present in the interstitium. This was not a prominent feature in the reaction and no eosinophils were present. Microbiologic culture and direct immunofluorescence findings were negative.

Multiple treatments have been attempted in an attempt to control our patient's progressive fibrosis, including oral prednisolone, methotrexate, hydroxychloroquine, and penicillamine, none of which have proved successful. Intralesional triamcinolone acetonide (10 mg/mL) injected into a fibrotic cord was not effective. The patient does not currently receive any treatment for his joints or skin lesions.

DISCUSSION

We describe a novel association of diffuse progressive polyfibromatosis of multiple joints and interstitial granulomatous dermatitis with arthritis. There has been one reported case that demonstrated polyfibromatosis associated with erosive arthropathy. Both the article by Lee, Chan and Black[1] and the one by Fenton, Yates, and Black[2] reported the same patient with bilateral Dupuytren's contractures with keloids and Peyronie's disease. In that patient, results of blood investigations were normal with x-rays showing bilateral erosive arthropathy. The condition was resistant to therapy that included systemic corticosteroids, penicillamine, and *para*-aminobenzoic acid. Our case has some components of polyfibromatosis syndrome, including Dupuytren's contractures and fibrosis of joints, but not keloid formation or Peyronie's disease.

Several cases of skin fibrosis in linear configurations have also been described.[3-5] In two cases, the patients had rheumatoid arthritis with rheumatoid nodules that developed in linear bands.[3] These subcutaneous linear bands were histologically compatible with rheumatoid granuloma. A few patients have also been described with linear granulomatous fibrotic bands without joint involvement.[4,5]

Ackerman et al[6] described the new entity of "interstitial granulomatous dermatitis with arthritis" and used the "rope sign" to describe the prominent,

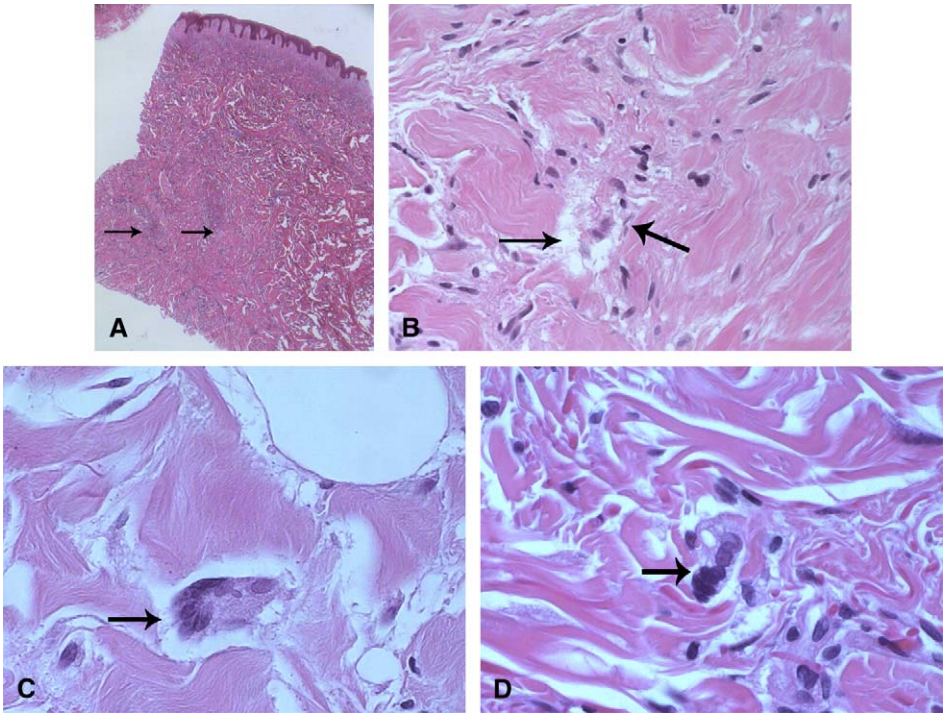

Fig 2. A, Low power. Diffuse histiocytic reaction is present throughout thickened dermal collagen with concentration of the reaction in lower third of the reticular dermis. *Arrows* indicate areas of reaction. **B**, Medium power. Areas of collagen degeneration with sparse histiocytic reaction (*arrows*). **C**, High power. Multinucleate histiocytic giant cell at periphery of some mildly degenerate collagen bundles (*arrow*). **D**, High power. Short palisade of histiocytes (*arrow*) is seen along edge of a degenerating collagen bundle. (**A-D**, Hematoxylin-eosin stain.)

linear cutaneous bands which was pathognomonic for this disorder. There have been several cases of interstitial granulomatous dermatitis with arthritis, although the "rope sign" has not always been present.[7-10] Several cases of interstitial granulomatous dermatitis with arthritis were associated with erythematous plaques[7] or with annular plaques.[8,9] A case of interstitial granulomatous dermatitis with arthritis, in which the patient displayed a linear erythematous band (rope sign) with an ANA of 1:160 has also been described. That patient did not have fibrosis affecting the joints.[10]

Overall, this is a complex group of disorders with overlapping features. The clinical and histologic features of these cases are summarized in Table I.

Histologically, the characteristic central collagen necrobiosis and "discontinuous" pattern of reaction seen classically in granuloma annulare[11] were not present in the biopsy specimens. The reaction was also haphazard throughout the dermis, being most prominent in the lower third of the reticular dermis. The clinicopathologic correlation of the histologic and clinical findings were more in keeping with an interstitial granulomatous dermatitis pattern than of granuloma annulare.

Recently, cutaneous drug eruptions showing a histopathologic pattern of interstitial granulomatous dermatitis have been described.[12] The implicated drug classes included calcium channel blockers, angiotensin-converting enzyme inhibitors, beta-blockers, lipid-lowering agents, antihistamines, anticonvulsants, and antidepressants. Our patient had been taking pravastatin since 1993, enalapril since 1995, and metoprolol after 2004. As the cords and contractures occurred many years before commencement of the aforementioned drugs, the possibility of cutaneous granulomatous drug eruption is very unlikely.

Cutaneous lesions of *Borrelia burgdorferi* may closely resemble the interstitial type of granuloma annulare.[13] However, there have not been any conclusive cases of *B burgdorferi* infection in Australia.[14,15]

To our knowledge, there have been no previous reports of an association between interstitial granulomatous dermatitis with arthritis and polyfibromatosis. This disorder has been progressive, disabling, and recalcitrant to treatment.

Table I. Clinical and histologic features of interstitial granulomatous disease with arthritis, polyfibromatosis, and erosive arthropathy

	Age (y)/ Sex/ Ethnicity	Skin features	Histologic features	Association	Investigation	Progress
Interstitial granulomatous dermatitis with arthritis						
Aloi, Tomasini & Pippione[7]						
Case 1	58/F	Erythematous oval patches in inner aspect of thighs, lateral chest wall	Similar findings of dense diffuse inflammatory infiltrate in entire reticular dermis, mostly of histiocytes with small area of severe collagen degeneration	Symmetric seronegative arthritis	Positive circulating immune complexes, antithyroglobulin antibodies, increased ESR	Skin lesions resolved spontaneously over 1 y
Case 2	65/F	Erythematous plaques with uneven borders in thighs, lateral aspect of upper trunk, flexor surfaces of elbows	Same as above	Symmetric seronegative arthritis	Negative	Skin lesions spontaneously resolved over 6 mo
Altakan et al[8]	53/F	Erythematous annular papules and plaques on dorsum of hands, feet, extending to extensor surfaces of both extremities	Diffuse inflammatory granulomatous infiltrate within papillary and reticular dermis composed of histiocytes, lymphocytes, and multinucleate giant cells	Arthritis in both wrists	Raised ESR and CRP, ANA (1:40)	Skin lesions resolved with topical class II steroid
Long et al[9]						
Case 1	56/F	Annular plaques on anterior and posterior thighs	Diffuse interstitial mononuclear cell infiltrate predominantly in reticular dermis, with focal areas of necrotic collagen bundles. Infiltrate composed of lymphocytes, histiocytes, and eosinophils	Diffuse myalgias, migratory polyarthralgia of fingers, toes, wrists, ankles	Elevated anti-SS-A antibodies; antihistone antibody positive; ANA 1:1280 homogeneous pattern; ESR, 40 mm/h	Persistent skin lesions

Continued

Table I. Cont'd

	Age (y)/ Sex/ Ethnicity	Skin features	Histologic features	Association	Investigation	Progress
Case 2	26/M/W	Annular plaques on posterior aspect of both thighs	Similar to above	Diffuse myalgia, migratory polyarthralgia	ESR, 26 mm/h; otherwise all normal	Lost to follow-up
Case 3	78/M/W	Erythematous papules coalescing into plaques on temples, scalp, and neck	Similar to above	Diffuse myalgia, leukopenia, low fever	RF, 1 in 640; ANA, 1:5120; ESR, 111 mm/h	Skin and arthralgia cleared in 1 mo with oral prednisolone
Verneuil, Dompmartin, & Comoz[10]	73/M	Linear and arched erythematous bands on lateral part of chest	Dense infiltrate of histiocytes in lower reticular dermis, foci of palisading histiocytes surrounded by few degenerated collagen bundles	Polyarthralgia of shoulders, wrists, fingers of both hands	ANA, elevated 1:160 homogeneous pattern; anti-dsDNA (6700), anti-ssDNA (1400)	No effective treatment; exacerbations and partial remissions, disease still active
Polyfibromatosis with erosive arthropathy						
Lee, Chan, & Black[1]; Fenton, Yates, & Black[2]	48/M/ African Caribbean	Keloids on chest and arms	Consistent with early proliferative phase of keloid formation	Symmetric erosive arthropathy of hands, feet, and shoulders; PD; bilateral palmar contractures	Normal	Resistant to therapy
Rope sign with rheumatoid arthritis						
Dykman, Galens, & Good[3]						
Case 1	39/M	Linear skin cords on R flank in posterior axillary line	Lower end of dermis showed areas of collagen degeneration with adjacent inflammatory cells including histiocytes and fibroblasts	RA with rheumatoid nodules	Widespread symmetric cartilage destruction and subchondral bone formation	Not applicable
Case 2	41/M	Nontender linear skin cord in L anterior axillary fold	No biopsy	RA with rheumatoid nodules	No investigation	Resolved over 6 wk spontaneously

ANA, Antinuclear antibodies; *CRP*, C-reactive protein; *dsDNA*, double-stranded DNA; *ESR*, erythrocyte sedimentation rate; *F*, female; *L*, left; *M*, male; *PD*, Peyronie's disease; *R*, right; *RA*, rheumatoid arthritis; *RF*, rheumatoid factor; *ssDNA*, single-stranded DNA; *W*, white.

We thank Rebecca Davies and Kathy Teagno, medical photographers, and the Skin and Cancer Foundation, Victoria, for their assistance in producing the images.

REFERENCES

1. Lee YC, Chan HH, Black MM. Aggressive polyfibromatosis: a 10-year follow-up. Australas J Dermatol 1996;37:205-8.
2. Fenton DA, Yates DAH, Black MM. Aggressive polyfibromatosis. J R Soc Med 1986;79:482-3.
3. Dykman CJ, Galens GJ, Good AE. Linear subcutaneous bands in rheumatoid arthritis. An unusual form of rheumatoid granuloma. Ann Intern Med 1965;63:134-40.
4. Harpster EF, Mauro T, Barr R. Linear granuloma annulare. J Am Acad Dermatol 1998;21:1138-41.
5. McDow RA, Fields JP. Linear granuloma annulare of the finger. Cutis 1987;39:43-4.
6. Ackerman AB, White WL, Guo Y, Umbert I. Granuloma annulare, interstitial types; interstitial granulomatous dermatitis with arthritis. In: Ackerman BA, Troy JL, Rosen LB, Jerasutus S, White CR, King DF, editors. Differential diagnosis in dermatopathology IV. Philadelphia: Lea & Febiger; 1994. pp. 34-7.
7. Aloi F, Tomasini C, Pippione M. Interstitial granulomatous dermatitis with plaques. Am J Dermatopathol 1999;21:320-3.
8. Altakan A, Erkin G, Boztepe G, Gokoz A. Interstitial granulomatous dermatitis with arthritis. Hum Pathol 2004;35:779-80.
9. Long D, Thiboutot DM, Majeski JT, Vasily DB, Helm KF. Interstitial granulomatous dermatitis with arthritis. J Am Acad Dermatol 1996;34:957-61.
10. Verneuil L, Dompmartin A, Comoz F. Interstitial granulomatous dermatitis with cutaneous cord and arthritis: a disorder associated with autoantibodies. J Am Acad Dermatol 2001;45: 286-91.
11. Weedon D. Skin pathology. The granulomatous reaction pattern. 2nd ed. Edinburgh: Churchill Livingstone; 2002.
12. Magro CM, Crowson AN, Schapiro BL. The interstitial granulomatous drug reaction: a distinctive clinical and pathological entity. J Cutan Pathol 1998;25:72-8.
13. Moreno C, Kutzner H, Palmedo G, Goerttler E, Carrasco L, Requena L. Interstitial granulomatous dermatitis with histiocytic pseudorosettes: a new histopathologic pattern in cutaneous borreliosis. Detection of Borrelia burgdorferi DNA sequences by a highly sensitive PCR-ELISA. J Am Acad Dermatol 2003;48:376-84.
14. Russell RC, Doggett SL, Munro R, Ellis J, Avery D, Hunt C, et al. Lyme disease: a search for a causative agent in ticks in south-eastern Australia. Epidemiol Infect 1994;112: 375-84.
15. Piesman J, Stone BF. Vector competence of the Australian paralysis tick, Ixodes holocyclus, for the Lyme disease spirochete Borrelia burgdorferi. Int J Parasitol 1991;21: 109-11.