CASE ESSAY 4

35-Year-Old Woman with Arthritis And Papular Skin Lesions

Robert Gniadecki[1], Poul Halberg[1], Susanne Ullman[1], Takasi Kobayasi[1] and Henrik Skjødt[2]

[1]Department of Dermatology D, Bispebjerg Hospital, DK-2400 Copenhagen and [2]Department of Rheumatology, Hvidovre Hospital, University of Copenhagen, Denmark. E-mail: rg01@bbh.hosp.dk

A 35-year-old woman was referred from a dermatologist in private practice because of papular and nodular skin lesions on the fingers. One year before the onset of skin lesions the patient developed polyarthritis of the wrists and the distal interphalangeal joints of the first, second and third fingers of both hands. She was treated with salazopyrine and prednisone without improvement of the condition. Three months before referral she developed several 5–6 mm indolent, dark-red papules and nodules on the fingers (Fig. 1). Laboratory findings showed slightly elevated lactate dehydrogenase (LDH), the haematology and other biochemistry parameters were normal.

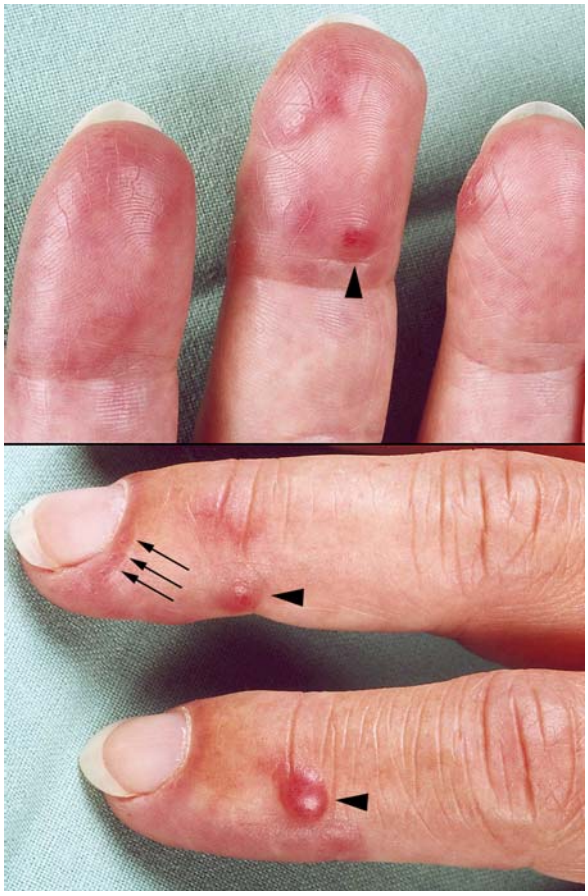

Fig. 1. Skin lesions comprising reddish papules arranged side-by side in the "coral beads" pattern in the periungual region (arrows) and as single lesions on the fingers (arrowheads). The coral bead pattern has been reported to be characteristic for multicentric reticulohistiocytosis.

We are presented with a young, previously healthy woman, who over a year developed arthritis and papular skin changes. Unless proven otherwise, we would assume that her skin and joint symptoms represent one single disease entity. The combination of skin symptoms and arthritis may be seen in several diseases (by some authors called DERMOARTHRITIDES) which are listed in Table I. Considering the patient's age, RHEMATOID ARTHRITIS should certainly top the list of differential diagnoses. The papules might represent rheumatoid nodules. PSORIATIC ARTHRITIS is another frequent cause of the distal, small joint arthritis, but is unlikely in this case due to the lack of typical psoriatic skin lesions or nail changes. Another possibility might be DERMATMYOSITIS, the papules representing Gottron's papules. Arthralgia and even joint swelling are sometimes seen in dermatomyositis. The patient even had periungual erythema which is known as Keining's sign in this disease. We need X-ray examination

of the joints and supplementary blood tests including creatine kinase, IgM rheumatoid factor, antinuclear antibodies (ANA), ANCA, and Jo-1 antibody.

The X-ray examination showed erosive changes in interdigital joints of both hands. She was negative for rheumatoid factor and antinuclear antibodies, and the creatine kinase was normal. The patient reported myalgias in the proximal limb muscles, but no muscle weakness. She denied photosensitivity or the presence of other types of skin rash.

The results are inconclusive, and we are unable to rule out any of the above–mentioned diagnoses. Dermatomyositis is, however, unlikely due to the lack of muscle involvement and absence of circulating autoantibodies. Gottron's papules are rarely situated on the digital pulps, rather on the cuticle and over the knuckles and the interphalangeal joints. Other characteristic features of dermatomyositis are also absent; photosensitivity, heliotrope eyelids, and muscle weakness. Erosive arthritis is not typical of dermatomyositis. We will, however, not abandon this diagnosis completely since up to 10% of the patients with dermatomyositis run an atypic course without muscle symptoms (amyotropic dermatomyositis).

Only 85% of the patients with rheumatoid arthritis are positive for rheumatoid factor so this diagnosis is still a distinct possibility. Rheumatoid nodules, however, tend to be larger than 5–6 mm and they are usually situated at pressure points like elbows or dorsal aspects of the interphalangeal joints. At this point we need a biopsy from a skin lesion.

A 3-mm punch biopsy was taken from a papule on the left finger. The histopathological examination showed slightly hyperkeratotic epidermis and diffuse infiltration of mononuclear and multinuclear histiocytic cells. No granulomas were found. The basement membrane was normal.

The histological findings are quite unusual and incompatible with either rheumatoid nodules or Gottron's papules of dermatomyositis. In the first case we would rather expect fibrosing dermal changes with fibrinoid necrosis surrounded by palisading fibroblasts and histiocytes. Gottron's papules have also a suggestive histology with mucin deposits, dermal fibrosis, and basement membrane thickening. The clue of the diagnosis is the presence of multinucleated cells which resemble histiocytoses. An immunohistochemistry examination should be performed to differentiate between Langerhans' cell and non-Langerhans' cell histiocytosis.

The cells stained with CD45 and CD68 antibodies, but were negative for anti-S100 antibody.

This profile is highly suggestive of a non-Langerhans' cell histiocytosis, a group of partially overlapping disease entities characterized by histiocyte infiltration of the skin and other organs. Several non-Langerhans' histiocytoses are characterized by multiorgan involvement including the bone where osteolytic lesions may be found. However, erosive arthritis is found only in MULTICENTRIC RETICULOHISTIOSYTOSIS **and in** FAMILIAL HISTIOCYTIC DERMATOARTHRITIS**. The two entities have overlapping clinical and histopathological features; however, familial histiocytic dermatoarthritis has an autosomal recessive trait, the disease usually starts in childhood or early adolescence, and it is characterized by eye involvement. Multicentric reticulohistiocytosis is predominantly seen in young and middle-aged Caucasian women and although rare in absolute terms, it is more common than familial histiocytic dermatoarthritis. For this reason we favour this diagnosis for our patient.**

The patient was treated with 25 mg methotrexate weekly. After 18 months the skin lesions disappeared and joint pain improved considerable. No further radiological progression of the erosive changes was seen by follow-up.

Table I. Differential diagnosis of dermatoarthritides and other conditions presenting with papular or nodular skin lesions and arthritis.

Disease	Papular skin lesions	Joint symptoms	Other symptoms and findings
Inflammatory diseases			
Rheumatoid arthritis	Rheumatoid nodules, interstitial granulomatous dermatitis, rheumatoid neutrophilic dermatitis, vasculitis, nail bed infarcts	Erosive arthritis	Rheumatoid factor (75%), positive ANA (25%), positive p-ANCA (25%), elevated platelet counts
Sarcoidosis	Red-brown nodules	40% patients present with arthritis that may be erosive or non erosive, mainly involving knees, ankles, sometimes hands and feet.	Multiorgan involvement
Dermatomyositis	Gottron's papules heliotrope rash, periungual cuticle erythema	Arthralgias, very rarely non-erosive arthritis	Proximal muscle weakness, myocarditis, dysphagia, increased creatin kinase, positive ANA (50%), positive Jo-1 (30%)
Scleroderma	Papular and nodular calcinosis	Non-erosive arthritis may be seen in some patients	Characteristic fibrotic skin changes, Raynaud' s phenomenon, systemic symptoms, positive ANA
Methotrexate noduli	Flesh coloured to dark brown dermal noduli resembling rheumatoid nodules	Rheumatoid arthritis or juvenile rheumatoid arthritis	Develop sometimes in patients treated with methotrexate for rheumatoid arthritis. Disappear after discontinuation of methotrexate
Degenerative changes			
Heberden's and Bouchard's nodes	Subcutaneous noduli composed of bone covered by cartilage. Localised at the proximal (Bouchard' s nodes) or distal (Heberden' s nodes) interphalangeal joints	Osteoarthritis	X-ray and ultrasound examination of the lesions reveals their bony character and contact with the joint.
Histocytoses			
Multicentric reticulohistiocytosis	Dark red papules and nodules on hands, face and ears	Erosive arthritis	Starts at the age 30-50. Predominantly Caucasian women. Possible multiorgan involvement. Risk of cancer
Familial histiocytic dermatoarthritis	Similar to multicentric reticulohistiocytosis	Similar to multicentric reticulohistiocytosis	Debut in childhood and adolescence. Ocular changes
Metabolic diseases			
Systemic amyloidosis	Hemorrhages, brusing, waxy papules predominantly on the face	Usually non-erosive arthritis of large joints.	Multiorgan involvement
Gout	Tophi: uric acid nodules mainly in digital joints, elbows and ears	Arthritis urica, starts usually as acute monoarthritis	Acute renal colic
Lipoid proteinosis (deposits of hyalin in the skin and mucosa)	Waxy papules on the face and dorsal hands	Arthralgias in a small proportion of patients	Starts in childhood. Hoarseness due to infiltrations of vocal cords
Juvenile hyaline fibromatosis (Murray-Puretic-Drescher syndrome)	Large subcutaneous nodules with tendency to ulceration, localized on the hands, elbows, knees and sometimes face	Osteolytic periarticular bone lesions, joint pain. Contractures	Starts in late childhood. Gingival hyperplasia, scoliosis, osteoporosis
Farber's disease (defect in acid ceramidase resulting in ceramide deposition)	Brown subcutaneous nodules localized near joints on the fingers, elbows, ears and knees	Erosive arthritis	Starts in childhood. High mortality. Hoarseness due to laryngeal infiltration
Infectious diseases			
Lepromatous leprosy	Nodular, skin-coloured lepromas on the face, ears and hands	Joint degeneration due to sensory neuropathy. Occasionally osteolytic periarticular changes	Sensory neuropathy

Diagnosis:

MULTICENTRIC RETICULOHISTIOCYTOSIS

Comment

The first description of multicentric reticulohistiocytosis was published in 1937 by Weber & Freudenthal (1) but the name was introduced by Goltz & Lymon in 1954 (2). Approximately 300 cases have been described in the world literature. A recent review summarized the clinical and the histopathological features of the condition (3). The disease has an insidious onset; the joint symptoms occur first in 40% of patients. The remaining cases first develop skin manifestations or the skin and joint symptoms simultaneously. The characteristic features are non-ulcerating cutaneous papules or nodules located predominantly in the face, on the ears and on the hands. Erosive, seronegative arthritis is present in virtually all patients with full-blown disease. The disease may be associated with other symptoms including dysphagia and dysartria due to mucosal nodules, myalgias, muscle weakness and heart symptoms. Approximately 20% of patients develop malignancy including lymphomas and various solid tumours. The diagnosis may be straightforward for the physicians familiar with this entity, but multicentric reticulohistiocytosis may mimick other more common entities, including psoriatic arthritis (which is a common cause of distal interphalangeal arthritis), dermatomyositis, rheumatoid arthritis, sarcoidosis, leprosy, neurofibromatosis and granuloma annulare. Other differential diagnoses are presented in Table I. Treatment is often unhelpful, but some patients respond to methotrexate (including our patient) or cyclophosphamide.

Further reading

1. Weber FP, Freudenthal W. Nodular non-diabetic cutaneous xanthomatosis with hypercholesterolemia and atypical histological features. Proc R Soc Med 1937; 30: 522–526.
2. Goltz RW, Laymon CW. Multicentric reticulohistiocytosis of the skin and synovia. Arch Dermatol 1954; 69: 717–731.
3. Luz FB, Gaspar AP, Kalil-Gaspar N, Ramos-e-Silva M. Multicentric reticulohistiocytosis. J Eur Acad Derm Ven 2001; 15: 524–531.