LESSON OF THE MONTH

Subcutaneous nodules in a patient with polyarthritis

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Case report

A 56 year old white male presented in May 1993 with a 12 month history of pain and stiffness affecting proximal interphalangeal and metacarpophalangeal joints of both hands, wrists and knees, and all metatarsophalangeal joints. This was associated with difficulties in performing activities of daily living.

Examination showed a well looking man who had synovitis of his knees. He had multiple soft tissue nodules at both elbows. The rest of the examination, including urine microscopy, was normal.

His rheumatoid factor was positive (titre not measured), though radiography of his hands, feet, and knees did not show any erosions. A diagnosis of seropositive rheumatoid arthritis was made, though his symptoms were out of proportion with his signs. He was treated with a non-steroidal anti-inflammatory drug, sulphasalazine 3 g per day, and prednisolone 5 mg per day.

In January 1994, he presented again, with a one month history of painful fingertips associated with lethargy and night sweats. There were no joint symptoms. He also reported three months of mild nasal stuffiness.

Examination showed areas of pulp infarction affecting the left index and the right middle fingers. His hands and feet were cold, and peripheral pulses were intact. There was no active synovitis. Nodules at both elbows were still present. Ear, nose, and throat examination

showed nasal crusting and areas of perforation along the nasal septum.

Mid stream urine analysis showed 150 000 glomerular red blood cells/ml (normal value (NV) <13 000/ml). There was proteinuria of 1.45 g/day (NV <0.15 g/day). Full blood count showed haemoglobin 131 g/l (NV 130-180 g/l), total leucocyte count $11.1 \times 10^9/l$ (NV $4-11 \times 10^9/l$), neutrophil count $8.32 \times 10^9/l$ (NV $2.5-7.5 \times 10^9/l$), platelet count $400 \times 10^9/l$ (NV $150-400 \times 10^9/l$). The erythrocyte sedimentation rate was 37 mm/1st h (NV 0-15 mm/1st h). Urea, creatinine, electrolytes, liver function tests, complement, immunoglobulin and cryoglobulin values were normal. Antinuclear antibody titre was weakly positive, with a speckled pattern; extractable nuclear antigens were negative. Rheumatoid factor was now negative. Antineutrophil cytoplasmic antibody titre was increased to 1:160, with cytoplasmic staining (cANCA). Hepatitis B and C serology was negative.

Kidney biopsy specimens showed focal segmental necrotising glomerulonephritis (figure). Nasal mucosa biopsy specimens showed areas of necrosis including erosion of cartilage and extensive fibroblastic repair with residual chronic inflammatory cells including many plasma cells. Biopsy of one elbow nodule showed granulomas with a necrotic centre surrounded by palisading histiocytes with some degree of fibroblastic fibroplasia externally, and some chronic inflammatory cell infiltrate.

The patient was treated with oral cyclophosphamide 100 mg/day, prednisolone 60 mg/day, persantin, nifedipine, and captopril. At four month follow up, his fingers had completely healed, his haematuria had resolved, and his 24 hour urinary protein had been reduced to 0.55 g/day. He was slightly cushingoid and was mildly hypertensive (160/90 mm Hg), but there were no other major iatrogenic complications. He remained well at 12 month follow up.

Discussion

We have reported a case of Wegener's granulomatosis (WG) with an unusual presentation. The finding of polyarthritis, subcutaneous nodules and positive rheumatoid factor led initially to the mistaken diagnosis of seropositive nodular rheumatoid arthritis (RA). However, there are other causes of subcutaneous nodules in a patient with

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A necrotising segmental lesion in one of two glomeruli. Silver methenamine-masson trichrome. Horizontal bar represents 200 μ m.

Causes of subcutaneous nodules and arthritis⁷

Connective tissue disease	Rheumatoid arthritis Spondyloarthropathies Systemic lupus erythematosus Scleroderma
Vasculitis	Polyarteritis nodosa Wegener's granulomatosis Behçet's disease Churg-Strauss angiitis
Metabolic	Tophaceous gout Amyloidosis
Infectious	Hepatitis B Subacute bacterial endocarditis
Miscellaneous	Erythema nodosum

arthritis (table). With the second presentation, the ischaemic lesions affecting the fingers were considered likely to be the result of a rheumatoid vasculitis, although renal involvement in RA is uncommon.¹ The diagnosis of Wegener's granulomatosis was eventually made on the evidence of the development of nasal symptoms, segmental necrotising glomerulonephritis on renal biopsy, and high cANCA titre. This provided three of four criteria for the classification of WG according to the American College of Rheumatology 1990 criteria (traditional format).²

In a large cohort study of 158 patients with WG over 24 years, 33% of patients had significant arthralgias or arthritis as the presenting complaint.³ In other studies, 44% of 85 patients⁴ and 55% of 50 patients⁵ presented with joint symptoms. Polyarthralgias are common, and polyarthritis may also be seen. Less frequently, monoarticular, pauciarticular, or a migratory polyarthritis occur. Previous experience has taught that such a presentation, particularly in association with positive rheumatoid factor present in 25% of patients with WG,⁴ may lead to a misdiagnosis of RA.

Rheumatoid nodules are classically associated with seropositive RA, with patients more likely to have severe disease, fewer remissions, and other extra-articular manifestations.⁶ Subcutaneous nodules histologically identical to the classic rheumatoid nodule of seropositive patients have also been reported rarely in patients with seronegative RA, spondyloarthropathies, and systemic lupus erythematosus, and in otherwise asymptomatic adults and children.⁷ Granuloma annulare and necrobiosis lipoidica diabetorum are con-

ditions in which nodules identical to those found in RA may occur in association with skin rash.

Cutaneous lesions occur in 40–50% of patients with Wegener's granulomatosis,⁸ though subcutaneous nodules are uncommon: of 118 patients with WG reviewed, none had subcutaneous nodules.⁹ Amongst 73 patients with cutaneous lesions from 158 studied,³ some had subcutaneous nodules, but the exact number was not given. Histologically, these may show granulomas with well defined palisading cells indistinguishable from the classic rheumatoid nodule, as was seen in our patient.

Whilst rheumatic complaints may often be the presenting symptoms in WG, subcutaneous nodules are seen infrequently. They can be histologically indistinguishable from the classic rheumatoid nodule and, when associated with joint symptoms, may lead to a misdiagnosis of rheumatoid arthritis.

The lesson

- Not all subcutaneous nodules are rheumatoid nodules.
- Not all 'rheumatoid' nodules are associated with rheumatoid arthritis.
- Renal involvement (not in association with drug therapy) should lead to consideration of diagnoses other than RA.

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