

A case of chronic non-erosive sero-negative polyarthritis associated with pyoderma gangrenosum

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Abstract

We report a patient presenting with a seronegative polyarthritis who later developed pyoderma gangrenosum. The presumptive diagnosis was seronegative rheumatoid arthritis and associated pyoderma gangrenosum. However, the arthritis, although steroid responsive, did not respond to treatment with the usual DMARD therapies and appears to mirror the activity of the pyoderma gangrenosum. The normal X-rays, the negative rheumatoid factor and the normal colonoscopy are also consistent with a diagnosis of primary pyoderma gangrenosum with associated arthritis.

Keywords

Pyoderma gangrenosum; seronegative arthritis.

Case report

A 43-year-old woman presented in March 2000 with a 2 year history of pain and swelling of the left wrist and of the small joints of the hands and feet. This was associated with early morning stiffness lasting for 1 h. There was no history of bowel disease, skin rash or eye symptoms. Her mother had rheumatoid arthritis. She was a smoker with a 30-pack year history. Examination revealed tenderness and swelling of the proximal interphalangeal (PIP) joints predominantly, with some metacarpophalangeal (MCP) joints also affected. Investigations at that stage revealed normal X-rays of the hands, feet and chest. Thyroid function, immunoglobulins and protein electrophoresis were normal as were inflammatory markers with erythrocyte sedimentation rate (ESR) 11 mm/h and C-reactive protein (CRP) <10 mg/l. The full blood count was normal. Rheumatoid factor, antinuclear antibody (ANA) and anti-extractable nuclear antigens (ENAs) were negative. Anti-neutrophil cytoplasmic antibody (ANCA) was positive at 1:320 but negative for myeloperoxidase and proteinase 3.

She was treated initially with anti-inflammatories but her symptoms did not improve. An isotope bone scan in July showed increased uptake in the wrists, MCP and PIP joints and all the fingers of the right hand thought to be consistent with an inflammatory polyarthritis. She was started on methotrexate in August.

Prior to starting the methotrexate, however, she developed an abscess-like lesion on her back and then a nodule on the left calf which developed into an ulcerated lesion measuring 8 × 9 cm. The methotrexate was stopped after only three doses. A biopsy of the skin lesions confirmed the

Table 1: The neutrophilic dermatoses (modified from Moscella^[1])

Sweet's syndrome
Pyoderma gangrenosum
Generalised pustular psoriasis
Reiter's syndrome
Palmoplantar pustulosis
Subcorneal pustular dermatosis
Bowel-associated dermatosis-arthritis syndrome
Behcet's disease
Rheumatoid neutrophilic dermatoses associated with rheumatoid arthritis
Neutrophilic eccrine hidradenitis

diagnosis as pyoderma gangrenosum. At this time she also developed abnormal liver function with elevated aspartate aminotransferase (AST) 528 IU/l (normal range (NR) 7–40), alkaline phosphatase 720 IU/l (NR 70–320) and γ -glutamyl transpeptidase (GGT) 133 IU/l (NR 7–32) and an inflammatory response with an ESR of 27 mm/h. Liver autoantibodies and hepatitis serology were negative. A liver ultrasound scan was normal. The liver function gradually normalised. She later underwent liver biopsy, which revealed no evidence of hepatitis but a slight increase in inflammatory cells in the portal tract, of questionable significance. As this was performed 4 months after the methotrexate dosing, it was not possible to determine whether this had been a methotrexate-induced reaction. In view of the diagnosis of pyoderma gangrenosum she was also investigated for inflammatory bowel disease. Colonoscopy and biopsies of the colon and terminal ileum were normal.

She was started on prednisolone 60 mg daily and cyclosporin 50 mg tds for the pyoderma gangrenosum in September 2000. By November the skin lesions had healed well and she was on a reducing dose of prednisolone 5 mg. In January 2001 the arthritis was active and sulphasalazine was started. Her arthritis did not respond and intramuscular myocrisin was commenced in May 2001.

In July she presented again with a mouth ulcer and three lesions of pyoderma gangrenosum on the buttocks, leg and back. Oral steroids were recommenced along with minocycline resulting in rapid healing of the skin lesions and no evidence of active arthritis. She remained well and asymptomatic on a reducing dose of corticosteroids, but 2 weeks after stopping the prednisolone, her arthritis flared again. At this stage myocrisin was withdrawn and leflunomide was commenced but she has remained responsive thus far to steroids alone.

Repeat X-rays of the hands and feet have shown no evidence of arthritis. In particular, there is no periarticular osteopenia, no joint space narrowing and no erosive change. Her rheumatoid factor and ANA remained negative.

Discussion

This case describes a patient presenting with a seronegative polyarthritis who later developed pyoderma gangrenosum. The presumptive diagnosis was seronegative rheumatoid arthritis and associated pyoderma gangrenosum. However, the arthritis, although steroid responsive, does not respond to treatment with the usual disease modifying anti-rheumatic drug (DMARD) therapies and appears to mirror the activity of the pyoderma gangrenosum. The normal X-rays, the negative rheumatoid factor (RF) and the normal colonoscopy are also consistent with a diagnosis of primary pyoderma gangrenosum with associated arthritis.

Pyoderma gangrenosum is classified as one of the neutrophilic dermatoses. These are skin disorders characterised, on histological examination, by an intense dermal infiltration of neutrophils with no evidence of a primary vasculitis or infection^[1]. A spectrum of skin lesions occurs in the neutrophilic dermatoses, ranging from nodules in Sweet's syndrome to ulceration in pyoderma gangrenosum. Although there are distinct disease entities described (Table 1), it is more appropriate to consider the disorders as a continuum as they share similarities in clinical features, disease associations, systemic manifestations and responses to treatment. The pathogenesis of the neutrophilic dermatoses is unknown but it is thought that there is a defect in the immune response. Accordingly they respond to steroids and immunosuppressive therapy.

Sweet's syndrome is the classical neutrophilic dermatosis, first described in 1964 by Sweet in eight female patients who presented with fever, peripheral neutrophilia and erythematous skin

lesions infiltrated with neutrophils. It is an uncommon disease predominantly affecting females (F/M 4:1). Up to 25% of patients with Sweet's syndrome have an associated malignancy, most often haematological, but adenocarcinoma of the breast, gastrointestinal or renal tracts are also associated^[2]. Apart from fever, systemic manifestations may occur in the eyes, lungs, liver, kidneys and nervous system and up to one-third of patients have arthritis. This is usually an asymmetrical, non-erosive arthritis most often affecting the knees and wrists and activity mirrors the course of the skin disease^[3]. Laboratory investigations reveal raised inflammatory markers, peripheral neutrophilia and mildly elevated serum alkaline phosphatase, aspartate aminotransferase and γ -glutamyl transferase. ANCA may be positive but with weak and diffuse fluorescence pattern.

Pyoderma gangrenosum is an ulcerating skin condition most commonly occurring on the legs. The lesion starts as a tender erythematous papule and then ulcerates and spreads to form a purulent necrotic lesion that may resemble an abscess. Histological examination reveals a sterile abscess with necrosis, haemorrhage, capillary thrombosis and a dense neutrophilic infiltrate. Scarring is usual.

Around half the cases of pyoderma gangrenosum are associated with a systemic disease, most commonly inflammatory bowel disease but also arthritis, especially rheumatoid and ankylosing spondylitis, and lymphoproliferative disorders such as non-Hodgkins lymphoma. As with Sweet's syndrome, arthritis may be associated with the skin manifestations. This may be classical seropositive rheumatoid, but is more commonly seronegative and may be erosive or non-erosive^[4]. In a review of 86 patients with pyoderma gangrenosum, 32 had arthritis^[5]. In most patients this was seronegative, asymmetrical, large joint, non-erosive, relapsing remitting arthritis. Four patients had pyoderma associated with classical rheumatoid arthritis.

Lesions of pyoderma gangrenosum may also occur in patients with Sweet's syndrome and Behcet's disease. Treatment of the underlying disease usually results in healing of the skin lesions. Otherwise, systemic treatments include corticosteroids and steroid-sparing agents such as azathioprine, cyclophosphamide, cyclosporin and tacrolimus. Minocycline may also be effective^[1].

Teaching point

The neutrophilic dermatoses comprise a group of clinically distinct skin disorders, which share many characteristics of disease associations, systemic manifestations and treatment approaches. The diagnosis should be considered in a patient presenting with arthritis and a rash. Patients with a neutrophilic dermatosis should be thoroughly investigated for underlying disease conditions, especially inflammatory bowel disease and malignancy. Arthritis is common in these conditions and is usually asymmetrical, seronegative and non-erosive, mimicking the activity of the disease. Treatment should be directed at any underlying disease primarily; otherwise corticosteroids and immunosuppressive therapy may be commenced.

References

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