LESSON OF THE MONTH

Systemic vasculitis following an unreported rat bite

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CASE REPORT

A 56 year old man presented with a 10 day history of fevers, cough, sore throat, and loose stools. Two days after onset he developed an acute polyarthritis affecting the right wrist, left thumb, both feet, and the right ankle. This was followed by a rash over elbows, fingers, and feet. He had no rheumatological history, drank little alcohol and apart from antihypertensive treatment with atenolol and nifedipine, was fit and well.

On admission he was apyrexial with normal cardiorespiratory and abdominal examination. A maculopapular, non-blanching rash with pustules and necrosis was evident over the extensor surfaces of both elbows and left calf. In the web space of the index and middle finger of the right hand was a small crusted, healing lesion. Acute, erythematous synovitis affected his right elbow, wrist, and shoulder, left thumb metacarpophalangeal (MCP) joint, both mid-tarsal joints, and right ankle.

Laboratory investigations showed his haemoglobin was 112 g/l, white cell count 12.6×10^9/l, neutrophils 11.4×10^9/l, urea 17.7 mmol/l, and creatinine 169 µmol/l. The erythrocyte sedimentation rate was 79 mm/1st h and C reactive protein 225 mg/l. Chest radiograph, urine dipstick, blood cultures, abdominal ultrasound, and echocardiogram were normal. In view of his systemic symptoms, polyarthritis and rash, a provisional diagnosis of reactive arthritis or vasculitis was made. A test for autoantibodies, including antineutrophil cytoplasmic antibodies, was requested and subsequently proved negative.

With rehydration and analgesia the patient felt better and his renal function returned to normal. Eighteen hours after admission his right hand rapidly developed critical ischaemia from the mid-palm distally. Pulses were present and arterial Doppler results normal. Atenolol was stopped and intravenous methylprednisolone and cyclophosphamide were given for presumed medium vessel vasculitis. The ischaemia resolved. After 24 hours, the hand again became painfully ischaemic and further intravenous methylprednisolone was given, again with improvement.

Over the next few days the patient continued to feel better, but with only minimal objective improvement in the rash and arthritis. He developed intermittent pyrexia.

On day 7 his joint symptoms worsened acutely, with his left ankle and thumb particularly affected. A left ankle aspirate yielded urate crystals. Serum urate was 371 µmol/l (normal 180–420). A diagnosis of gout was made and colchicine started. Joint inflammation promptly responded except in the left thumb MCP joint (fig 1). This became increasingly erythematous with threatened skin necrosis and was also aspirated. Initial microscopy suggested an "odd" Gram positive coccus had been isolated. Intravenous benzylpenicillin and flucloxacillin were started. After four days, culture revealed a Gram negative pleomorphic coccobacillus *Streptobacillus moniliformis* (confirmed by DNA sequencing). This organism causes rat bite fever (RBF). Further questioning disclosed that the patient had been bitten three weeks previously by a friend's rat causing the scab in the web space of his right hand noted on admission.

The final diagnosis was rat bite fever complicated by polyarticular gout. After six weeks treatment with oral doxycycline, physiotherapy, and occupational therapy, gradual recovery occurred, with persistent damage to the right wrist and left hand extensor tendons.

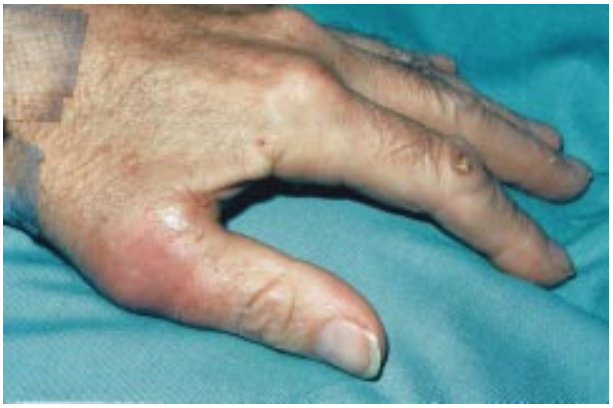

Figure 1 Left hand of the patient showing acute synovitis of the metacarpophalangeal joint of the thumb. Aspiration of this joint grew *Streptobacillus moniliformis*. A further vasculitic lesion is present over the proximal interphalangeal joint of the index finger.

DISCUSSION

Classically, RBF describes single cases of systemic illness associated with *Streptobacillus moniliformis* infection from rat or rodent bite. This bacterium (carried in the nasopharynx of 50% of healthy rats[1]) is non-encapsulated, non-motile, non-acid fast, and on solid media exhibits characteristic pleomorphism.[2 3] In RBF, the bite heals and, as other symptoms develop, becomes reinflamed. There is abrupt onset of fever remitting in 2–5 days and recurring three days later with the onset of other symptoms.[1] Commonly these are centrifugal rash with erythematous macules, petechial haemorrhages,[2] and discharging pustules with an asymmetrical arthralgia/arthritis and sore throat.[1] Less commonly, there is desquamation,[1] abscesses, endocarditis, pericardial effusion, and suppurative arthritis.[3]

Our patient developed polyarticular gout during this illness. Although his serum urate remained normal, the numerous uric acid crystals in synovial fluid and prompt response to colchicine led us to this diagnosis. This has been previously reported in RBF[4] and in rare association with other septic arthritides,[5] although the mechanism remains unclear.

Blood cultures provide definitive diagnosis and guide treatment (commonly penicillin and tetracycline[2]) but are technically difficult. Additives in culture broth may inhibit the growth of *Streptobacillus moniliformis*.[3] Serology is possible, but not readily available.

Streptobacillus moniliformis organisms may be cultured from synovial fluid, but are easily mistaken for proteinaceous debris on microscopy.[3] Skin biopsy has shown leucocytoclastic vasculitis. Synovial biopsy is also of limited diagnostic use, showing typical non-specific changes of acute and chronic inflammation associated with septic arthritis.[2]

RBF is a rare cause of systemic vasculitis which is not notifiable and therefore underrecognised. The mechanisms underlying infection related vasculitis are complex, with bacterial antigens causing a series of endothelial and immunological reactions with vessel walls.[6]

THE LESSONS

- RBF is a rare but important cause of systemic vasculitis.
- Detailed inquiry about rat exposure and unexplained skin lesions may provide essential diagnostic clues.
- Specific antimicrobial treatment is available for RBF, but identifying the organism requires diligence. Liaison with local microbiology services is essential.

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