Salmonella osteomyelitis in aplastic anaemia after antilymphocytic globulin and steroid treatment

S Allard, J O'Driscoll, A Laurie

Abstract
A 22 year old patient with severe aplastic anaemia responded to antilymphocytic globulin but developed recurrent fever despite treatment with steroids and then antibacterial, antifungal, and antituberculous drugs. There was progression, with severe joint pains and immobility associated with radiological evidence of a symmetrical destructive process. A bone marrow specimen showed no evidence of malignancy, and cultures of blood, urine, and stool were negative but enriched broth cultures of an open biopsy specimen of the humeral head grew Salmonella enteritidis phage type 4. Treatment with ciprofloxacin resulted in considerable symptomatic improvement: a total of 12 months of treatment is planned. Salmonella osteomyelitis, particularly with this unusual pattern of disease, has not previously been described in aplastic anaemia.

Case report
Bone and joint infections due to Salmonella are uncommon, although various predisposing conditions are recognised, particularly sickle cell anaemia.1-3 We describe a patient with aplastic anaemia who responded well to treatment with antilymphocytic globulin (ALG) but who developed severe Salmonella enteritidis (type 4) osteomyelitis.

A 22 year old Greek woman presented with anaemia and thrombocytopenia (haemoglobin 5 g/dl; platelets 42 x 10^9/l; white cell count 3-3 x 10^9/l, with 46% neutrophils, 48% lymphocytes, and 6% monocytes), and investigations confirmed idiopathic aplastic anaemia. She received 15 mg/kg equine ALG (Merrieux) daily for five days infused into the subclavian vein via a line inserted into the antebrachial fossa. Five days later a typical syndrome of fever sickness developed with fever, rash, and arthralgia and this responded promptly to hydrocortisone.

High fever with negative blood cultures
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was performed in an attempt to make a definitive diagnosis. The bone marrow had an abnormal rubbery texture with a discoloured grey brown appearance. Histological examination of the specimen showed severe chronic inflammation; no organisms or crystals were seen and no neoplastic infiltrate was identified. In view of her deteriorating condition she was given empirical antibiotic treatment with intravenous vancomycin (1 g twice a day), intravenous ciprofloxacin (200 mg twice a day), and oral fusidic acid (500 mg three times a day).

Enriched broth cultures from the bone biopsy specimen now grew an organism that was identified as *Salmonella enteritidis* (phage type 4) which was fully sensitive to ciprofloxacin; this was therefore continued as single agent treatment. Over the next three weeks the high fevers settled completely, bone pain at rest resolved, and there was gradual improvement in mobilisation with physiotherapy. She returned to Greece with a plan to continue oral ciprofloxacin (750 mg twice a day) for a total of 12 months after which joint replacement surgery may be considered.

Discussion

Salmonella osteomyelitis has been attributed to use of steroids, but such cases generally involve one or two sites only. Cherubin et al described a young woman receiving steroids for systemic lupus erythematosus who developed osteomyelitis due to *Salmonella enteritidis* after undergoing pin repair of a fracture of the ankle. In a review of 37 cases of bone infection due to *Salmonella*, three patients were receiving immunosuppressive treatment for connective tissue disorders; all three presented with localised osteomyelitis, though there was subsequent involvement of a second site in one case.

Our patient showed an extensive symmetrical osteomyelitis rarely reported except in sickle cell anaemia, and not previously reported in aplastic anaemia. This unusual clinical picture posed considerable diagnostic difficulties and, we feel, probably reflects impaired immunity due to prolonged steroid treatment aggravated by impaired marrow function. The use of a central venous catheter raises the possibility of a sustained bacteraemia and it is interesting to speculate whether coincident serum sickness modified the extent of the infection.

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