Suspected immune-mediated polysynovitis and serositis in a horse

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A 2-year-old, un raced, 450 kg Thoroughbred colt, when initially presented to a practising veterinarian for routine anthelmintic treatment, was lethargic, febrile (38.9°C), showed marked abdominal splitting and had oedema of all limbs and effusion of both tarsi and carpi. Moderate pain was elicited on flexion of all limbs. The veterinarian performed abdomino-centesis, thoraco-centesis and arthro-centesis of the left carpus and tarsus. Synovial protein concentration (10 g/l) and total nucleated cell count (3x10^9/l) were elevated in the tibiotarsal joint fluid. The predominant cells were non-degenerate neutrophils. No significant organisms were cultured. Examination of blood revealed a marked microcytic anaemia (PCV 0.23 l/l, MCV 38.3 fl, RBC 6.02x10^12/l) and a mild rise in globulins (34 g/l).

The horse was treated twice daily with procaine penicillin G, 15 mg/kg, intramuscularly (IM) and neomycin sulphate, 10 mg/kg, intravenously (IV) for 5 d. No improvement was seen after 2 d of this regime. On the third day symptomatic therapy was instituted. A combination of anti-inflammatory agent (isopyrin 140 mg, phenylbutazone sodium 70 mg, dexamethasone 0.5 mg, cimetidine HCl 2.2 mg/ml, IV) and diuretic (furosemide, 0.05 mg/kg, IV) was administered morning and night. Dramatic improvement in the horse's condition was reported overnight. Anti-inflammatory therapy was maintained, in addition to the antibiotic regime, for 5 d, during which time the horse appeared to make a good recovery.

The day after cessation of this regime the horse again became dull, febrile and showed increasing effusion of the joints and digital sheaths. The reoccurrence of clinical signs prompted referral to this centre.

At our initial examination, the horse had a rectal temperature of 38.9°C, heart rate of 60/min and respiration rate of 12/min and was depressed, with reduced borborygmi. Visible abnormalities included marked symmetrical swelling of synovial structures, including both tarsi and digital tendons sheaths of all limbs. Oedema was also present distally in all limbs. Lameness was minimal, although there was moderate pain on flexion of all 4 limbs and constant shifting of weight from limb to limb. Mucous membranes were pale pink with a normal capillary refill time; no mucusosal petechiation was observed. Absorption of fluid from pleural and peritoneal cavities was unsuccessful on day 1. Clinical laboratory evaluation of samples collected on day 1 included a complete blood count, serum chemistry analysis, urinalysis, prothrombin time, blood culture and joint aspiration from pleural and peritoneal cavities was unsuccessful on day 1. Additional tests performed included Coombs and Coggins tests, serum agglutination for Brucella abortus, rheumatoid factor (RF) and antineutrophil antibody (ANA) assay. Haematological analysis revealed a mature neutrophilia (9.4x10^9/l) without a leucocytosis. The haematocrit (0.26 l/l), haemoglobin (103 g/l) and erythrocyte count (6.42x10^12/l) all fell below reference values. A platelet count of 3x10^9/1, and small quantities of erythrocytes and platelets. The peritoneal sample had a total nucleated cell count of 19.4x10^9/l, of which 94% were non-degenerate neutrophils. Both fluid samples were interpreted as inflammatory exudates, although the peritoneal fluid protein concentration was low (10 g/l) for this.

Results of Coombs, Coggins and R. abortus tests were negative. Estimated prothrombin time was within normal limits. No significant bacteria were isolated from pleural, peritoneal and blood cultures. Both ANA and RF titres were negative.

Initial therapy included twice daily procaine penicillin G (15 mg/kg, IM) and neomycin sulphate (10 mg/kg, IV) and 1 g phenylbutazone paste per os. On day 2, rectal temperature, heart and respiration rates were normal, though borborygmi were still depressed. Resolution to costal pressure and the presence of a pleuritic ridge were observed. Symmetrical synovial swelling of tarsi, carpi, fetlocks and digital tendon sheaths was pronounced. Lameness was assessed as minimal and the demeanour of the horse unaltered. Antibiotic therapy was supplemented with dexamethasone sodium phosphate (0.2 mg/kg, IV) once daily.

Dramatic improvement in synovial effusion was seen on day 3, at which time antibiotic therapy ceased, based on a negative bacteriological culture from all fluid samples, a history of failure to respond to broad spectrum antibiotics and the favourable response to steroid treatment. The horse was maintained on 100 mg dexamethasone sodium phosphate, IV, and 1 g oral phenylbutazone paste daily, till day 5. Oral prednisolone treatment (1.5 mg/kg once daily) was maintained till day 6. The horse was clinically normal when discharged from hospital on day 7. The owner was advised to rest the horse for 3 months and maintain it on an extended course of oral prednisolone, decreasing the daily dose every 2 by 100 mg. The treatment was discontinued after 12 w.

Subsequently, 3 recurrences of similar clinical presentation were reported over a 2-year period. Two of these occurred during race preparation and one following surgery for an intra-articular carpal fracture. All 3 episodes were treated with steroid therapy, as described previously. On each occasion the response was dramatic and the horse rapidly returned to clinical normality. The corticosteroid regime in 2 of these occurrences incorporated rest, while the horse was maintained during race preparation following one of the episodes.

Cyclic polyarthritis with periods of complete clinical remission, such as was present in this case, also occurs in canine idiopathic polyarthritis (Bennett 1987), which includes cases of non-infective polysynovitis that cannot be classified into more defined groups. This immune-mediated, non-erosive, polyarthritic condition of the dog has close parallels to conditions in man and may well have a similar aetiopathogenesis to non-infectious polysynovitis in the horse. The few documented cases of immunemediated polysynovitis in the horse most commonly have a history of lethargy, symmetrical synovial effusion and stiffness (Yrins and Feldman 1983; Byars et al 1984; Madison and Scarratt 1988). Affected horses may be euthanased because of debilitating polyarthritis, or may, more often in young horses, recover spontaneously (Byars et al 1984).

Cytological analysis of synovial fluid from our case was similar to that from cases of non-erosive polysynovitis reported in the dog and horse, where leucocyte counts characteristically are elevated, and up to 93% of cells are non-degenerate neutrophils (Peder sen et al 1976; Krawiec 1985; Byars et al 1984). Elevated synovial protein levels in our case are consistent with that reported in both dog (Peder sen et al 1976) and horse (Byars et al 1984; Madison and Scarratt 1988).

The steroid responsive nature of the case presented may also be observed in other non-infectious arthritides. In contrast, the severity of the disease process associated with septic arthritis is typically increased with steroid therapy. The dramatic response to dexamethasone in the light of ineffective antibiotic treatment is suggestive of an immunological pathogenesis, but the significance of the anti-inflammatory versus immunosuppressive action of the steroid, and the effect of concurrent rest, need to be considered.

Non-specific ANA may be found in 5% of normal horses (WJ Penhale, personal communication) as well as in animals with diseases of a non-immune nature (Day and Penhale 1986). High titres found in systemic lupus erythematosus (SLE) are thought to be more diagnostic than the lupus erythematosus cell (Vrins...
and Feldman 1983), which has as yet undetermined significance in the horse (Byars et al 1984). Although simultaneous onset of polyserositis with joint effusion was seen in this case, the lack of an ANA titre makes an autoimmune SLE-like syndrome unlikely.

Non-infectious, non-erosive arthritis frequently develops after several systemic states in human beings. A similar pathogenesis has been proposed in dogs (Pedersen et al 1976), calves (Van Pelt and Langham 1966) and horses (Madison and Scarratt 1988) and is possibly the result of the deposition of immune complexes in synovial membranes (Jasin and Cooke 1978). Investigation of immunemediated polyarthritis secondary to a distant focal infection in foals (Madison and Scarratt 1988) revealed both negative ANA and RF titres, but these by no means preclude the possibility of an immunological pathogenesis. In addition, these tests must be interpreted with consideration to previous steroid therapy and the stage of the disease process.

A study of non-infectious, non-erosive polyarthritis in dogs revealed almost half had SLE and the remainder had an associated infectious disease process, or were idiopathic in origin (Pedersen et al 1976). Idiopathic polyarthritis is uncommon in the horse.

In the absence of definitive diagnostic aids, common to diseases of an immunological pathogenesis, the case presents clinically as an idiopathic, non-erosive polyarthritis. A presumptive diagnosis may be made on the basis of clinical signs of stiffness, distension of multiple joints and tendon sheaths, near-normal results of cytologic examination of synovial fluid, absence of infectious agents in affected joints and the clinical response to steroid therapy. Further investigation of this case with histological and immunofluorescent examination of synovial biopsies was, unfortunately, not possible.

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CORRESPONDENCE

Treatment of Yersinia infection with tetracyclines

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In a recent article describing Yersinia pseudotuberculosis enteritis, Slee and Button (1990) state the tetracyclines may be useful in the treatment of the disease in sheep, goats and pigs based on the effectiveness of this drug for the treatment of yersiniosis in cattle. Since clinical signs are not pathognomonic for yersiniosis, as is pointed out in the same article, I would like to suggest that the parental use of tetracyclines is inadvisable until culture and sensitivity results are available.

Salmonella is one of the major diagnostic differentials and the use of parenteral tetracyclines as an adjunct in the treatment of this disease is not generally recommended (Beveridge 1983; Blood et al 1983; Divers and Johnston 1987). Indeed, tetracyclines may be ineffective and can lead to the development of a carrier state, though this carrier state also may be incurred from the use of other antibiotics (A1 Frost personal communication 1990).

If enteric yersiniosis is suspected, I suggest the parenteral antibiotic of first choice should be trimethoprim plus sulfadiazine for cattle, sheep and goats, used in conjunction with supportive therapy. This antibacterial combination is recommended for the treatment of salmonellosis (Beveridge 1983; Blood et al 1983; Divers and Johnston 1987) and also has been shown to be effective in vivo against most isolates of Y. pseudotuberculosis (Callinan et al 1988). In their study, all of 30 isolates of Y. pseudotuberculosis from cattle were sensitive to neomycin, 29 of 30 to sulfamethoxazole-trimethoprim and 28 of 30 to tetracycline.

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Reply

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Both Yersinia enterocolitica and Y. pseudotuberculosis are sensitive in vitro to a wide range of antibiotics including tetracyclines, sulphonamides, trimethoprim, streptomycin and neomycin (Callinan et al 1988; Slee et al 1988; Robins-Browne 1989). Y. enterocolitica is, however, inherently resistant to the penicillins, including ampicillin (Robins-Browne 1989).

The results of in vivo drug sensitivity tests on Yersinia spp, in common with many other bacteria, do not necessarily correlate with clinical efficacy. For example, doubt has been cast on the value of streptomycin in the treatment of Y. enterocolitica infection of humans (Robins-Browne 1989) and Y. pseudotuberculosis infection of buffalo (Behra et al 1984). Pia et al (1984) found that a combination of sulphonamide and trimethoprim had no clinical value in the treatment of human infections due to Y. enterocolitica. Experience with Y. pseudotuberculosis infections in cattle in both New Zealand (B Stephen et al 1988) and sheep (K Slee, unpublished), producing both a clinical and bacteriological cure.

While the use of antibiotics in the treatment of human Salmonella sp enteritis does not affect the course of disease, and may prolong the faecal excretion of the bacterium (Aserkoff and Bennett 1969), we are unaware of any information to suggest that this is the case in livestock species treated with tetracyclines. In fact, this possibility is suggested to have little practical significance by Blood and Radostits (1989).

Until a combination of sulphonamide and trimethoprim is demonstrated to be effective in the treatment of yersiniosis or until tetracyclines are demonstrated to carry a significantly increased chance of inducing a persistent carrier state of Salmonella sp in livestock species, it would seem wise to continue the recommendation that long-acting tetracyclines be used in the treatment of both Y. enterocolitica and Y. pseudotuberculosis infections in animals.

References
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