

A case of periosteal proliferative polyarthrititis in a cat

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S U M M A R Y

In this paper a case of periosteal proliferative polyarthrititis is described in an 11-year old, female Siamese cat, that was admitted to the Surgery Clinic of the Veterinary School, A.U.Th., with a 6-month history of non-weight bearing lameness of the left thoracic limb. At physical examination, restricted range of motion of the left elbow joint, local swelling and pain were detected. In the radiological examination of the affected joint the main finding was an extensive periarticular and irregular periosteal new bone formation. The results of the complete blood count and routine serum biochemistry were within normal limits and the cat was serologically negative for FeLV and FIV. Synovial fluid examination showed a lymphoplasmacytic pleocytosis, while the bacterial culture was negative. Prednisolone given at an anti-inflammatory dose for two consecutive weeks resulted in a marked improvement of the clinical signs. However, two months after the end of the treatment lameness reappeared, but this time in the contralateral thoracic limb, due to the involvement of the same joint. Radiology revealed the same type of lesions in the right elbow joint, while the left became ankylosed. Again, prednisolone given at an immunosuppressive dose for two weeks gave only moderate improvement in both the clinical conditions and the radiological changes in the animal. For this reason azathioprine at the dose of 1 mg/kg BW, every 48 hours, was added to therapy that lasted for 5 months. Transient mild leukopenia, that resolved after decreasing the dose of azathioprine by 25% was the only adverse side effect noticed. At the end of the treatment, regression of the radiographical lesions in both elbows enabled the cat to walk with a stilted gait despite the development of joint ankylosis bilaterally. The disease was kept in remission during the 12-month follow up period.

INTRODUCTION

Periosteal proliferative polyarthrititis (PPP) is the most common form of feline chronic progressive polyarthrititis (CPP), an uncommon erosive joint disease that was first studied by Pedersen and associates in 1980. Despite its association with FeSFV, FeLV (Pedersen et al 1980, Lipowitz 1985, Schrader 1995, Tizard 2000) or occasionally FIV infection (Taylor 2003), PPP is still considered an immune-mediated disorder, although the precise mechanism that triggers the immunologic reaction remains unknown (Nelson and Couto 1992, Bennett 1994,

This paper originally appeared in: *The Journal of the Hellenic Veterinary Medical Society** (2004) **55**, p 46-54

Schrader and Sherding 1994, Thomson 1994, Roush 1997, Day 1999, Hay and Manley 2000); however, synovial immune-complex deposition may be involved (Day 1999, Davidson 2002). Joint diseases, similar to feline PPP, have been described in both humans (Reiter's arthritis) (Bennett and Nash 1988, Goring and Beale 1993, Thompson 1994, Schrader 1995, Pedersen et al 2000) and dogs (Bennett and Nash 1988, Bennett 1990, May and Bennett 1994, Day 1999). In general, the prognosis is guarded to poor, as CPP tends to be progressive making euthanasia necessary when the quality of life becomes unacceptable (Day 1999). The purpose of this article is to present the clinical and radiological

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* Presented by HVMS (Greece)

findings, as well as the response to treatment of a cat with PPP, which, to our knowledge, has never been reported in the greek literature.

CASE DESCRIPTION

An 11-year old, female Siamese cat, weighing 6 kg, was admitted to the Surgery Clinic, School of Veterinary Medicine, Aristotle University of Thessaloniki, Greece, with a 6-month progressive and non-weight bearing lameness of the left thoracic limb as the main complaint; no medical treatment, of any kind, had been attempted prior to admission. At physical examination, restricted range of motion of the left elbow joint, local swelling and pain were detected upon palpation. Radiological examination of the affected joint showed excessive periarticular soft tissue radiopacity accompanied by extensive and irregular periosteal new bone formation (figure 1). The other limb joints as well as the thoracic and abdominal cavity and the vertebral column appeared radiographically normal. The results of complete blood count (haematocrit, haemoglobin, leucocyte and platelet counts, differential white blood cell count), routine serum biochemistry (total protein, albumin, ALP, ALT, γ -GT, BUN, creatinine) and FeLV+FIV ELISA serology were found to be within normal limits or negative, respectively. Synovial cytology of the affected joint disclosed the presence of numerous lymphocytes and plasma cells, while the bacterial culture came back negative. Synovial biopsy was also suggested but declined by the owner.

Figure 1. Lateral radiograph of the left elbow on the day of first admission, showing the increased radiopacity of the expanded periarticular soft tissues, as well as the extensive periarticular new bone formation



Subsequently, the cat was put on oral prednisolone (Prezolon®) at the anti-inflammatory dose of 2 mg/kg BW, once daily, for two consecutive weeks which resulted in a marked improvement of the functional state of the affected limb. A gradual tapering of the prednisolone dosage was further suggested, but the owner stopped giving it on his own initiative.

Approximately two months after the end of the aforementioned treatment, the cat started limping, but on the right thoracic limb this time. The painful swelling of the ipsilateral elbow joint, along with the already ankylosed left elbow joint, made the cat reluctant to jump and walk. Radiological examination of the right elbow showed the presence of periosteal proliferation at the attachment site of the joint capsule (figure 2); the left elbow lesions were well demarcated and had more regular margins than the first time. Again, the radiographs of the other limb joints did not disclose anything abnormal. Oral prednisolone was re-instituted, but at an immunosuppressive dose this time (4 mg/kg BW, per os, once daily) for two consecutive weeks, tapered gradually over a period of three additional weeks. The radiological examination, at the end of the treatment, revealed that the lesions of the left elbow joint remained unchanged while those of the contralateral joint appeared much worse (figure 3). Thereupon, it was decided to use azathioprine (Azathioprin®), at the dose of 1 mg/kg BW, per os, every 48 hours, along with 1 mg/kg BW prednisolone, every 24 hours, tapered to 0.5 mg/kg BW. This dose was subsequently used along with azathioprine, on an alternate day basis. The combination therapy was administered for a 5-month period, during which the cat was being monitored clinically and clinicopathologically (every 15 days), as well as radiographically (every month). Because of a transient leukopenia (4,900/ μ l) that appeared approximately one month after the beginning of the treatment, the dose of azathioprine was lowered by 25% until the number of WBC's was restored to normal range (5,000-18,900/ μ l). The radiological examination of the right elbow showed a substantial regression of the lesions at the end of the

Figure 2. Lateral radiograph of the right elbow just before the institution of the immunosuppressive treatment, demonstrating periosteal new bone formation at the attachment site of the joint capsule.





Figure 3. Lateral radiograph of the right elbow after the immunosuppressive treatment with prednisolone, showing the worsening of the periarticular new bony tissue formation.

treatment period (figure 4a). At the same time, a decreased radiopacity of the periarticular new bony tissue in the left elbow was clearly visible (figure 4b). In spite of the fact that ankylosis was well established in both elbow joints, the absence of pain enabled the cat to walk with a stilted gait. The clinical condition of the animal remained unchanged within the 12-month follow-up period, whereas the lesions did not deteriorate further in the left and improved moderately in the right elbow joint.

DISCUSSION

PPP occurs exclusively in intact or neutered male adult cats, regardless of their breed (Pedersen et al 1980, Moise and Crissman 1982, Bennett and Nash 1988, Schrader and Sherding 1994, Roush 1997, Pedersen et al 2000). The appearance of PPP in female or elderly patients, like the cat of our report, is only seldom witnessed (Pedersen et al 1980, Bennett and Nash 1988). The disease in this cat was not associated with either FeLV or FIV infection, which have not been proven to cause PPP, at least experimentally (Taylor 2003). Synovial fluid testing for FeSFV was not considered necessary because the virus has been isolated from either the affected or normal feline joints (Day 1999). Lesions tend to have a symmetrical distribution, with the carpal and tarsal joints being more frequently affected compared to the stifle, shoulder, hip or the elbow joint, as was the case in

this cat (Pedersen et al 1980, Bennett and Nash 1988, Schrader and Sherding 1994).

The typical radiological finding in PPP is a periarticular extensive and profound periosteal proliferation, that ultimately may lead to ankylosis of the affected joint(s) (Bennett and Nash 1988, Nelson and Couto 1992, Schrader and Sherding 1994, De Haan and Beale 1995) and was also noticed in this cat. Subchondral erosions of mild degree, usually located at the margins of the articular cartilage, may also occur in PPP (Bennett and Nash 1988, Bennett 1994, May and Bennett 1994, Schrader and Sherding 1994, Day 1999); but they were not demonstrated in either of the elbow joints of our feline patient, as it has also been reported in other cases (Lipowitz 1985, Nelson and Couto 1992, Goring and Beale 1993, De Haan and Beale 1995, Schrader 1995, Hay and Manley 2000). In the deforming erosive or rheumatoid-like form of feline CPP, subchondral erosions and cysts are quite visible in radiographs and may eventually lead to the subluxation or luxation of the affected joint (Bennett and Nash 1988, Goring and Beale 1993, Schrader and Sherding 1994, Hay and Manley 2000, Pedersen et al 2000, Taylor 2003). Also, the frequently observed deformity and instability of the carpal and other distal joints (Taylor 2003) was not part of the clinical picture in this cat.

Since the idiopathic form of feline immune-mediated nonerosive polyarthritis shares some clinical features with PPP, the diagnosis was mainly based on the marked periarticular new bone formation over the affected joints of the cat (Bennett and Nash 1988, Nelson and Couto 1992, Day 1999, Pedersen et al 2000). The same kind of polyarthritis, that appears secondarily to infections, neoplasms, drugs or vaccines (Day 1999, Hay and Manley 2000, Pedersen et al 2000, Taylor 2003), was also excluded from the list of differentials from a historical and clinical standpoint. Systemic lupus erythematosus, an extremely uncommon cause of nonerosive polyarthritis in cats (Bennett and Nash 1988, Pedersen et al 1989) was also ruled out from the beginning because its polysystemic nature did not fit into the clinical picture of this cat. Interestingly, this animal did not exhibit anorexia, fever and / or peripheral lymphadenopathy, which are, at least initially, common manifestations in PPP, (Pedersen et al 2000, Taylor 2003). This could be explained by the delayed first admission of the animal, although these symptoms were not manifested on the second admission, as well.

In the erosive types of feline polyarthritis the continual assessment of the animals is important because the true nature of the disease may only become apparent as it progresses, while certain individual factors will decide how it will be finally manifested (Bennett 1995). Since the radiographic changes (periosteal new bone formation, cyst-like metaphyseal defects, destruction of articular cartilage, subchondral bone development) in both the bacterial L-form and mycoplasmal (*Mycoplasma gatae*, *Mycoplasma felis*) polyarthritis are similar to those of PPP (Carro 1994, Schrader and Sherding 1994) these differentials should have also been pursued diagnostically. However, these wall-less and prokaryotic bacteria necessitate the use of specific media to grow (Carro et al. 1989), which



Figure 4. Lateral radiograph of the right (a) and the left (b) elbow, immediately after the end of the 5-month immunosuppressive therapy with azathioprine and prednisolone, showing substantial regression (a) and decreased radiopacity (b) of the periarticular new bony tissue.

unfortunately were not available. Since these bacterial infections cannot be excluded on clinical and radiological grounds alone, tetracyclines, lincomycin and tylosin (Carro et al. 1989) should have been tried prior to institution of the immunosuppressive treatment.

Periarticular exostoses in hypervitaminosis A, that may also lead to lameness, are very similar to those of PPP, but the dietary history (commercial cat food) of the cat ruled-out this possibility (Bennett 1994, Schrader and Sherding 1994, Harari 1997, Johnson and Watson 2000); furthermore, no exostoses could be seen in the radiographs of the cervical spinal column (Bennett 1994, Harari 1997, Johnson and Watson 2000).

In PPP, lifelong immunosuppressive therapy is often required in an attempt to halt the progression of the lesions and to obtain clinical remission, because in the majority of cases the clinical signs relapse when there is a decrease of the dosage or no medication at all (Schrader and Sherding 1994, Day 1999, Pedersen et al 2000, Taylor 2003). In this cat, the initial use of prednisolone at an antiinflammatory dose could be justified by the one joint involvement of the lesions, which made the diagnosis of PPP uncertain. The clinical improvement, noticed initially, would have been more prolonged had the owner complied with the full course of treatment. The recurrence of clinical signs in both frontlimbs made the diagnosis of PPP more certain and, therefore, the use of prednisolone at immunosuppressive dosage necessary. Azathioprine had to be added subsequently, because of the aggravation of the right elbow lesions, along with the development of ankylosis in the contralateral joint. Combination immunosuppressive therapy is recommended in small animal immune-mediated arthritides, not only for the achievement of longer remission periods, but to lower the risk of side effects that are associated with the prolonged use

of glucocorticosteroids (Beale 1988, May and Bennett 1994, Hay and Manley 2000, Pedersen et al 2000, Tizard 2000).

The use of azathioprine in cats is reportedly associated with a life-threatening leukopenia and thrombocytopenia (Beale 1990, Beale et al 1992, Plumb 1999, Scott et al 2001), that could be attributed to the low erythrocyte thiopurine methyltransferase activity in this animal species (Foster et al 2000, Papich 2000, White et al 2000). Lower doses of azathioprine, such as 0.3 mg/kg BW, once daily (Papich 2000), 0.3-0.5 mg/kg BW every 48 hours (Birchard and Sherding 2000) or 1.5-3.125 mg/cat every 48 hours (Papich 1995), are thought to be relatively safer. The dose of 1 mg/kg BW every 48 hours, that was used in this cat, has also been recommended, provided that a close monitoring for early detection of side effects is regularly pursued (Plumb 1999, Pedersen et al 2000, Boothe and Mealey 2001); however even this dose is still considered unacceptably high (Papich 2000).

Since azathioprine is generally considered unsafe for the cat (Bennett 1995, Papich 2000, Taylor 2003) it is strongly advised to use cyclophosphamide or chlorambucil instead, along with prednisolone at low immunosuppressive dosage (Taylor 2003). Combination therapy with the use of prednisolone, azathioprine (7.5 mg/cat every 48 hours) and cyclophosphamide was applied in 5 CPP cats with moderate to poor results (Pedersen et al 1980). In the same study, two of the treated animals died of drug-induced side effects, although the detrimental role of azathioprine could not be assessed. Transient leukopenia, that was also noticed in our feline patient at the 16th azathioprine administration, subsided when its dose was lowered by 25%. When a similar dosage (1.1 mg/kg BW, every 48 hours) was used in 8 cases of feline pemphigus foliaceus, 4 of these cats developed leukopenia after the 8th administration (Caciolo et al

1984), while doses twice as high (2.2 mg/kg BW, every 48 hours) led to severe leukopenia (<3000 leukocytes/ μ l) after approximately 1.5 months of continuous administration (Beale 1992). The absence of life-threatening side effects in our feline patient, even after the 5-month treatment period, may indicate that this dose can be tolerated, at least by some cats.

Interestingly, the higher degree of periosteal bony tissue regression in the right elbow joint, where the immunosuppressive treatment started as early as two weeks after the appearance of the clinical signs, indicates that its early application is associated with a better outcome (Wilkinson and Robins 1979, Schrader and Sherding 1994).

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