Surgery NOTE

Three Cases of Idiopathic Sterile Pyogranulomatous Inflammation of Epidural Fat in Miniature Dachshunds

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Running head: EPIDURAL PYOGRANULOMATOUS INFLAMMATION
ABSTRACT. Progressive ataxia and paralysis in three Miniature Dachshunds were found to be caused by idiopathic sterile pyogranulomatous inflammation of epidural fat between T5 and L4. All dogs were managed by hemilaminectomy and removal of epidural compressive material. Surgical findings and histopathological evaluation were necessary to diagnose epidural pyogranulomatous inflammation. A dog did not regain motor and sensor function after the surgery. Two dogs had exhibited improved neurological function after the surgery, but they recurred. Oral cyclosporine treatment was useful for their long remission. Idiopathic sterile pyogranulomatous inflammation of epidural fat can be considered to be a cause of thoracolumbar myelopathy in dogs.

KEY WORD: dog, epidural, pyogranulomatous inflammation, spinal cord
Idiopathic sterile pyogranulomatous inflammation or sterile panniculitis is characterized as inflammation of the subcutaneous fat [14, 15]. Skin lesions, which can ulcerate, may be solitary or multiple; multiple lesions are more commonly associated with systemic signs such as pyrexia, lethargy, depression, and anorexia [15]. Relatively few cases have been reported in dogs, and the cause and pathogenesis of these conditions are unknown. Dogs with sterile pyogranulomatous inflammation are controlled mainly with systemic corticosteroid [14, 15, 18]. A recent study found that idiopathic sterile pyogranulomatous inflammation of epidural fat caused spinal cord compression in five Miniature Dachshunds [3]. In this report, five out of 520 dogs that suspected involvement with intervertebral disk herniation (IVDH) were idiopathic sterile pyogranulomatous inflammation of epidural fat. All five dogs had good neurological outcome and some dogs needed systemic corticosteroid. However, there is little information about recurrence and long-term management with immunosuppressive drug therapy of idiopathic sterile pyogranulomatous inflammation of epidural fat.

We report three dogs with idiopathic sterile pyogranulomatous inflammation of epidural fat that is causing spinal cord compression. We describe clinical signs, imaging, surgical findings, histopathological findings, recurrence, and long-term management with immunosuppressive drug therapy in dogs with idiopathic sterile pyogranulomatous inflammation of epidural fat.

Case-1 was a 3-year-old spayed female Miniature Dachshund with a body weight of 3.4 kg, referred to the hospital with a 14-day history of back pain. There was no improvement following administration of nonsteroid anti-inflammatory drug (NSAIDs) for 3 days (drug unknown). Lumbar myelography was performed at L5-6 using 0.45 ml/kg of iotrolan (Iosvist, 240 mg iodine/ml, Shering, Osaka). Myelographic findings
were characteristic of an extradural lesion on the right lateral aspect of T10-11. A right-sided hemilaminectomy was performed in this area. Although ill-defined soft nodules were observed, these were different from the typical compressive lesion caused by nucleus pulposus extrusion, and we removed the nodules. Histopathological analysis of the nodules was not performed. The dog was relieved of the back pain following this decompressive surgery.

Back pain and paresis in the pelvic limbs recurred 2 months later. Up on reexamination, hematologic analysis showed elevated leukocytosis (19900 cells/μl, normal range: 6000-17000 cells/μl). Serum biochemical analysis revealed elevated C-reactive protein concentration (18 mg/dl, normal range: 0-1 mg/dl). Myelographic findings were characteristic of an extradural lesion on the left lateral of L3-4 (Fig. 1). The previous lesion at T10-11 was normal. Cerebrospinal fluid analysis was not performed. A left-sided hemilaminectomy was performed at L3-4. Ill-defined soft nodules were again observed, and the boundary of the nodules with adjacent laminae and muscles was unclear. All the degenerated tissues were excised. The dura matter did not coalesce with the nodules and was normal macroscopically. The histopathological diagnosis of nodules removed at surgery was pyogranulomatous inflammation (Fig. 2). Microbial culture of surgical specimens was not performed, but infectious pathogenic bacteria were not evident by histology.

The dog regained motor and sensor function after the 2nd surgery and therapy was initiated with prednisolone (1 mg/kg, orally once a day) to prevent relapse of pyogranulomatous inflammation. When the dosage of prednisolone was reduced (0.5 mg/kg, orally once a day), the pain returned and the C-reactive protein concentration was elevated. Survey radiographics of the entire spine revealed hypertrophic
ossification in L1 and L3 at 7 months after the 2nd surgery (Fig. 3). The dog had also clinical signs of iatrogenic hyperadrenocorticism (polyuria, polydipsia, and increased serum alkaline phosphatase). Prednisolone was therefore disconitinued, and further treatment was initiated with cyclosporine (5 mg/kg, orally once a day) for 1 month. The dog thereafter showed no sign of recurrence, and the C-reactive protein decreased. Cyclosporine was decreased gradually (5 mg/kg, orally once 4 days), after which the dog has shown no sign of recurrence for 29 months.

Case-2 was a 5-year-old castrated male Miniature Dachshund with a body weight of 4.1 kg, which entered the hospital with a 7-day history of paresis of the pelvic limbs. Although prednisolone (1 mg/kg, orally once a day) had been administered for 7 days, the dog had paraplegia and loss of nociception in the pelvic limbs. The dog had histories of pyogranulomatous inflammation as a reaction to the surgical silk used in the castration at 3 years of age in inguina, and subcutaneous sterile panniculitis at 3 years old. Myelographic findings were characteristic of an extradural lesion on the right lateral aspect of T10-11. A right-sided hemilaminectomy was performed in this area. Ill-defined soft nodules were observed, and the boundary of the nodules with adjacent laminae and muscles was unclear. All the degenerated tissues were excised. The dura matter did not coalesce with the nodules and was normal macroscopically. The histopathological diagnosis of nodules removed at surgery was pyogranulomatous inflammation. Microbial culture of surgical specimens was undertaken, but no bacteria were isolated. Although prednisolone (1mg/kg, orally once a day) was administered for 30 days after the surgery, the clinical signs were not changed. The owner declined additional examinations and treatments. The dog had not regained motor and sensor function by 12 months after the surgery.
Case-3 was a 4-year-old spayed female Miniature Dachshund with a body weight of 4.9 kg, referred to the hospital with a 14-day history of paraplegia, with intact nociception in the pelvic limbs. There was no improvement despite administration of NSAIDs for 14 days (drug unknown). Myelographic findings were characteristic of an extradural lesion on the ventral aspect of T5. A left-sided hemilaminectomy was performed in the T5-6 area. The mass was confirmed at this area. Well-circumscribed firm nodules were observed, distinct from cases 1 and 2. The boundary of the nodules with adjacent dura matter, laminae and muscles was clear, therefore the nodules were excised completely. The dura matter was normal macroscopically. The histopathological diagnosis of nodules removed at surgery was pyogranulomatous inflammation. Microbial culture of surgical specimens was not performed, but no infectious pathogenic bacteria were evident according to histology.

The dog regained motor and sensor function after the decompressive surgery. It suffered anorexia 2 months after the surgery, and the C-reactive protein concentration was elevated (20 > mg/dl). A mass, caudal to the left kidney, was confirmed by ultrasonography. On exploratory celiotomy, this mass was excised. The histopathological diagnosis of the mass was pyogranulomatous inflammation caused by the surgical silk used at spaying. Microbial culture of surgical specimens was undertaken; no bacteria were isolated. The C-reactive protein concentration was elevated (20 > mg/dl), and the mass caudal to the left kidney was confirmed by ultrasonography at 12 months after the exploratory celitomy. The owners declined further surgical therapy, so therapy was initiated with prednisolone (1 mg/kg, orally once a day, for 14 days) and cyclosporine (5 mg/kg, orally once a day). The dog showed no sign of recurrence, and the C-reactive protein was decreased. Cyclosporine was
decreased gradually (5 mg/kg, orally once 4 days), after which the dog showed no sign of recurrence for 16 months.

We have reported 3 dogs with idiopathic sterile pyogranulomatous inflammation of epidural fat causing spinal cord compression. A recent study found that idiopathic sterile pyogranulomatous inflammation of epidural fat caused spinal cord compression in Miniature Dachshunds, and all dogs experienced good neurologic outcome after decompressive surgery [3]. In the present report, one of the three dogs did not regain motor and sensor function after decompressive surgery. It was possible that spinal cord compression by the nodules caused axonal injury irreversibly. These dogs had similar symptoms of intervertebral disk herniation (IVDH), including back pain, paresis, or paraplegia. The Miniature Dachshund is predisposed to sterile pyogranulomatous inflammation, as well as IVDH [17, 18]. Idiopathic sterile pyogranulomatous inflammation of epidural fat may therefore be a cause of thoracolumbar myelopathy in dogs.

All dogs in this report had been castrated or spayed; two of the 3 dogs had a history of pyogranulomatous inflammation caused by the surgical silk which was used at castration or spaying. It has been reported that castrated or spayed dogs are predisposed to sterile panniculitis [18]. Physical invasion in a surgical process, or the local inflammatory reaction caused by foreign materials (i.e. residual sutures), may have triggered the development of this disease. Multiple factors might be implicated in the etiology of sterile panniculitis in dogs, including bacterial and fungal infections, foreign bodies, nutritional deficiency, vasculopathy, pancreatic disorders, and further immunological and physicochemical factors [5, 14, 15]. A further study would be needed to determine the etiology of idiopathic sterile pyogranulomatous inflammation.
Myelography was used to confirm the location of the compressive lesions. This was because we had doubt about IVDH, which is one of the major differential diagnoses of thoracolumbar spinal cord injury in middle-aged Miniature Dachshunds. Surgical findings and histopathological evaluation were required for diagnosis of idiopathic sterile pyogranulomatous inflammation of epidural fat. In a case, the boundary of well-circumscribed nodules with adjacent tissues was clear, therefore the nodules were excised completely. In two cases, the boundary of ill-defined soft nodules with adjacent laminae and muscles was unclear, therefore it was uncertain whether degenerated tissues were excised completely. Case-1 had hypertrophic ossification in L1 and L3. This symptom has never been recognized in the other spinal diseases. It may be caused by extension of pyogranulomaous inflammation. Computed tomography or magnetic resonance imaging could be useful to provide more detailed information about idiopathic sterile pyogranulomatous inflammation of epidural fat. In this report, C-reactive protein was consistently elevated when the dogs showed signs of recurrence. In IVDH, most of the cases did not exhibit elevated C-reactive protein concentration [12]. The measurement of C-reactive protein may be useful in differentiating IVDH and estimating recurrence. However, Bathen-Noethen et al reported that serum C-reactive protein concentration was high in dogs with steroid responsive meningitis-arteritis [4]. Further studies would be needed to evaluate the availability of measurement of C-reactive protein.

Concurrent inflammation of fat in the abdomen [8], epidural space [3], and bone [7] may occur in dogs with idiopathic sterile pyogranulomatous inflammation. The present report indicates that there was generally multiple region involvement. Dogs with sterile pyogranulomatous inflammation have a good outcome by systemic corticosteroid [14,
However, long-term management with corticosteroid is difficult because of the drug's side effects, for example, hepatotoxicity, iatrogenic hyperadrenocorticism, gastrointestinal ulceration, polyuria-polydipsia, and polyphagia [1, 11]. In human medicine, cyclosporine is an immunosuppressant drug used for organ transplant patients to decrease the risk of organ rejection [6]. In veterinary medicine, cyclosporine has been widely used for dermatologic diseases and other systemic immune-mediated diseases [1, 2, 13, 16]. Recent reviews and a meta-analysis of prospective clinical trials concluded that cyclosporine was highly effective compared with placebo and was as effective as prednisolone for treatment of atopic dermatitis in the dog [13, 16]. Some reports have suggested that cyclosporine is an effective therapeutic option for CNS inflammation in dogs [1, 2]. Moreover, cyclosporine plus prednisolone therapy could decrease the required prednisolone dosage, which consequently could reduce the side effects of the drug for the long term [9]. Cyclosporine may be useful for long-term management of idiopathic sterile pyogranulomatous inflammation. Further studies would be needed to evaluate the effectiveness of cyclosporine. These results match those of another study of dogs which were successfully treated with tacrolimus [10]. Allowing for the fact that the dogs needed immunosuppressive drugs after surgical excision, it is possible that pyogranulomatous inflammation is a systemic disease.

In conclusion, we diagnosed three castrated or spayed Miniature Dachshunds with idiopathic sterile pyogranulomatous inflammation of epidural fat causing spinal cord compression. Idiopathic pyogranulomatous inflammation of epidural fat has different forms such as ill-defined soft nodules and well-circumscribed nodules. Surgical findings and histopathological evaluation were required for diagnosis of idiopathic sterile pyogranulomatous inflammation. In addition, the measurement of C-reactive protein
could be useful in estimating recurrence. Cyclosporine may be useful for treatment of idiopathic sterile pyogranulomatous inflammation for the long term. Idiopathic sterile pyogranulomatous inflammation of epidural fat can be considered to be a cause of thoracolumbar myelopathy in dogs.

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REFERENCES


Figure legends

Fig. 1. Myelographic of ventral 45° right-dorsal left oblique view. There is deviation of the contrast medium column on the left between L3 and L4.

Fig. 2. Case-1 photomicrographs. A) Low magnification (scale bar = 100 μm). B) High magnification (scale bar = 50 μm). Inflammatory cells, mainly macrophages and neutrophils, have infiltrated into the adipose tissue. Hematoxylin and eosin stain.
Fig. 3. Survey radiographic, lateral view. There were hypertrophic ossification in L1 and L3 (arrow heads).
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