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Case Report

VERTEBRAL OSTEOMYELITIS DUE TO CANDIDA ALBICANS IN A DOG

Sv. Krastev¹, G. Simeonova¹*, V. Urumova², R. Simeonov³

¹Department of Veterinary Surgery; ²Department of Veterinary Microbiology, Infectious and Parasitic Diseases; ³Department of General and Clinical Pathology, Faculty of Veterinary Medicine, Trakia University, Stara Zagora, Bulgaria

ABSTRACT

Candida species uncommonly cause vertebral osteomyelitis both in animals and human. We present a case of lumbar vertebral osteomyelitis in a dog caused by *Candida albicans*. The dog was 3-year-old female kurtzhaar weighing 19kg. The patient had a history of loss of appetite and weight, and several fistulas on the left lumbar area for three months that appeared after injury. Clinical signs were related to neurological dysfunction but were observed later in the course of the disease. The diagnosis was made on the basis of history, clinical symptoms, x-ray examination, cytology and cultural conformation. The treatment was successful after surgical debridement and oral ketoconazole for 35 days.

Key Words: vertebral osteomyelitis, Candida albicans, dog

INTRODUCTION

Candidal vertebral osteomyelitis is a rare disease. *Candida albicans* is a normal fungal inhabitant of the gastrointestinal, upper respiratory, and genital mucous membranes of dogs Opportunistic infections may develop as a result of breaks in the normal mucosal barrier, immunosuppression, and treatment with broad-spectrum antibiotics (1).

Laboratory, X-ray, and clinical data are consistent with spondylitis independently on the underlying causative factor. On the initial presentation the patients may reveal some other non-specific symptoms such as depression, anorexia, weight loss, sometimes fever that may confuse the prompt diagnosis. Neurological symptoms that appear later in the course of the disease may also be attributed to many other diseases.

The definitive diagnosis requires culture of a biopsy specimen, cyto- or histological identification. Some advanced diagnostic techniques such as computed tomography, magnetic resonance imaging (2), and immunohistochemical investigations (3) are recommended but they are not always available.

Systemic candidiasis is very devastating disease with high mortality rate whereas local mycoses have favourable prognosis. The successful treatment of candidal vertebral osteomyelitis was reported in 85% of the cases with prolonged antifungal and surgical therapy starting as early as possible (2).

CASE HISTORY

A 3-year-old female kurtzhaar, weighing 19kg was admitted to the Small Animal Clinic in the Faculty of Veterinary Medicine of the Trakia University in Stara Zagora, Bulgaria. The dog presented a three-month history of multiple fistulas on the left lumbar region, progressive anorexia and weight loss. The owner explained that the dog had sustained an injury a month before fistulas appeared. It had not been treated at that time but later fistulas were treated by antibiotics symptomatically and unsuccessfully.

Physical examination did not reveal significant disorders, except that the fistulas led to the vertebral column when a probe was inserted into their canals.

Neurological examination showed moderate pain on deep palpation of the cranial lumbar region, listlessness, slight spasticity in

^{*} Correspondence to: Galina Simeonova, Department of Veterinary Surgery, Faculty of Veterinary Medicine, Trakia University, Stara Zagora – 6000, Bulgaria; E-mail: gpsimeonova@uni-sz.bg

the walk and lumbar rigidity. Postural reactions and spinal reflexes were normal at the time of presentation (**Figure 1**), but soon after the condition deteriorated. On the 10^{th} day the animal showed abnormal positioning of the hind limbs with increased muscle tone (**Figure 2**), dorsal deviation of the trunk, proprioceptive deficit of the hind limbs detected by flexing the paw to lie with its dorsal surface on the floor, depressed anal sphincter reflex, and loss of superficial sensation caudal to L₄-L₅.



Figure 1. Normal position of the body except slight stiffness of the back and hind legs. Several fistulas are visible on the left lumbar area in a dog (arrow).



Figure 2. Proprioceptive deficit and rigidity of the hind limbs. Profound dorsal back deviation.

Venous blood samples were obtained from heparinised v.cephalica tubes. in Haematological and biochemical blood tests were made using automatic cell counter (Serono 150 plus, Germany), biochemical blood analyser (BA-88 Mindray, China) and commercial diagnostic tests (GIESSE Diagnostics test-Italy; Chema Diagnostica *test-Italy*). The results did not show abnormalities in the investigated parameters (table 1).

Table 1. Results of haematological and biochemical investigations of a dog with candidal vertebral osteomyelitis.

Morphological	Detected	Reference	Biochemical	Detected	Reference
parameter	value	values	parameter	value	values
Hgb, g/L	136	120-180	Total	66	51-72
PCV, 1/1	0.44	0.37-0.55	protein, g/L	16	19-59
RBC, T/L	5.39	5.5-8.5	ALT, U/L	25	20-50
MCV, fl	63.1	60-77	AST, U/L	2.19	2.5-11.4
WBC, G/L	9.4	6-17	BUN,	46.1	41-121
Seg,G/L	6.016	3.6-11.5	mmol/l		
Bands, G/L	0.282	0-0.3	Creatinine,		
Metamyelo,	0.188	0	µmol/l		
G/L	0	0			
Myelo, G/L	0.376	0.01-1.25			
Eos, G/L	0	0-0.1			
Basos, G/L	2.256	1-4.8			
Lymphs, G/l	0.282	0.15-1.35			
Monos, G/L					

An X-ray examination (*TUR-800*, *Germany*; 60kW, 16 mAs) of thoracolumbar spine was compatible with L_3 spondylitis or vertebral neoplastic process. The presence of irregular shape of L_3 vertebral body with lytic

and sclerotic changes in it, irregular shape of intervertebral foramina L_2 - L_3 and L_3 - L_4 , ventral osseous proliferation and slightly decrease dorsal L_3 - L_4 intervertebral space was observed on the lateral view (**Figure 3**).



Figure 3. On the plain radiographs in a lateral view are visible deformation and sclerosis of L_3 ; irregular shapes of L_2 - L_3 and L_3 - L_4 intervertebral foramina (white arrowhead), new bone proliferation ventrally (black arrows). Note sharply-outlined intervertebral space and end-plates of L_3 .

A sterile swab was used to obtain material for cultural examination after surgical approach to the affected vertebra. Material was incubated in blood agar and Saburo dextrose medium by 37°C in anaerobic conditions for 48 hours. Whitish colonies with smooth surfaces and size 4-5mm were observed. After Gram and methylenblue staining of the colonies, a Saccharomyces cells with typical thin cell walls and round shape were observed by microscopic examination. A small amount of inoculums was suspended in 0.5ml sheep's serum and was incubated by 37°C for 2 hours. Drops of inoculums were observed by light microscopy. Candida albicans was identified by its typical germinal cell forms.

After skin incision and soft tissue retraction a vertebral body biopsy using Rochester Bone Biopsy needle was made by sampling cells from different areas of the affected vertebra. Several touch preparations were made. The material for cytologic evaluation was fixed with Merckofix spray (Merck, Darmstadt, Germany) and stained Hemacolor[®] (Merck with Darmstadt. Germany). Cytologycally, a granulomatous inflammation with many macrophages, neutrophils, plasma cells and erythrocytes was found. Numerous fungal organisms (hyphae and spores) were seen throughout the slide (Figure 4).

According to these results, a presumptive diagnosis of vertebral osteomyelitis was established and treatment with oral



Figure 4. Vertebral candidiasis in a dog – cytological finding: Pyogranulomatous inflammation, presented by multiple macrophages, neutrophils, plasma cells and erythrocytes. Note the spores [1] and fungal hyphae [2] (arrows). There is no evidence of neoplasia. Hemacolor stain, x 1000.

ketoconazole (Nizoral®. Janssen *Pharmaceutica*, *Belgium*) 20mg/kg per 12 hours was prescribed along with local tissue debridment. An intensive curettage after exploration of all sinus tracks was made. No foreign body was found. All necrotic tissues and debris were removed. The wounds were washed with 0.05% chlorhexidine gluconate (Hibitane[®]. Medical solution gmbh, Steinhausen) and 10% povidon-iod (Braunol®, B. Braun Melsungen AG, Melsungen) for several days and left to heal by second intention.

After the initial deterioration, which was probably due to the surgical treatment, a slight clinical improvement with increased appetite and activity was observed on the 18th day. Full recovery was achieved after 35 days. The dog was still well on the check-up made 1.5 year later.

DISCUSSION

Vertebral osteomyelitis is defined as infection confined to the vertebral body whereas diskospondylitis is an infection of the intervertebral disk with concurrent osteomyelitis of adjacent vertebral end-plates and vertebral bodies (4). The two diseases often go together.

In the dog, the infection has been attributed mostly to *Staphylococcus aureus*, *Brucella canis*, *Streptococcus spp*, , *Escherichia Coli* (5), *Nocardia spp*. (6), *Corynebacterium spp*, *Paecilomyces sp*. (7), and grass-seed foreign body penetration with secondary infection (8). Other organisms reported in dogs and cats include some anaerobes - Actinomyces viscosum, Bacteroides spp., Clostridium vilosum (9), Actinobacillus spp. (10), Pseudomonas spp., Pasteurella spp. and various mycotic organisms, particularly Aspergillus spp. (11).

Candida species uncommonly cause vertebral osteomyelitis but 62% of all candidal vertebral osteomyelites are due to *C. albicans* (2). Candida species are typically considered commensal organisms and a part of the normal microflora. Candidiasis is an opportunistic infection and principally manifests as a superficial mycosis of mucous membranes such as oral mucosa, and skin. Systemic candidiasis is less common and may affect several organs including lymph nodes, kidneys, pancreas, prostate gland, spleen, thyroid glands, heart, and spine and very often lead to dead (3).

The nidus arises from haematogenous spread (12), from migrating foreign bodies, penetrating bite or gunshot wounds, or previous surgery (11). In our case the presumed source of infection was also a soft tissue injury of the lumbar region.

Possible sources for a septicaemia and access include haematogenous dental extraction - 66% of dogs and 80% of humans (13), genitourinary infection, and some diagnostic procedures such as endoscopy, biopsy, urinary catheterisation, which may damage the respiratory, digestive, or urogenital mucosa, that harbour a saprophytic microbial flora. According to Cabassu and Moissonnier (12) haematogenous osteomyelitis is very rare whereas Walker et al. (14) claimed that infection of the spine via the bloodstream was the most common route in dogs. The presence of fungi in bone alone is not enough to cause disease. Several risk factors were associated with fungaemia and invasive candidiasis, including local and systemic conditions.

Alterations in the vertebral microcirculation, which occur in trauma and important surgery, are cofactors in development of a vertebral focus of infection. Microorganisms tend to accumulate in vertebral circulation, because of reduced concentration of phagocyte cells here, the presence of nonanastomotic branches of capillary loops, and easy microtrombus formation (11).

The changes of the normal microbial flora, that occur in prolonged antibiotic use, and immunosuppression after steroid use, surgery, parvovirus and feline panleucopaenia virus infection, and diabetes has been implicated in the susceptibility to a haematogenous spread of mycoses (15, 7, 16, 3).

As in our case, a history of trauma was noted in the most of cases with osteomyelitis (9, 17) and the trauma was considered a contributing factor of susceptibility to disease localization. Direct extension of an infective process through foreign body migration from a percutaneous entrance or through the bowel wall has been described (8. 18). Diskospondylitis (diskitis) has occurred after disk surgery in humans and in dogs after prophylactic disk fenestration (4).

Age at presentation was generally less than 4 years but was reported to range from 8 months to 10 years. Large and giant breed dogs predominate, with affected males outnumbering females approximately 2 to 1 and purebred dogs, especially German shepherds and Great Danes were most often represented (4, 5).

The clinical and laboratory characteristics of patients with candidal vertebral osteomyelitis were similar to those described for patients with bacterial and Aspergillus vertebral osteomyelitis (2). The signs vary in severity and may mimic other diseases. Spinal pain and neurological deficit are readily recognized, but the subtleties of depression, sometimes fever, loss of appetite, and weight loss (4) may be confusing early in the course of the disease. Back pain is the primary and may be the only sign of spondylitis and discospondylitis (19). We also found a back pain in the present case. Fistulas are typical for the presence of foreign body but such was not found.

Neurological signs occur later as an aftermath of the infection. If the disease progresses and involves the nerve roots and spinal cord, more definitive signs referable to the nervous system are noticeable, primarily as paresis/paralysis caudal to the lesion. The latter seldom occurs in the absence of pathologic fractures. We observed neurological signs later in the course of the disease comprising of an increased muscle tone and proprioceptive deficit of hind limbs,

dorsal deviation of the trunk, depressed anal sphincter reflex, and loss of superficial sensation caudal to L₄-L₅. A stilted gait or arched back are considered nonspecific, because they could be caused by numerous conditions from intervertebral disk disease to prostatitis, renal or urethral calculi, to hip dysplasia. In children with intervertebral disk inflammation, the most common symptoms are back or hip pain and a refusal to walk (20). Reluctance to walk in a dog with no preexisting or documented musculoskeletal or neurological problems could be an early premonitory sign but was not observed in this case. The severity of the lesion does not always correspond to the clinical signs. The duration of signs prior to presentation vary but usually last at least 1 month.

The diagnosis of candidal vertebral osteomyelitis is based on the clinical signs, radiographic confirmation of a compatible lesion, and identification of the etiological agent.

The radiographic changes are essential to obtain the diagnosis and reflect the underlying pathophysiologic processes but the radiographic changes may not occur until 4 to 6 weeks after the infection is established (21). The most common site affected are lower thoracic and lumbosacral spine (2). Plain radiographs show varying degrees of vertebral lysis, sclerosis, and proliferative bony changes, which lead to vertebral body deformation and with shortening possible fractures or instability. In the present case, radiographic mentioned examination revealed afore characteristics of spondylitis.

The disease should be differentiated from diskospondylitis, vertebral alterations associated with plant-derived foreign bodies and bone neoplasia. The classic appearance of diskospondylisis was bony destruction on both sides of the disk with irregular end-plates` surfaces and widening or narrowing of the disk space (4), which was not obvious in our case. Plant-derived foreign bodies tend to migrate along fascial planes, because of their shape and aided by active muscle contractions. They radiographic induce typical images characterized by osseous proliferations along the ventral surfaces of the vertebral bodies from L₂ to L₄. The letter two diseases were excluded later by histological examination and surgical exploration of the sinus tracks.

Blood chemical and haematological values are usually normal, as we observed, although a nonspecific leukocytosis may be present. In human, an elevated erythrocyte sedimentation rate was frequently found (2) but it was not measured in our case.

Because of the number of bacteria, actinomycetes, mycobacteria, and fungi are capable of causing spondylitis, an exact discovery of the cause is very important. Moreover, these causative agents require vastly different therapies and some are associated with toxicities.

The definitive microbiological diagnosis of candidal vertebral osteomyelitis is made by culturing of biopsy specimen or histocytological examination (1). Bone and blood isolates have similar identical sensitivities (22), which provides reasonable assurance that the organism from the bone is the causative agent. Both the microbiologic and histological results confirmed the presence of *Candida spp*. in the affected vertebra in our case.

The treatment of patients with candidal vertebral osteomyelitis consisted of both surgical and medical interventions. The surgical primary interventions were debridement and if necessary bone grafting, vertebral fusion, or prosthetic support (2). An accurate microbiologic diagnosis followed by appropriate antimycotic therapy is extremely important. The specific Candida species should also be definitively identified to guide therapy, because antifungal susceptibilities of Candida species are variable. C. albicans is routinely susceptible to fluconazole and ketoconazole, whereas C. krusei is routinely resistant (23). C. albicans was the predominant organism responsible for the most cases of candidal vertebral osteomyelitis (2).

Antifungal therapy should last for at least 4 to 6 weeks. Some authors recommend systemic application of amphotericin B initially, followed by oral azole treatment (2). of high nephrotoxicity Because its amphotericin B is not recommended for longterm treatment in dogs. Ketoconazole alone has been used successfully to treat even disseminated candidiasis after drug abuse in human (24). Fluconazole is often selected as the first line treatment because it is effective. has low incidence of adverse effects and is cost-effective (1).

The prognosis for patients with candidal vertebral osteomyelitis is good. The majority of patients had an outcome profile similar to that for patients with bacterial vertebral osteomyelitis (20). The cure rate for local vertebral mycosis was 85% (2) whereas systemic candidiasis is very severe disease with high mortality rate both in human and dog (1).

A successful outcome is most likely diagnosis with early and appropriate antimycotic therapy for prolonged periods of time in conjunction with surgery. Surgery is indicated in select cases for diagnostic and therapeutic procedures, but the prognosis is heavily influenced by the degree of neurological dysfunction with or without surgery. A successful endpoint is the elimination of infection, relief of pain, and return of neurological function.

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