



Hypertrophic Osteopathy in a Two-years-old Belgian Shepherd Associated with a *Pantoea agglomerans* Infective Endocarditis

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Received: March 22, 2021

Published: April 28, 2021

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Abstract

The association of an infective valvular endocarditis and a hypertrophic osteopathy in a young dog is considered as rare. The latter case is usually due to an intra-thoracic lesion but the association with a cardiac disease has only been reported in a few numbers of cases.

A 2 years old Belgian shepherd military dog is presented to the French Army Referral Center, 24th Veterinary Group of Suippes, for an hypertrophic osteopathy due to an infective valvular endocarditis caused by *Pantoea agglomerans*, confirmed by a blood culture.

To our acknowledgement, it is the first published case of dog infection by *Pantoea agglomerans*, an emerging, zoonotic, soil related and nosocomial bacteria in human infectious diseases.

Keywords: *Pantoea agglomerans*; Infections; Endocarditis; Hypertrophic Osteopathy; Dog

Key Clinical Message:

- Endocarditis must be included in the hypertrophic osteopathy differential diagnosis in the dog.
- *Pantoea agglomerans*, an emerging, bacteria in human infectious diseases can also be found in dogs.

Introduction

Hypertrophic osteopathy, formerly known as osteoperiostitis, is a rare condition in dogs, mainly occurring in association with a thoracic disease [1]. But unusual association can occur.

This case is one of them, associating an emerging and never described in dogs bacteria: *Pantoea agglomerans*.

Pantoea agglomerans is a Gram-negative, non encapsulated, non spore-forming ubiquitous bacterium formerly known as *Enterobacter Agglomerans*, *Erwinia herbicola* [11].

Case Description

A two-years-old sexually intact male Belgian Shepherd was presented at the 24th Veterinary Group of Suippes (French Army Vet-

erinary Referral Center) for a bilateral forelegs lameness and a history of lethargy, decreased appetite. The dog was housed in a kennel of 600 congeners and was used as a military working dog. He never left French territory and was up to date with his vaccinations and deworming and had no history of trauma.

Clinical and radiographical results

On physical examination, the dog had a normal rectal temperature, a regular heart rhythm with no heart murmur. Transrectal prostate exam shows no anomaly. Mild lameness and bilaterally symmetrical nonoedematous soft tissue swelling on both forelimbs were determined in clinical evaluations. Pain was detected on all legs by palpation. No other abnormality was observed and the patient's life conditions seemed normal.

No abnormality was detected in the chest X-rays (three views) or in the abdominal ultrasound examination performed. In addition, new periosteal bone formation was observed in all appendicular bones, compatible with hypertrophic osteopathy (Image 1 - Right carpus; Image 2 - Left carpus; Image 3 - Carpus, front view; Image 4 - Tarsus, front view; Image 5 - Left Tarsus; Image 6 - Right Tarsus).

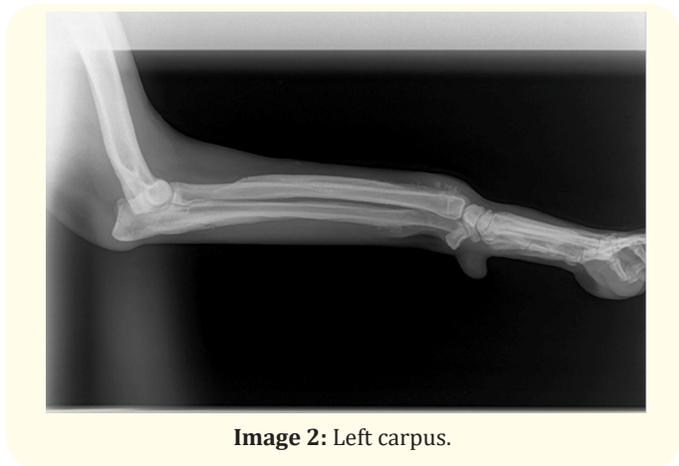


Image 2: Left carpus.

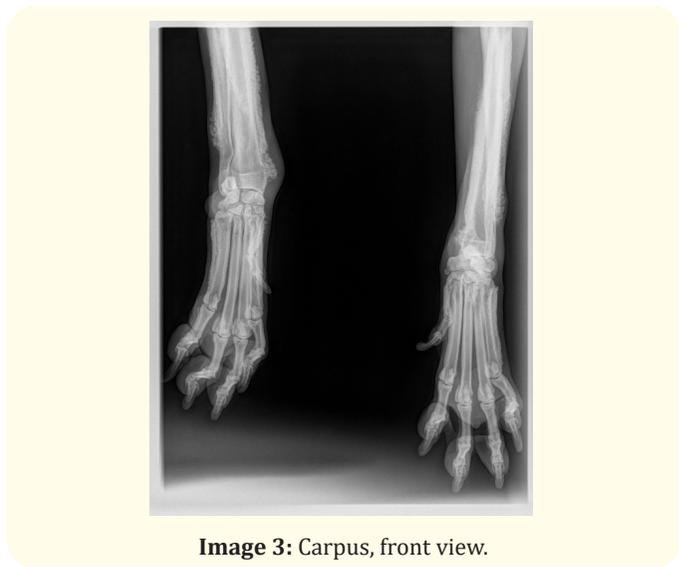


Image 3: Carpus, front view.

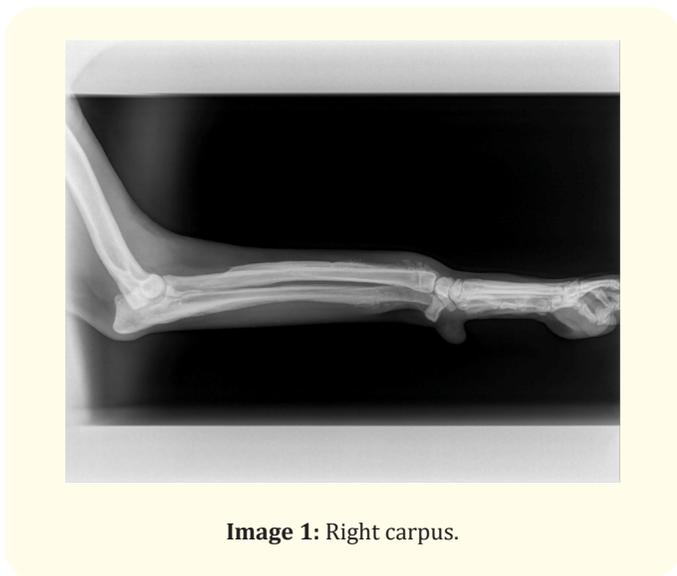


Image 1: Right carpus.

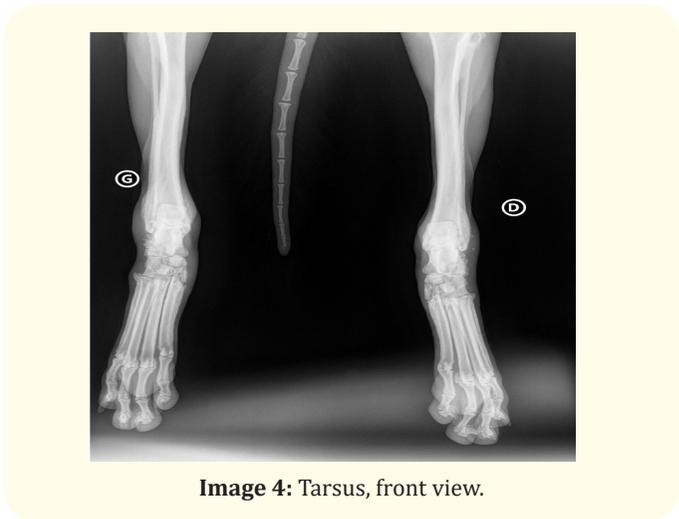


Image 4: Tarsus, front view.



Image 5: Left Tarsus.



Image 6: Right Tarsus.

Additional tests

A routine haematological and biochemical examination was carried out and showed an inflammatory syndrome (marked leucocytosis, biochemistry in the usual values). A heartworm test (Idexx 4DX) was performed and negative. An electrocardiogram and an echocardiography were performed. The last one revealed a one cm diameter irregular mass attached to the mitral valve highly suggestive signs of vegetative endocarditis with a slight pericardial effusion (Image 7 - Echocardiography of the dog). Bacterial endocarditis was suspected and a blood culture is performed by multiple phlebotomies. It highlights the *Pantoea agglomerans* Bacteria.



Image 7: Echocardiography of the dog.

Clinical evolution

Probabilistic antibiotic therapy was performed with a combination of amoxicillin and clavulanic acid (20 mg/kg TID intravenously). Unfortunately, the dog died of cardiac decompensating associated with a systemic inflammatory response syndrome before getting the blood culture results within a week.

Post-mortem examination

The autopsy showed severe endocarditis lesions on the mitral valve. A sterile sample of the abnormal tissues was taken and sent for histological analysis. This revealed the presence of the same bacteria confirming our diagnosis of endocarditis caused by *Pantoea agglomerans*. Disseminated abscesses, in particular at the renal and splenic level, were also revealed.

Discussion

Hypertrophic osteopathy, was first described in humans in the late 1800s [1]. There is archaeological evidence for its occurrence even in the ancient world, and it was almost certainly described by Hippocrates [2]. Hypertrophic osteopathy is also known by different names, including osteoperiostitis, hypertrophic osteoarthropathy, hypertrophic pulmonary osteopathy, hypertrophic pulmonary osteoarthropathy, pulmonary osteoarthropathy, osteoporosis, and Marie's disease and Pierre Marie-Bamberger syndrome [3]. In ani-

mals, hypertrophic osteopathy is most commonly seen in dogs, but has also been reported in various other domestic animals, including horses, cow, sheep, cat and in exotic species [3-5].

In humans and animals, hypertrophic osteopathy is a rare disease process, secondary in nature, and usually occurs due to neoplastic or infectious masses in the chest cavity or, less often, a mass in the abdominal cavity [1,3].

In response to these masses, bilateral symmetrical, non-oedematous soft tissue swellings affect the distal portions of all forelimbs. These are quickly accompanied by a characteristic diffuse periosteal new bone formation outside the diaphysis of the long bones of the limbs, without destruction of the cortical bone. These changes cause mild to severe lameness. Bone changes start distally and spread proximally to involve the humerus and scapula, femur, and pelvis. Other bones such as the ribs and vertebrae are also sometimes affected. These bone changes are not primary neoplasia or metastatic bone lesions [1,3,5]. Although the joints are not affected, range of motion of the joints may be reduced due to periarticular soft tissue swelling; however, inflammatory changes in the synovial membrane of painful swollen joints have been reported in humans [1]. The formation of new periosteal bones has been described as 'palisades' or 'scalloped', resembling a city skyline, as these proliferations are either irregularly shaped perpendicular to the cortex or smooth in shape parallel to the cortex [1]. Intrathoracic lesions associated with the disease include metastatic lung neoplasms, lung abscesses, bacterial endocarditis, *Spirocerca lupi* granulomas, and canine tuberculosis, right to left shunting with a patent ductus arteriosus, oesophageal foreign body and congenital megaesophagus [1]. Intra-abdominal lesions associated with the disease include embryonic bladder rhabdomyosarcoma, liver adenocarcinoma, prostatic adenocarcinoma, and adrenocortical carcinoma [6,7].

Hypertrophic osteopathy is a rare sequel to infective endocarditis in dogs and there are only three published reports of dogs with suspected infectious endocarditis and hypertrophic osteopathy [8,9]. No further details are given and *Dirofilaria immitis* are often associated with no idea of the putative cause of the endocarditis [9]. In our case the Heartworm test was negative.

Infective endocarditis is an uncommon and very often lethal disease in veterinary medicine. The reported prevalence is low

[0,09%-6,6%] in dogs but the true prevalence in the general population is likely to be highly underestimated because of the difficulty to establish a diagnosis [10]. It arises from microbial colonisation and infection of the endothelial lining of the heart that are normally resistant to adherence and colonisation by microbial agents. The mitral and aortic valves are the most affected in small animals [10]. Dogs usually have an ill-defined history of nonspecific signs of extracardiac systemic illness including lethargy, weakness and weight loss (all seen in our case). Medium to large breed and middle-aged to older male dogs are most commonly affected with a German Shepherd predisposition in one study [10]. Murmurs and arrhythmias are heard in majority of dogs (respectively 89%-96% and 40%-70%) but were not heard in our case [10]. Echocardiography is the most important tool to diagnose infectious endocarditis. The pathognomonic lesion is a hyperechoic, oscillating, irregular-shaped mass adherent to, yet distinct from, the endothelial cardiac surface [10]. The main differential for echocardiographic diagnosis of infectious endocarditis of the mitral valve is valve degeneration with a better prognosis.

Once diagnosed, infective endocarditis is almost invariably associated with a poor prognosis and the death by acute congestive heart failure, fatal cardiac arrhythmias and/or thromboembolic diseases of one or several organs, and thus despite the treatment [9,10]. In one study the median survival was only 3 days [10].

Blood culture before treatment with antibiotics is an essential tool to support the diagnosis and aid proper selection of antimicrobial treatment, which is the cornerstone therapy owing to the bacteraemia and endothelial disruption necessity for creating an infective endocarditis. Transient bacteraemia can occur after a medical or surgical procedure involving mucosal trauma, localised infection such as abscesses, pyoderma, prostatitis, pneumonia, diskopyndylitis, urinary tract infection, periodontal disease, and long-term indwelling central venous catheter [10].

Some bacterial characteristics may facilitate bacterial adhesion and vascular colonisation.

Pending the results of the blood culture and the antibiogram, empiric treatment with a broad spectrum antibiotic and good serum concentration and tissue penetration is necessary. Betalactams and cephalosporins are thus indicated. We decided to start with an association of amoxicillin and clavulanate.

Staphylococcus species (*aureus*, *intermedius*), *Streptococcus* species (*canis*, *bovis* and β -hemolytic) and *Escherichia Coli* account for over half of the infectious agents isolated in canine infectious endocarditis in order of frequency. Less common bacterial isolates include *Pseudomonas*, *Erysipelothrix rhusiopathiae*, *Enterobacter*, *Pasteurella*, *Corynebacterium* and *Proteus*. Rare causes include *Bordetella avium*, *Actinomyces* species [10]. Recently *Bartonella* species has been identified as an important infectious agent in both canine and human endocarditis [10].

To date, no case has been described with *Pantoea agglomerans* in the dog.

Pantoea agglomerans is a Gram-negative, non encapsulated, non spore-forming ubiquitous bacterium formerly known as *Enterobacter Agglomerans*, *Erwinia herbicola* [11]. It is both an epiphytic microbe developing on the surface of plants and an endophytic organism living inside plants [12]. The bacterium also occurs abundantly in plant, animal products, body of arthropods and other animals, in water, soil, dust and air, and occasionally in humans [12,13]. In people, it is mainly known as the cause of byssinosis and other respiratory disorders by exposition to inhalation of organic dusts, mainly from cotton [14]. However, it can also produce substances effective in the treatment of cancer, and other diseases of humans and animals, suppresses the development of various plant pathogens by antibiotic production and/or competition [15-17].

There are only few reports on infections caused by *Pantoea agglomerans* in vertebrate animals [17]. It has been identified as a possible cause of equine abortion, as one of the causative agents of equine placentitis, and as a possible cause of allergic pulmonary diseases in cows [17]. It can be isolated on healthy vertebrate animals on skin, digestive tracts and in fishes where it can be the cause of a hemorrhagic disease [17].

It is also isolated from arthropods, mostly insects and ticks such as *Dermacentor reticulatus* [17,18].

Pantoea agglomerans is the most prominent species of the genus *Pantoea* in humans [19]. Because of the few cases described, there is not enough information on the pathogenic mechanism, but can be a cause of the opportunistic human infections in two situations: wound infection (35,7% of the cases) with plant material

and hospital acquired infection occurring mostly in immunocompromised persons [19,20].

P. agglomerans wound infection could follow piercing or laceration of the skin with a vegetal thorn, made of wood fragments or other plant material, usually during execution agricultural occupations, during gardening or children playing and following inoculation of plant bacteria [21-24]. Recently, Vaiman., *et al.* [25] found in a retrospective study that the nine patients with one to two months of ineffective post-traumatic wound treatment showed the presence of foreign bodies of plant origin infected with *Pantoea agglomerans*. Withdrawal from abroad the bodies led to rapid healing of the wounds within two to three days. Septic arthritis or synovitis appears as a common clinical finding exogenous infection with *P. agglomerans*, others include endophthalmitis, acute unilateral dacryocystitis, specific by the genus eye contaminant - not plant material but dog feces, corneal infiltrate in a farm worker after rice pod lesions, caused by *Pantoea ananatis*, a closely related species linked to *P. agglomerans*, periostitis, endocarditis, osteomyelitis after injury with rose thorn or after closed fracture, tibial osteitis after open grade IIIB tibial shaft fracture and tumor-like muscle cyst the thigh [21,22,24,26-30]. Exposure of hospitalized, often immunocompromised individuals, medical equipment or fluids contaminated with *P. agglomerans* is another major reason for clinical infections with this bacterium. Some nosocomial infections are described as "sporadic" or "endogenous" since they are not clearly explained but all seen in immunocompromised patients [31-35]. *P. agglomerans* may cause serious morbidity and mortality, especially in young patients with underlying comorbidities. Community acquired and hospital acquired cases of *P. agglomerans* infection may have different pathogenic and clinical features [20].

Conclusion

Pantoea agglomerans is widespread among invertebrate and vertebrate animals. It has an opportunistic pathogen character and, because of the real diverse clinical picture, then this bacteria has been classified as an emerging pathogen in human medicine and further large-scale studies are needed to investigate its clinical and pathogenic characteristics. Its clinical significance in domestic and farm animals is almost unknown.

It appears here to be a possible cause of infectious endocarditis in dogs. Our hypothesis is that our dog has suffered from a plant

trauma that went unnoticed with a secondary bacteraemia causing an infectious endocarditis.

Moreover, it should henceforth be sought in the rare combination of endocarditis and hypertrophic osteopathy.

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