**Candida glabrata Septicemia in a Piglet**

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**ABSTRACT**

**Background:** *Candida* organisms are ubiquitous pathogens that may cause mucosal or systemic infection in humans and animals. *Candida albicans* was the main *Candida* specie associated with cases of systemic candidosis, and *Candida glabrata* is the second most isolated in those cases. In animals there are few reports of candidosis. In pigs *C. albicans* was described as mucocutaneous disease affecting oral mucosa, esophagus and aglandular stomach of pigs affected by porcine circovirus type 2. Systemic invasion by *Candida* species in pigs is rare. This report describes the pathological changes observed in a case of systemic candidosis due to *C. glabrata* infection in a piglet.

**Case:** In a nursery facility with 500 piglets a 47-days-old piglet showed lateral recumbency that progressed to inability to stand, paddling and death. In the necropsy it was observed valvular vegetative endocarditis in the left atrio-ventricular valve and in the kidneys multifocal to coalescing whitish foci in the sub-capsular and in the cut surface. Microscopical examination of the cerebral cortex, brain steam and cerebellum revealed multifocal random necrotic suppurative foci surrounded by mononuclear cells, epithelioid and multinucleated giant cells together with discret linfoplasmocitic meningitis. In the kidneys there was embolic suppurative nephritis with multifocal abscesses in renal parenchyma, characterized by large amount of neutrophils surrounded by mononuclear cells. In the left valve surface of the hearth there was extensive proliferation of connective tissue with large amount of fibrin, neutrophils and intralesional Gram-positive bacterial colonies with coccoid shape morphology. In brain, hearth and kidneys slides stained with Grocott´s methenamine silver and periodic acid-Schiff technique a large amount of yeasts cells round to ovoid in shape were observed associated with necrotic foci and in multinucleated giants cells.

**Discussion:** In the present report, a 47-days-old weaned piglet showed neurological signs that suggested a *Streptococcus suis* meninitis, and a presumptive diagnostic was reached based on those signs. Antibiotic therapy with amoxicillin was attempted, but there was no improvement in the clinical signs and the piglet died. *S. suis* was not isolated in the bacteriological analysis, however, PCR technique allowed the detection of the pathogen from the heart, raising the possibility for a role of the agent in the endocardial lesion, but not in the brain. *Candida glabrata* was detected in the hearth, kidneys and brain suggesting a septicemic spread candidosis in the piglet. Due to the presence of *C. glabrata* in the piogranulomatous lesions observed in the brain we assumed that the neurological signs were associated with the candidal infection. In humans, it is described the association among intracardiac candidal infection and an increased risk for the development of central nervous system infection. A recent study in slaughter pigs have shown that brain lesions associated with bacterial valvular endocarditis are common. Immunosuppression, low birth weight and broad spectrum antibiotic therapy are among the predisposing factor to the development of septicemic candidosis. In our case report, the piglet was the lighter in the litter at weaning and in the day of necropsy, besides antibiotic therapy was attempted twice in the piglet what could act as another predisposing factor for the septicemic candidosis. This was an unusual case of systemic candidosis with brain involvement and neurological clinical signs associated, due to *C. glabrata* infection in a piglet.

**Keywords:** *Candida glabrata*, systemic candidosis, systemic candidiasis, piglet.
INTRODUCTION

Candida organisms are ubiquitous pathogens that may cause mucosal (mucocutaneous) or systemic (invasive) infection in humans and animals. Invasive candidosis has increased significantly and is an important cause of nosocomial infection in hospitalized patients [3]. Broad spectrum antibiotic, immunosuppression, intravascular catheters and babies with low birth weight are among the major risk factors for septicemic candidosis [3]. Candida albicans was the main Candida specie associated with cases of systemic candidosis, however in recent years the role of non-albicans Candida species are increasing and Candida glabrata is the second most isolated in those cases [1].

In animals there are few reports of candidosis [10] in comparison to the high number of cases reported in humans, besides, the occurrence of Candida infections in domestic animals is not as well known as it is in humans [2]. In pigs C. albicans was described as mucocutaneous disease affecting oral mucosa, esophagus and aglandular stomach of pigs affected by porcine circovirus type 2 (PCV-2) [13]. C. glabrata was associated with pre-ulcerative changes to the pars oesophagea [8], however systemic invasion by Candida species in pigs is rare [5]. This report describes the pathological changes observed in a case of systemic candidosis due to C. glabrata infection in a piglet associated with S. suis endocarditis.

CASE

In a nursery facility with 500 piglets ranging from 21 to 65 days-old, a 47 days-old piglet showed incoordination and received antibiotic treatment with amoxicillin during 3 days. Five days after the ending of the treatment the piglet was found in lateral recumbency with inability to stand and paddling. The treatment with amoxicillin was repeated in the therapeutic dose with no improvement in the clinical signs and evolution to death. Necropsy was performed for diagnostic purpose and sections from several tissues were collected and fixed in buffered 10% formalin, prepared by standard histological methods and stained with haematoxylin and eosin. Brain, kidney and heart were additionally stained with Grocott’s methamine silver (GMS) and periodic acid–Schiff (PAS) to detect fungal structures and Brown Gram stain to detect bacterial structures. The main macroscopical findings were valvular vegetative endocarditis in the left atrio-ventricular valve and in the kidneys multifocal to coalescing whitish foci in the sub-capsular and in the cut surface with predominant involvement of the renal cortex.

Histological findings of the cerebral cortex, brain steam and cerebellum revealed multifocal necrosis in the gray and white matter with large amount of degenerated neutrophils surrounded by mononuclear cells (Figure 1), epithelioid and multinucleated giants cells together with discrete linfoplasmocitic meningitis. Perivascular edema with slight multifocal cuffing of mononuclear cells around small capillaries was also observed. In the kidneys there was embolic suppurative nephritis with multifocal abscesses in renal parenchyma, characterized by large amount of neutrophils surrounded by mononuclear cells. In the valvular surface of the hearth there was extensive proliferation of connective tissues with large amount of fibrin, neutrophils and intralesional Gram-positive bacterial colonies with coccoid shape morphology. Adjacent to the valvular surface, there was myocarditis with few neutrophils, macrophages and lymphocytes. In brain, hearth and kidneys slides stained with GMS and PAS technique a large amount of yeasts cells round to ovoid in shape were observed associated with necrotic foci and in multinucleated giants cells (Figure 2).

Immunohistochemical (IHC) to detect porcine circovirus type 2 (PCV-2) was performed in mesenteric lymph node, spleen and lung using polyclonal rabbit antibody to PCV2 [11] at 1:1000 dilution, incubated for 1 h and stained by the streptavidin-biotin immunoperoxidase technique using diaminobenzidine¹ as chromogen. PCV-2 IHC results negative.

Lymph node, spleen, kidney, lung and liquor were submitted to bacteriological identification. There was no bacterial growing or isolation of pathogenic bacteria in the tissues tested.

Brain and kidney fragments were submitted to mycological analysis. The material was inoculated in Agar Sabouraud Dextrose medium² with the presence of round to oval blastoconidia without the production of chlamydospores and negative germinative tubes. To the identification of the species the API ID32C³ yeast identification gallery was applied [12]. The tests results were positive to C. glabrata.

PCR to detect Streptococcus suis (S. suis) type 2 was performed in frozen fragment from brain and lung and in formalin-fixed, paraffin-embedded (FFPE) fragment from heart [7]. The heart fragment was positive to S. suis type 2, the brain and lungs were negative.
DISCUSSION

The current study presents a case of septicemic candidosis due to *C. glabrata* infection in a piglet associated with *Streptococcus suis* endocarditis and describes the pathological changes observed. Meningitis is the most striking feature of *S. suis* infection in weaned piglets, although, in slaughter pigs endocarditis due to *S. suis* infection is a common finding [6]. In the present report, a 47-days-old weaned piglet showed neurological signs that suggested a *S. suis* meningitis, and a presumptive diagnostic was reached based on those signs. Antibiotic therapy with amoxicillin was attempted, but there was no improvement in the clinical signs and the piglet died. *S. suis* was not isolated in the bacteriological analysis, however, PCR technique allowed the detection of the pathogen from the heart, raising the possibility for a role of the agent in the endocardial lesion.

*Candida glabrata* is a haploid fungus that grows only in the yeast form and does not form hyphae, which is an important mechanism to penetration to the deeper tissues and the bloodstream. A possible route for *C. glabrata* to reach the circulatory system is breaching the natural barriers (via trauma, catheters, surgery). In some cases, *C. glabrata* may exploit the tissue destruction caused by *C. albicans* to gain nutrients and possibly even to access blood stream [1]. In the reported case, *S. suis* endocarditis possibly facilitated *C. glabrata* dissemination to the arterial bloodstream and presence of the fungus in the kidneys and brain.

Immunosupression is a well known and described predisposing factor associated with candidosis in humans and animals [3,5]. In pigs, immunosupression due to PCV-2 infection was associated with mucocutaneous candidosis in piglets [13]. In our case, PCV-2 was not detected in the piglet. Low birth weight is a predisposing factor associated with the development of systemic candidosis in babies [3]. In swine production, birth weight is a major determinant of colostrum intake, an important factor for the survival and development of the piglet. Lower birth weight piglets had lower vitality and are less likely to have an adequate colostrum intake, which is important to the acquisition of good passive immunity and in the development of the active immunity [4]. In our case report, the piglet was the lighter in the litter at weaning and in the day of necropsy. It is possible that the low weight of this piglet predisposed him to the infection with *S. suis*, due to a lack of a good passive immunity, facilitating the invasion with *C. glabrata* and the development of systemic candidosis. Broad spectrum antibiotic therapy is another predisposing factor to the development of Candida infection well described in humans [3] and animals [10]. Antibiotic therapy was attempted twice in the piglet what could act as another predisposing factor for the systemic candidal infection, together with the low birth weight.

The neurological signs showed by the piglet were supposed to be caused by a Streptococcal infection, however, *Streptococcus* was not found in the brain. Due to the presence of the fungus in the piogranulomatous lesions observed in the brain we assumed that the neurological signs were associated with the candidal infection. In humans, it is described the as-
Association among intracardiac candidal infection and an increased risk for the development of central nervous system infection [9]. A recent study in slaughter pigs have shown that brain lesions associated with valvular endocarditis are common [6]. Although, in those report only bacterial agents were identified in the endocardial valves and associated with the brain lesions.

This was an unusual case of systemic candidosis with brain involvement and neurological clinical signs associated, due to Candida glabrata infection in a piglet.

Sources and manufacturers
1 DAKO LSAB 2 kit, DAKOCorp., Carpinteria, CA, USA.
2 Agar Sabouraud Dextrose Medium, Oxoid, Hampshire, U.K.
3 API ID32C, BioMerieux, Marcy l’Etoile, France.

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