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Review

Trueperella pyogenes infections in swine: clinical course and pathology

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Abstract

Trueperella pyogenes is an opportunistic pathogen causing purulent infections in pigs and other animal species. T. pyogenes infections in pigs are local and/or generalized depending on the immune status of the animals, their individual susceptibility and environmental factors. The occurrence of these infections on pig farms causes substantial economic losses in breeding and rearing. In sows from the breeding herd, the disease leads to infertility, embryonic death, abortion, and disorders of the menstrual cycle and lactation. Mastitis is the major cause of losses in piglets. Disorders of the musculoskeletal system, including inflammatory polyarthritis, fractures and degenerative joint disease results in the culling of animals with high breeding value. In other technological groups, multi-organ inflammations and movement disorders dominate, leading to a reduction of the slaughter value and elimination of pigs from breeding. Understanding of the clinical and pathological aspects of T. pyogenes infections in pigs will enable the development of effective methods of combating this disease on pig farms.

Key words: *Trueperella pyogenes*, swine, clinical course, pathology

Trueperella pyogenes infections - predisposing and risk factors

Trueperella pyogenes is a ubiquitous opportunistic pathogen causing purulent infections in various species of domestic, wild and exotic animals as well as birds (Brinton et al. 1993, Billington et al. 2002, Lehnen et al. 2006, Hassan et al. 2009, Lin et al. 2010, Hijazin et al. 2011b, Al-Tarazi et al. 2012, Rzewuska et al. 2012). This microorganism is part of the commensal flora of the mucous membrane of the respiratory and urogenital tracts, and thus the cause of the infection, the clinical course of the disease and the risk of its occurrence in animals are often difficult to estimate. T. pyogenes infections in pigs have recently become a growing clinical and epidemiological problem, particularly evident on medium and large scale farms.

Pyogenic infections in swine are also important from the point of view of the economics of pig production. The most common consequence of the occurrence of these infections in farming is the culling of animals, as a result of the development of a generalized purulent process and in connection with reproductive disorders, leading to a reduction in reproductive rates, and thus a decline in profitability (Bradley 2002, Ertas et al. 2005, Silva et al. 2008).

The factors that lie at the root of the growing

threat posed to swine by opportunistic pathogens, such as T. pyogenes, are multiple. Intensification of pig production and the creation of large commodity farms foster the emergence of a variety of endogenous and exogenous factors that may affect the animals; health and the occurrence of infections, mainly of bacterial aetiology. Disorders of immune homeostasis associated with a decrease in immunity are a major cause of the occurrence of infections induced by conditionally pathogenic microorganisms. Such disorders are particularly likely to occur when the local and/or general immune response of the body is suppressed by the action of stress factors, contamination of the environment, preventive and therapeutic use of formulations reducing the activity of the immune system (immunosuppressants), prolonged antibiotic therapy and associated infections. An important group of factors predisposing to the development of overt T. pyogenes infections are functional disorders of the immune system, especially immunosuppression caused by concurrent infections with other pathogens, such as porcine reproductive and respiratory syndrome (PRRSV) and Aujeszky's disease virus (Pejsak et al. 2006).

The bacterial species most frequently isolated from clinical cases of infection with pathogens from the genus Trueperella occurring in different species of farm animals are T. pyogenes, T. bernardiae and T. abortisuis (Bradley 2002, Hijazin et al. 2011b, Yassin et al. 2011, Hijazin et al. 2012). The species which is the most often isolated from diseased pigs is T. pyogenes (Christensen et al. 2007, Azuma et al. 2009, Hijazin et al. 2012), which, as a common commensal of the skin and mucosae of the respiratory, genitourinary and gastrointestinal tracts, gives rise to purulent lesions in the co-presence of a variety of risk factors (Bradley 2002, Hassan et al. 2009). The development of endogenous infections is fostered, among others, by inflammation-initiating mechanical injuries, injuries to the skin and other tissues, or improperly performed surgical procedures (Sundberg 2000, Lin et al. 2010, Al-Tarazi et al. 2012). Purulent lesions generally form in tissues which have previously undergone an inflammatory process or tissues whose viability has been weakened by the action of other factors. For example, an improperly performed tail docking can lead to suppuration of the incision site, and, in consequence, to purulent osteomyelitis. Injuries to the mammary gland lead to mastitis and metastatic arthritis. Similarly, contamination and inflammation of the umbilical cord in neonates can lead to inflammation of the umbilical vein, which in turn causes sepsis due to T. pyogenes (Van Amersfoort et al. 2003, Meyer et al. 2005). The formation of purulent lesions involving T. pyogenes is often observed after castration and intramuscular injection performed without adherence to the principles of asepsis (Sundberg 2000, Houser et al. 2004, Hassan et al. 2009). These types of procedures may be complicated by spreading of the local inflammatory process within the scrotum, leading to the development of peritonitis; inflammation at the injection site, on the other hand, may favour the development of lymphangitis.

Disorders of the osteoarticular system

Disorders of the musculoskeletal system, including polyarthritis, fractures and osteoarthritis, which occur due to T. pyogenes infections, are an important cause of culling of sows from the breeding herd (Pejsak and Truszczyński 2013). It has been shown that in infected pig farms, 2 to 44% of female swine and pigs in the other sectors of production are culled and directed for slaughter each year (Yoshimura et al. 2000, Pejsak et al. 2006). The exact pathogenesis of the development of inflammatory lesions in the osteoarticular system is not fully understood. Presumably, their formation is additionally affected by genetic and nutrition-related factors, rapid growth of the animals, mechanical injuries and abnormal formation of joints (Houser et al. 2004, Ide et al. 2006). The consequences include aseptic necrosis of cartilage and bone, separation of epiphyses, mainly of the femur and ankylosing arthritis. The sequelae of polyarthritis in the course of T. pyogenes infection include bone fractures that occur most frequently within the metaphysis and the proximal epiphysis of the humerus and the femur. It has been shown that the pathological fractures observed in connection with T. pyogenes infections constitute up to 48% of all reported cases of fractures in pig farms (Jost et al. 2005). As a rule, they occur in the early stages of the development of the systemic form of the disease, in the period before the appearance of purulent lesions. 11% of cases of arthritis present with concurrent inflammation of bones, bone marrow and intervertebral discs, manifested in paralysis and recumbence of the animals, while 49% of cases show osteochondrosis (Jones and Ward 1989). It has been demonstrated experimentally that intravenous administration of T. pyogenes leads to accumulation of the bacteria in the bone marrow, predominantly in the epiphyses of the long bones, causing osteolysis, abscesses and the formation of bony projections called osteophytes (Lin et al. 2010). These types of lesions have been demonstrated, among others, in the case of experimental infection with T. pyogenes in turkeys (Brinton et al. 1993). Migration of bacteria from abscesses located in the joints or in the muscle tissue can lead to extensive myocarditis and



Fig. 1. Inflammatory and degenerative lesions of the mammary gland in the course of T. pyogenes infection.

associated heart valve damage (Van Amersfoort et al. 2003, Levy et al. 2009).

Osteoarthritis, which may occur in the course of *T*. pyogenes infection, is caused by cartilage fibrillation, mainly in the proximal epiphyses of the long bones, as well as erosions and ulcers of articular cartilage, the formation of so-called corrosion holes on the surface of cartilage and cracks and crevices with accompanying intra-articular ossification. Often at the root of these types of inflammatory lesions' are improper animal handling and inadequate structure of the bedding, which causes microtraumas to the hoof and facilitates infection. Other factors predisposing to the occurrence of joint diseases due to T. pyogenes include improper nutrition and genetic selection leading to the production of fast-growing efficient meat breeds at the cost of the proper function of the animals' musculoskeletal system.

The abscesses produced by *T. pyogenes* in the soft tissues around the bone lead to *osteomyelitis*, whose main clinical symptom is lameness (Ide et al. 2006). This process is often accompanied by symptoms of polyarthritis or intra-articular inflammation. The animals take the weight off the affected limb by extending it forward; they take a sitting stance, and in extreme cases recumbence is observed. The affected

joints are heavily swollen, deformed, painful, hot, and filled with yellow-green pus that drains outside through multiple fistulas (Fig. 3). The synovial membrane and the joint capsule are congested, swollen and thickened and are yellow or brown in colour. These lesions often lead to deforming, ankylosing arthritis, and in severe cases even to the development of sepsis. Sometimes diseased pigs present with hind limb paralysis and pyogenic osteomyelitis, leading to pathological fractures of the long bones and vertebrae and spinal cord compression (Ide et al. 2006). The pathogens that are most commonly isolated from inflamed joints are *T. pyogenes* and *Streptococcus spp.*, and more rarely *Staphylococcus aureus* and *Mycoplasma spp* (Zhao et al. 2011).

T. pyogenes infections of reproductive tract in sows

T. pyogenes-induced inflammations of the reproductive tract of breeding herd sows are characterized by individual specificity, which is connected with their different clinical courses and frequent difficulties in their diagnosis *in vivo* (Hassan et al. 2009, Ülbegi-Mohyla et al. 2010, Murakami et al. 2011). Sometimes the



Fig. 2. Lesions in the mammary gland of a sow infected with T. pyogenes. Visible purulent fistulas.

only, periodically appearing clinical sign of inflammation is a purulent discharge from the cervix and vagina. It is worth noting that such a condition is usually the result of mixed infections, most commonly caused by T. pyogenes, E. coli and F. necrophorum. A common clinical consequence of T. pyogenes infections in swine is a low reproductive rate, which is especially strongly expressed in asymptomatically infected sows (Kaneko et al. 2013, Pejsak and Truszczyński 2013). These disorders are manifested in reduced litter sizes, hard and long deliveries, delivery of weak piglets, and a lack of desire for mating in boars due to soreness in the extremities. An important issue in pig farming is also the need for early culling of sows from the breeding herd on farms infected with T. pyogenes (Jones and Ward 1989, Christensen et al. 2007, Azuma et al. 2009). The necessity to cull the sows is mainly associated with the occurrence of lesions in the reproductive system, leading to infertility, embryonic death, abortion, disorders of the menstrual cycle and the resulting lack of heat (Lehnen et al. 2006, Hijazin et al. 2011). Another important reason for culling from the herd are lactation disorders in sows manifesting in reduced milk yields or agalactia, which may result in nearly 50% of piglets dying in the period from birth to weaning (Zastępowska and Lassa 2012, Pejsak and Truszczyński 2013). The lesions caused by T. pyogenes in the sow's mammary gland make it impossible for piglets to properly intake colostrum and milk (Hijazin et al. 2011), (Fig. 1,2). As a consequence, the malnourished piglets become weak, runted and usually die within the first few days of life (these are "minus variants"). Damage to the mammary gland caused by infection with T. pyogenes also contributes to increased aggressiveness of sows induced by the pain felt during the act of sucking (Waage et al. 1999, Christensen et al. 2007, Murakami et al. 2011).





Fig. 3. Extensive swelling of the tarsal and knee joints in a grow-finish pig. Massive abscesses in the muscle tissue of the periarticular area, a fistula, and phlebitis are visible.

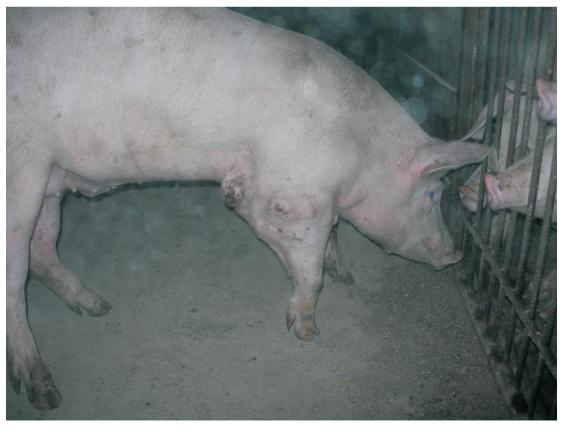


Fig. 4. Lesions in the elbow and shoulder joints and numerous superficial abscesses in a grow-finish pig.

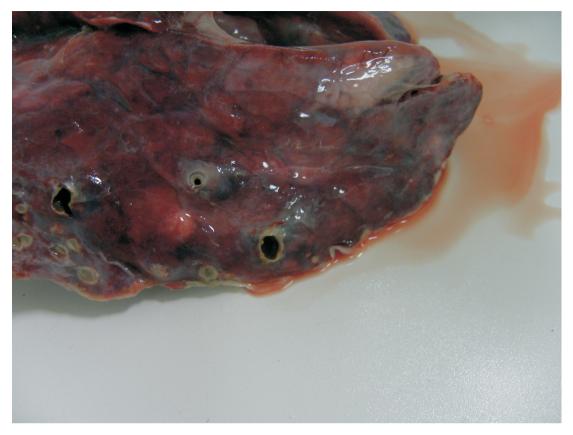


Fig. 5. Cavities in the lung tissue in the chronic form of infection with *T. pyogenes*.

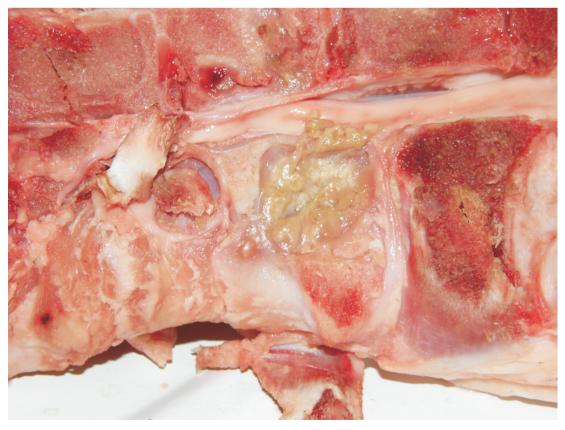


Fig. 6. A metastatic purulent focus causing spinal cord compression in the course of infection with *T. pyogenes*.





Fig. 7. A cross-section of a large muscular abscess and the surrounding tissue originating from a pig infected with T. pyogenes.

Suppurative processes in organs – the most typical clinical course of *T. pyogenes* infection in swine

The most typical clinical symptom of overt infection with T. pyogenes for all technological groups is the presence of abscesses in the subcutaneous tissue, organs or within muscles, which are only observable posthumously or during a post-mortem examination (Brinton et al. 1993, Lawson et al. 2001, Billington et al. 2002, Ertas et al. 2005, Jost et al. 2005, Ide et al. 2006, Moore et al. 2010, Ülbegi-Mohyla et al. 2010, Shahbazfar et al. 2013). A factor that contributes to the development of purulent lesions is the production by T. pyogenes of pyolysine and serine protease. The occurrence of abscesses in animal carcasses indirectly brings significant financial losses associated with the necessity to qualify the meat as unfit for human consumption (Levy et al. 2009, Kavitha et al. 2010), (Fig. 6). The size of the abscesses varies and ranges from a few millimetres to several centimetres in diameter (Fig. 7). Abscesses are surrounded by a rigid thick fibrous capsule with greenish-yellow pus inside that has a fluid or granular consistency (Yoshimura et al. 2000, Hermida et al. 2004, Zhao et al. 2013). Abscesses can be localized in various parts of the body, and a consequence of their formation is the development of purulent inflammations of bones, bone marrow, joints, lungs, cardiac muscle, uterus, kidneys, liver and mammary gland (Fig. 4). In the lung, Trueperella pyogenes usually produces a purulent-necrotic inflammation accompanied by pleurisy, multifocal vasculitis and thrombosis. The purulent process usually starts in the deeper layers of the lungs, gradually covering large areas of tissue with subsequent necrosis of pulmonary alveoli (Palmer and Whipple 1999, Hermida et al. 2004, Al-Tarazi et al. 2012, Rzewuska et al. 2012). Histopathological examination of the lung tissue reveals multifocal, confluent areas of necrosis containing cellular and fibrinous debris separated from healthy tissue with an infiltration consisting of neutrophils (Hoie et al. 1991). The multiple neutrophils present in these foci exhibit a significant degree of degeneration, manifested as hyperchromatosis and nuclear pyknosis. The remaining areas of the alveoli are filled with a fluid containing proteins, erythrocytes, neutrophils, macrophages and lymphocytes. A similar appearance is seen in small bronchioles, which are additionally filled with fibrin. Affected lungs are congested, and pulmonary veins, in each of their three layers, contain cellular-fibrinous clots with numerous neutrophils. The pus accumu-

lated in the lung tissue sometimes evacuates from the sites of inflammation, leaving empty cavities in places affected by the disease (Fig. 5). This leads to the spread of the infection within a given part of the lung or extension of the process to the neighbouring organs (Hermida et al. 2004).

In the case of abscesses located on a pig's extremities, the microorganisms isolated from the lesions usually constitute a mixed flora containing, besides T. pyogenes, also Fusobacterium necrophorum (Seimiya et al. 2004, Truszczyński and Pejsak 2005). It has been shown that the presence of F. necrophorum rods in infected tissues facilitates the proliferation of T. pyogenes, which in turn stimulates the growth of F. necrophorum (Seimiya et al. 2004, Silva et al. 2008). Purulent foci located on the extremities favour the formation of oedema and impose increased pressure on hoof tissues, which causes pain within the diseased sites, especially in the first phase of infection in the period of increased inflammatory response. Strongly expressed laminitis is usually diagnosed in obese animals and often coincides with the presence of abscesses in the central nervous system (Billington et al. 2002). The formation of purulent lesions on limbs is promoted by the adverse effect of environmental factors such as high air humidity and inadequate housing conditions. For example, the wrong type of bedding can cause limb injuries, and too high a density of the animals, formation of new groups, droving and transportation are major stressors. Laminitis develops quite rapidly, and the toxin produced by T. pyogenes may sometimes cause a fatal outcome within 48-72 hours. The limbs affected by the disease, usually the front legs, are swollen and hot; there is swelling at the coronary band with purulent exudate leaking from under the band. The skin at the coronary band and the metacarpal joint shows many focal necrotic lesions demarcated by an infiltration of neutrophils. Sick animals generally lie down, trying to decrease the load on the affected limb; coarse hair and hair loss as well as significant weight loss are observed. Radiographic examination shows small abscesses within the hoof wall and frequent fractures of phalanx bones, bone defects caused by osteolysis, numerous periosteal reactions, degenerative joint lesions and tissue necrosis. The long-term disease process in the extremities inevitably leads to the separation of the hoof wall (Edwards 2002).

In *T. pyogenes* infections in pigs, an affinity of the bacteria for the gastrointestinal tract and parenchymatous organs is also observed (Yoshimura et al. 2000, Jost et al. 2005, Al-Tarazi et al. 2012). PCR tests of gastric mucosal microflora using primers specific to the *T. pyogenes plo* gene performed in 5-19-week-old pigs showing signs of bleeding from the gastrointes-

tinal tract, have demonstrated that the microbe is found in the mucous membrane in 39% of cases of haemorrhagic gastritis (Jost et al. 2002a). It has not been elucidated so far whether these microorganisms are present in the stomach on a permanent basis or whether they locate themselves there temporarily but originally come from the oral cavity and the respiratory system, in which they live as commensals. Colonization of the gastric mucosa of pigs by T. pyogenes leads to considerable damage to the membrane, which may occur, for example, in inflammatory conditions of the stomach or in the presence of ulcers (Jost et al. 2002a). In these cases, the bacteria can pass through blood vessels into the liver and other parenchymatous organs, causing the formation of abscesses in them. White nodules, 1-5 mm in diameter, are then found in the liver and the renal cortex. Sometimes pulmonary congestion and vibices on the mucous membrane of the cecum are observed. T. pyogenes may also give rise to haemorrhagic necrotizing splenitis in pigs. In such cases, dark red haemorrhagic confluent nodules, 50 mm in diameter, with concurrent haemorrhagic inflammation of the regional lymph nodes, are observed. Histopathological preparations of the spleen show that the structure of the organ is impaired by the presence of necrotic cells saturated with hemosiderin.

Conclusion

The clinical symptoms and anatomopathological lesions observed in the course of infection with T. pyogenes in pigs show that the clinical course of the disease varies depending on the technology group and the organ-affinity of the bacterium. It is worth noting that beside the typical clinical course, T. pyogenes infections in pigs are often asymptomatic or the symptoms are atypical, which significantly restricts the diagnosis of the disease and effective medical and veterinary management. Detailed knowledge of all the clinical and pathological aspects of T. pyogenes infections in swine will contribute to the development of more effective methods of treatment and control of these infections in pigs. Early and immediate implementation of an appropriate medical program on infected farms is essential for reduction of the economic losses associated with the occurrence of T. pyogenes infections in pigs.

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