Perinatal mortality in dogs and cats

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Abstract

Canine and feline perinatal loss is a frequent and frustrating event for practitioners and breeders. Working on these cases can also be enigmatic and difficult for diagnostic pathologists to determine the cause of death. Typical conditions associated with canine perinatal loss include infectious disease, sepsis, pneumonia, congenital abnormalities, and trauma. Fading puppy syndrome is also a consideration. Currently, feline perinatal loss is not well characterized. Maternal health, a critical factor in perinatal losses, should also be assessed. Collecting an endometrial biopsy could constitute a critical part of this evaluation; however, more investigation is needed to correlate endometrial lesions to fertility.

Keywords: Abortion, fetal loss, dogs, cats, diagnostic pathology, perinatal mortality, necropsy

Introduction

Neonatal period in dogs is not well defined but is often referred to as a period from birth to 30 days. Additionally, the early neonatal period is defined as the first 7 days of life and the late neonatal period is considered 1 - 4 weeks. Perinatal mortality can be defined as death that take place before first week of life in addition to stillbirth. Defined percentages of litter loss in dogs are most frequently recorded in breeding colonies. Of all mortalities 55.6% occurred before the first week of life (including stillbirth) with a perinatal death percentage of 11.9%.[1] Perinatal loss in 10,810 litters in a Norwegian kennel club study was 8%.[2] Only limited information is available regarding feline perinatal loss, and studies performed were less discriminatory and lacked clear distinction between early and late neonatal loss. However, the percent of stillbirth has been characterized. In 14 litters, 4.7% of the kittens were stillbirths.[3] Analysis of a database comprised of French breeder litters described a rate of 8.5% over a 3-year period.[4]

Causes of perinatal death

It is important to specify the types of infectious diseases that are related to stillbirth and the death of puppies and kittens within the first week of life. Since infectious diseases commonly affect litters in the late neonatal period, confirmation of similar infectious agents as a cause of stillbirth or early neonatal loss is more difficult.[5] In addition, there is conflicting information regarding the incidence of perinatal loss due to infectious disease.[2,6]

Causes of perinatal loss in dogs	Comments
Fading puppy syndrome	Pathogenesis unknown; refer to subheading below
Bacterial pathogens	Beta-hemolytic *Streptococcus* spp., *Escherichia Coli*, *Brucella canis*[7,8]
Viral pathogens	Canine herpesvirus-1, canine adenovirus-1, canine parvovirus-2
Congenital defects	Losses from 1.0 to 2.2%[1,9]
Parasitic pathogens	Toxoplasma gondii[10]
Maternal infections	Refer to bacterial and viral pathogens
Maternal trauma	N/A
Dystocia	N/A

Many of the etiologies listed above are not limited to the perinatal period, specifically, infectious agents that overlap with canine abortion and late neonatal loss.

Causes of perinatal loss due to infectious disease are fairly well established despite the difficulty in detecting pathogens in many cases. However, many noninfectious causes are poorly characterized. Specifically, noninfectious placental disease is not well characterized in dogs and cats. Guidelines for the

pathologic evaluation of human placenta are provided by the College of American Pathologists.[11] These guidelines classify the causes into 3 major categories; maternal conditions, fetal conditions, and placental abnormalities. Maternal conditions include conditions such as placental abruption, systemic disorders at term, and severe oligoamnios. Stillbirth and perinatal death are among the criteria of the fetal category. Placental conditions include thrombosis, umbilical cord torsions, and retroplacental hemorrhage. Placental abruption, hematoma and infarction are well-established causes of growth restriction and fetal death in humans.[12] Placental abruption represents hemorrhage in the retroplacental region at the location of the basal plate. Abruption is also most commonly associated with this location; however, hemorrhage at the margin of the placental disc is possible.[13]

Ischemic lesions can be categorized as fetal vascular malformation or maternal vascular malformation. Fetal vascular malformation is typically associated with macroscopic abnormalities such as umbilical cord torsion, true umbilical cord knots, or excessive umbilical cord lengths.[14] These parallels exist in horses and cattle; however, these are not well characterized or reported in dogs and cats. Maternal vascular malformation is related to the remodeling process that takes place in the maternal vasculature. Spiral arteries are a unique vascular arrangement in the primate placenta in which trophoblastic invasion results in modified blood flow to the fetal membrane. Ultimately, this results in less vascular resistance and increased blood flow to the placental disc. Abnormalities in this process can result in a myriad of lesions in the chorioallantois including infarction, hypoplasia, and retroplacental hematoma formation.[14] Infarction can result from both maternal and fetal vascular malformation; however, maternal vascular malformation appears to be the most commonly associated predisposing cause. Infarct affecting > 5% of the nonperipheral placental structure is worthy of consideration.[14] Vascular abnormalities, particularly ischemia, have not been well characterized in canine and feline labyrinths. Authors have commonly observed coagulation necrosis adjacent to the marginal hematomas in normal neonates. However, areas of coagulation necrosis and hemorrhage have also been observed in the middle region of the labyrinth in cases where the cause of fetal loss could not be determined from the analysis of fetal tissue. The potential for acute or chronic placental disease induced by vascular events should be considered and investigated in dogs and cats.

Fading puppy syndrome

Respiratory disease is a common feature of what many breeders call 'fading puppy syndrome,' a frequent cause of death in neonates. Recent and ongoing research at the Michigan State University suggests that developmental lung disease is likely a major cause of these cases, similar to a condition in human pediatric medicine.[15] Histologically, pulmonary dysplasia includes underdeveloped alveoli, pulmonary artery medial hypertrophy, increased numbers of thin-walled venous profiles, and increased capillary profiles. The 3-D reconstructions of the affected lungs have vascular abnormalities suggestive of arteriovenous shunts. Continued research, including genetic analyses, is required to better understand this condition in dogs and humans and will require rigorous examination of cases of respiratory disease in puppies.

Canine endometrial disease

Similar to cattle and horses, a means to assess the health and quality of the endometrium while maintaining the animal's fertility, is important. Endometrial biopsies have been the mainstay of endometrial diagnostics in horses for some time, and to a lesser extent in ruminants. However, this technique has been difficult to apply to the bitch for several reasons:

1. Zonary placentation and the regional nature of the placental sites make it difficult to extrapolate the findings from 1 endometrial sample to the entire surface of the uterus.
2. The size of the patient requires small instrumentation, blind sampling, and advanced operator technical skill.
3. The sensitivity of the endometrium to trauma during diestrus (sampling during this period may induce cystic endometrial hyperplasia).

However, given these limitations, there is still value to identify endometrial lesions in real-time. General procedure is as follows: sampling should ideally occur at the end of diestrus (progesterone is < 1 ng/ml), but it may be possible during anestrus or proestrus. Dogs are restrained manually (and sedated if necessary). An endoscope with a 5-French rigid instrument port is inserted transvaginally and upon visualization of the cervix, a 5-French biopsy instrument is passed transcervically into the uterus. Collection of at least of 3 separate samples is suggested. Sanitizing the endoscope is not required between samples. Samples can be fixed in 10% neutral buffered formalin, 4% paraformaldehyde, or Bouin's solution, according to pathologist's preference. Careful handling of very small and delicate samples is critical as they can easily be crushed or lost. A 26-gauge needle may help in removing tissue from the biopsy instrument. Some caution is necessary during anestrus, as the endometrium is so thin-walled that perforation of the uterus is very easy and the sample may be only adipose tissue. However, no negative sequela was noted from these events.

Full-thickness endometrial samples can also be taken during a laparotomy. It is tempting to take these samples during a Caesarian section; however, these samples can be difficult to interpret as inflammation, necrosis, and cystic change are a normal part of mid to late involution, placental delivery, and involution and other changes are likely masked by these features. Lesions described as most prevalent in cases of canine subfertility (lack of pregnancy or fetal resorption) include chronic endometritis, cystic endometrial hyperplasia, and endometrial fibrosis.[16-18] Endometritis and fibrosis were not described during the immediate postpartum period in a study of 98 bitches at various stages of involution.[19] The relative value of biopsies taken during diestrus versus other stages of the estrous cycle has not been determined. However, since canine endometrium morphology undergoes a variety of histological changes during the estrous cycle, evaluation by a pathologist familiar with canine endometrium is advisable.

Pyometra was not detected in transcervical endometrial biopsies; however, fibrosis, cystic endometrial hyperplasia, and inflammation (equal to the full thickness sections) were observed in endometrial samples obtained after ovariohysterectomy.[20] All samples with pyometra were from diestrous animals. Therefore, it is more likely that the sampling procedure itself induced pyometra. However, authors have identified multiple cases of pyometra and endometritis using transcervical endometrial biopsies. Whereas additional studies are needed, transcervical endometrial biopsies offer additional diagnostic information for bitch infertility, including repeated abortions.

Feline endometrial disease

Although there are many similarities between canine and feline placentation grossly, substantial variations can be observed microscopically, primarily in the chorionic labyrinth. Feline placental site involution studies are very limited and consequently it is difficult to elucidate endometrial association in subfertility. Although it is tempting to apply the knowledge that we have gleaned from bitch endometrium to queen, the endometrial lesions associated with feline infertility has to be explored. A systematic study of the lesions that affect feline endometrium and subsequent correlation of these lesions to subfertile queens would be an ideal starting point.

Conclusion

Investigation of canine and feline perinatal loss requires collaboration and cooperation among the owner, clinician, and pathologist as the determining specific causes can be difficult. Perhaps managing expectations is a critical aspect of the process. Majority of investigations often result in negative histological and ancillary diagnostic tests. However, the value of excluding infectious, particularly transmissible, causes of the perinatal death is often overlooked in this process. Diagnostic testing for infectious agents is well established and readily available in most commercial and state diagnostic laboratories. Critical investigations remain for noninfectious causes of death that may involve placental insufficiency and endometrial disease. Additionally, further investigation of potential causes of 'fading puppy syndrome' is necessary as the pathogenesis of this condition is poorly understood.

Conflict of interest

Authors have no conflicts of interest. No funding was received for this publication.

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