

HEMOTHORAX DUE TO VASCULAR NECROSIS OF THE VENA CAVA CAUDALIS IN AN ABORTED FOAL INFECTED WITH EQUINE HERPESVIRUS 1

Hemothorax ten gevolge van vasculaire necrose van de Vena cava caudalis bij een geaborteerd veulen, geïnfecteerd met equiene herpes virus 1

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ABSTRACT

An aborted foal was presented with the suspicion of equine herpes virus (EHV) infection. On gross pathology, there were no specific EHV lesions present. Histopathology revealed moderate necrotizing inflammatory reactions in several organs associated with (peri)vasculitis. The polymerase chain reaction (PCR) for EHV type 1 on several organs was positive, as well as the seroneutralization test on the mare's serum. The foal had an extensive hemothorax with blood clots due to leakage of blood through a focal necrotic area of the vena caval wall. The relation between the EHV-1 infection and the hemothorax is discussed.

SAMENVATTING

Een geaborteerd veulen verdacht van een equiene herpes virus (EHV) infectie werd aangeboden voor autopsie. Macroscopisch waren er geen specifieke EHV-letsels zichtbaar. Histopathologisch onderzoek toonde een matige necrotiserende ontstekingsreactie in verscheidene organen geassocieerd met (peri)vasculitis. Polymerase chain reactie (PCR) voor EHV-type 1 op verscheidene organen was positief, alsook de seroneutralisatietest op het serum van de merrie. Het veulen had echter een uitgebreide hemothorax met bloedklonters ten gevolge van een lek van een lokale necrotische zone in de wand van de Vena cava caudalis. De relatie tussen de EHV-1-infectie en de hemothorax wordt besproken.

INTRODUCTION

Herpesviruses are known to cause abortion in domestic animals (Acland, 1995). Equine herpes virus type 1 (EHV-1) is the most important viral cause of equine abortion (Allen and Bryans, 1986; Smith *et al.*, 2003), while equine herpes virus type 4 (EHV-4) is a major cause of acute respiratory disease (Crabb and Studdert, 1995). In one study, only 4% of EHV-induced abortions could be attributed to EHV-4 (Van Maanen *et al.*, 2000).

Up to 95% of EHV-1 abortions occur in the last third of pregnancy, and have rarely been observed under natural conditions before 4 months (Allen and Bryans, 1986). This increased susceptibility of the

late pregnant mare to abortigenic infection is likely related to anatomical and endocrine changes in the placental barrier, which facilitate cotyledonary infarction as pregnancy proceeds (Smith, 1997).

EHV-1 lesions such as lymphoid necrosis, together with multiple, small foci of necrosis, mild acute inflammation and intranuclear inclusion bodies in adjacent parenchymal cells in a wide range of organs (especially liver, lungs and adrenal glands) are commonly noticed in affected fetuses (Acland, 1995). Vascular lesions may be limited to endothelial swelling, but the effect can be pleural and peritoneal effusion and subcutaneous edema. Viral infection of maternal uterine endothelial cells plays a major role in the pathogenesis of abortion. The lesions include

thrombosis, perivascular inflammation, edema and subsequent avascular necrosis of endometrium. The fluid that escapes the damaged endometrium causes separation of maternal and fetal elements of the placenta and can allow virus from maternal leucocytes and lysed endothelial cells to enter the fetus (Edington *et al.*, 1991; Acland, 1995). If infection occurs close to term, the infected foal may be born weak, and usually dies within 7 days due to interstitial pneumonia and viral damage to the liver, lymphoreticular system and adrenal glands, often complicated by secondary bacterial infection (Hartley and Dixon, 1979).

The present case describes the abortion of a foal after EHV-1 infection. An extensive (lethal) hemothorax caused by leakage in the wall of the *Vena cava caudalis* was detected at necropsy. The damaged venous wall was associated with a severe necrotizing vasculitis.

CASE REPORT

A 9-year old mare aborted a foal 3 weeks pre-term and was presented for retentio secundinarium. After manual removal, the fetal membranes showed petechiae and a cooked aspect. The mare did not show any signs of illness. It was the second abortion on the farm in one week.

An autopsy of the foal was performed. There were no macroscopic soft tissue lesions or fractured ribs in the thorax region which would be indicative of traumatic injuries caused by the mare. The muscles and myocard were very pale. The lungs showed fetal atelectasis (still-birth). The thoracic cavity was filled with several liters of hemorrhagic fluid and blood clots. The blood originated from a leakage in the *Vena cava caudalis* near the diaphragm. Blood leaked from a necrotic area (about 2 cm in diameter) in the wall of the *Vena cava caudalis* (Figure 1) and filled the thoracic cavity completely. The venal wall of the necrotic zone was dark red to black in color.

Serum of the mare was collected and tested for the presence of antibodies against equine herpes virus (EHV) and equine viral arteritis (EVA) by a standard seroneutralization test (according to the O.I.E. manual). The serum was negative for EVA, while it had an antibody titer of = 1/256 against EHV. Virus isolation was performed by inoculation of tissue suspensions onto a monolayer of rabbit kidney (RK-13) cells. EHV1 was isolated from suspensions of the lung and spleen of the fetus. An EHV1-EHV4 specific PCR performed



Figure 1. Photograph of the vascular necrosis of the *Vena cava caudalis*. 1: *Vena cava caudalis* / 2: Diaphragma / Arrowhead: vascular necrosis with leakage of blood into the thoracic cavity.

on the lung and spleen suspensions demonstrated the presence of EHV1 in these organs.

Hematoxylin-eosin (HE) staining of the liver revealed a mild perivascular infiltration of neutrophils, macrophages and lymphocytes. Occasionally a single hepatocyte was necrotic. The lymphoid follicles of the spleen showed moderate lymphoid necrosis. In the lungs, miliary necrotic foci associated with mild mixed inflammatory reaction were noticed. No intranuclear inclusions of EHV1 could be observed. The examination of the vena caval wall revealed severe necrosis of the tunica media and mixed inflammatory reaction, hemorrhages and clots.

DISCUSSION

EHV-1 infected fetuses aborted in late pregnancy are often fresh and enclosed in the placenta, with death due to suffocation following rapid placental separation. Gross examination typically reveals a combination of icterus, meconium staining of the integument, transudation into the body cavities, splenomegaly, perirenal edema, pulmonary edema or hemorrhage and pale miliary foci on the capsule and cut surfaces of the liver. None of these typical characteristics were observed in the present case. Histological examinations show necrosis in the liver, adrenal gland, thymus, spleen, lung and small intestine consistent with an EHV-1 infection (Hong *et al.*, 1993; Smith, 1997). The present case showed mild mixed perivascular infiltration in the liver and lungs, moderate lymphoid necrosis in the spleen and miliary necrotic foci in the lungs, which could be attributed to the EHV-1 infection.

Literature on EHV-1 and vascular necrosis is sparse. Machida *et al.* (1997) found endothelial cell necrosis and fibrinoid changes in the media in the myocardial small arteries and arterioles of aborted equine fetuses. Walker *et al.* (1999) described congestion and necrosis of the middle layer of the trophoblast and chorionic necrosis in the placentae of EHV-1 infected dams. Del Piero and others (2000) described vascular necrosis, edema, and hemorrhage with near complete endothelial loss, including effacement of the tunica media and adventitia in the lung of a filly. However, this vascular necrosis had always been described in the smaller blood vessels. In the present case, the *Vena cava caudalis* was affected. The high titer of neutralizing antibodies against EHV of the mare is indicative of a recent EHV infection (the mare was not vaccinated). The presence of EHV1 in fetal organs was demonstrated by virus isolation and confirmed by PCR. Unfortunately, for technical reasons we were not able to demonstrate the presence of EHV1 in the region with vascular necrosis in the vena cava. However a primary traumatic etiology could be excluded, as there were no indications of traumatic injuries present on the aborted foal. Thoracic trauma occurs in newborn foals and may cause associated clinical signs and death (Schambourg *et al.*, 2003). Fractured ribs, hemothorax and subsequent pulmonary collapse were cited most commonly as the cause of death (Schambourg *et al.*, 2003).

In conclusion, EHV-1 is known to cause abortion and vascular necrosis of small blood vessels in equines. However, the present case showed vascular necrosis of a larger blood vessel, namely the *Vena cava caudalis*, resulting in hemothorax, associated with an EHV-1 infection (abortion). The presence of EHV-1 infected cells in the vena cava could not be demonstrated, but it is strongly suspected to be the causative agent of the vascular necrosis.

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REFERENCES

- Acland H. M. (1995). Chapter 12: Reproductive System: Female. In: Carlton W. W., McGavin M. D. (Eds.). *Thomson's Special Veterinary Pathology*. Second edition, Mosby-Year Book Inc., St. Louis, p. 529 - 530.
- Allen G. P., Bryans J. T. (1986). Molecular epizootiology, pathogenesis and prophylaxis of equine herpesvirus-1 infections. In: *Progress in Veterinary Microbiology and Immunology*, vol. 2, Basel, Karger, p. 78 - 144.
- Crabb B. S., Studdert M. J. (1995). Equine herpes virus 4 (equine rhinopneumonitis virus) and 1 (equine abortion virus). *Advances in Virus Research* 45, 153 - 190.
- Del Piero F., Wilkins P. A., Timoney P. J., Kadushin J., Vogelbacker H., Lee W., Berkowitz S. J., La Perle K. M. D. (2000). Fatal nonneurological EHV-1 infection in a yearling filly. *Veterinary Pathology* 37, 672 - 676.
- Edington N., Smyth B., Griffiths L. (1991). The role of endothelial cell infection in the endometrium, placenta and fetus of equid herpes virus 1 (EHV-1) abortions. *Journal of Comparative Pathology* 104, 379 - 387.
- Hartley W. J., Dixon R. J. (1979). An outbreak of foal perinatally mortality due to equid herpesvirus type 1: pathological observations. *Equine Veterinary Journal* 11, 215 - 218.
- Hong C. B., Donahue J. M., Giles R. C. (1993). Equine abortion and stillbirth during 1988 and 1989 foaling seasons. *Journal of Veterinary Diagnostic Investigation* 5, 560 - 566.
- Machida N., Taniguchi T., Nakamura T., Kiryu K. (1997). Cardio-histopathological observations on aborted equine fetuses infected with equid herpesvirus 1 (EHV-1). *Journal of Comparative Pathology* 116, 379 - 385.
- Schambourg M. A., Laverty S., Mullim S., Fogarty U. M., Halley J. (2003). Thoracic trauma in foals: post mortem findings. *Equine Veterinary Journal* 35, 78 - 81.
- Smith K. C. (1997). Review Herpesviral abortion in domestic animals. *The Veterinary Journal* 153, 253 - 268.
- Smith K. C., Blunden A. S., Whitwell K. E., Dunn K. A., Wales A. D. (2003). A survey of equine abortion, stillbirth and neonatal death in the UK from 1988 to 1997. *Equine Veterinary Journal* 35, 496 - 501.
- Van Maanen C., Vreeswijk J., Moonen P., Brinkhof J., de Boer-Luijtze E., Terpstra C. (2000). Differentiation and genomic and antigenic variation among fetal, respiratory, and neurological isolates from EHV1 and EHV4 infections in The Netherlands. *Veterinary Quarterly* 22, 88 - 93.
- Walker C., Perotti V. M., Love D. N., Whalley J. M. (1999). Infection with equine herpesvirus 1 (EHV-1) strain HVS25A in pregnant mice. *Journal of Comparative Pathology* 120, 15 - 27.