

## A perirenal fibrosarcoma in a newborn calf

*Een perirenaal fibrosarcoom bij een pasgeboren kalf*

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### ABSTRACT

**Congenital tumors are rare in cattle. In this case report, a calf with a congenital perirenal fibrosarcoma is described. A newborn Belgian Blue calf that succumbed shortly after caesarian section was submitted for necropsy at the diagnostic lab of the ARSIA (Association Régionale de Santé et d'Identification Animales). At necropsy, a hemorrhagic firm mass was found surrounding the left kidney. Histopathological examination of the mass revealed a neoplastic cell population. Additional immunohistochemical stainings were performed to identify the tumor. The majority of neoplastic cells stained positive for vimentin but were negative for neurofilaments (NFs), desmin, CD3, CD20, Von Willebrand factor and cytokeratin, indicating a mesenchymal origin. The tumor was diagnosed as a fibrosarcoma. To the authors' knowledge, this is the first case of a congenital perirenal fibrosarcoma reported in a Belgian Blue calf in Belgium.**

### SAMENVATTING

Congenitale tumoren zijn zeldzaam bij het rund. In dit artikel wordt een kalf met een congenitaal perirenaal fibrosarcoom beschreven. Een pasgeboren Belgisch witblauwkalf stierf kort na de keizersnede en werd aangeboden voor autopsie bij het diagnostisch labo ARSIA (Association Régionale de Santé et d'Identification Animales). Tijdens de autopsie werd er een hemorrhagische, vast aanvoelende, perirenale massa gevonden. Histopathologisch onderzoek van de massa toonde tumorale cellen aan. Bijkomend immunohistochemisch onderzoek werd uitgevoerd voor verdere identificatie van de tumor. De tumorale massa kleurde positief voor vimentine, maar bleek negatief voor neurofilament (NFs), desmine, CD3, CD20, Von Willebrand-factor en cytokeratine. Op basis van deze bevindingen werd de tumor getypeerd als zijnde van mesenchymale oorsprong, meer bepaald als een fibrosarcoom. Volgens de auteurs is dit het eerste beschreven geval van congenitaal perirenaal fibrosarcoom vastgesteld bij een Belgisch witblauw-kalf in België.

### INTRODUCTION

Fibrosarcomas are unusual in cattle, horses and pigs but are more commonly reported in dogs and cats. These malignant tumors of fibrous tissue mostly originate in soft tissue and can invade adjacent bone (Basheer et al., 2014; Britt et al., 1998). Congenital tumors in calves are uncommon (Sickinger et al., 2009; Moore, 2013; Misdorp, 2002a,b).

In calves, spontaneous tumors are referred to as congenital when they appear in fetuses, newborn and very young calves that are less than two months of age, (Turan Yaman et al., 2019; Misdorp, 2002a). When the tumors are present between two and twelve months of age, they are defined as tumors of the juvenile type (Misdorp, 2002a). Most cases turn out to be of mesenchymal origin and four main groups can be distinguished: malignant lymphomas, mesotheliomas,

embryonic tumors (medulloblastoma, nephroblastoma) and hamartomas (Misdorp, 2002b). These tumors all occur sporadically with the exception of malignant lymphoma in twin calves and medulloblastoma. Nephroblastomas in neonatal calves are not rare and often attain a large size (Kirkbride and Bicknell, 1972; Misdorp, 1965). Tumors in the same region but without the epithelial component have been histologically typed as mixed mesodermal tumors (Misdorp, 1965) or fibrochondrolipoma (Donnelly et al., 1975). Carcinoma is the most frequent tumor in adult cattle and humans but in calves and in children, carcinomas are virtually absent in the neonatal period (Moore et al., 2013; Misdorp, 2002a). Although rare, in cattle, the majority of fibrous tumors are diagnosed as fibroma or fibrosarcoma (Mc Entee and Nielsen, 1976; Takai et al., 2004; Michishita et al., 2016; Mohana et al., 2016). Congenital fibrosarcoma is rare (Misdorp, 2002b). In this report, the pathological, histological and immunohistochemical examination of a newborn Belgian Blue calf with a congenital fibrosarcoma is described.

## CASE DESCRIPTION

### Case history and diagnostic protocol

A female Belgian Blue calf (40 kg bodyweight) was born by cesarean section after a full term gestation. It died shortly after birth without any clear symptoms. The dam did well and recovered from the procedure without any complications. An abortion protocol which included necropsy, aerobic and fungal culture of the liver, culture for *Brucella abortus* spp. of the liver, PCR test for *Anaplasma phagocytophilum* and *Coxiella burnetti* of the spleen, ELISA test for *Bovine viral diarrhea virus* on skin ear biopsy and Stamp stain on liver was carried out. At necropsy, the thyroid gland was increased in volume (36.2 g) and the liver had an orange appearance. The lungs were inflated and the abomasum contained milk. Inspection of the abdomen revealed a congested, hemorrhagic, firm perirenal mass of 25x15 cm, which surrounded the entire left kidney (Figure 1). The kidneys appeared normal. The left kidney was attached to, but grossly not involved in the neoplastic process. No metastases were found in surrounding tissues or regional lymph nodes, more specifically the renal, sublumbar and iliac lymph nodes.

No relevant pathogenic bacteria could be cultured on regular culture media. A culture for *Brucella* spp. and fungal organisms was negative, as was the Stamp staining (modified Ziehl-Neelsen stain) for acid fast bacteria (*Brucella* spp., *Chlamydia* sp. and *Coxiella burnetti*). The PCR test for Q-fever (*Coxiella burnetti*) and *Anaplasma phagocytophilum* was negative. The ELISA test for *Bovine pestivirus* antigens (*Bovine Viral Diarrhea Virus*) also showed to be negative. Analysis of a serum sample from the dam was nega-

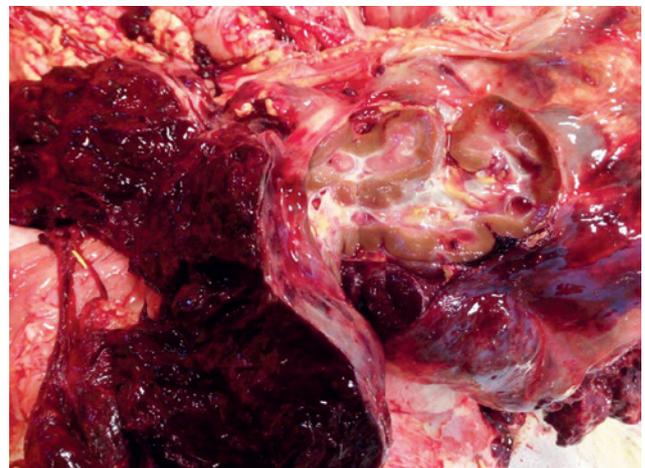
tive for antibodies to *Brucella* spp., *Coxiella burnetti* (Q fever), *Leptospira hardjo* and *Neospora caninum*.

### Histopathology and immunohistochemistry

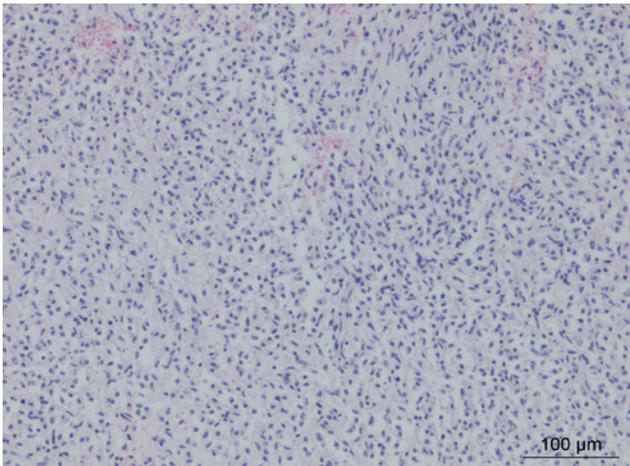
For histopathology, specimens of the perirenal mass, liver and thyroid gland were fixed in 10% neutral buffered formalin and embedded in paraffin wax. Tissue samples were processed routinely. Four-µm-thick sections were mounted and stained with hematoxylin and eosin for histologic examination.

Histology showed a densely cellular, well-demarcated, partially encapsulated, expansile and non-infiltrative mass composed of round to polygonal cells organized in bundles and separated by bands of fibrovascular stroma (Figure 2). The cells had indistinct cell borders, a round to polygonal, basophilic nucleus with coarse chromatin and clear eosinophilic cytoplasm. There was moderate anisokaryosis and anisocytosis. Mitoses were 0-2 per high powerfield. Severe multifocal to diffuse hemorrhages were present throughout the mass. There was multifocal karyorrhexis and karyolysis of neoplastic cells (lytic necrosis) and marked infiltration of intact and degenerated neutrophils. Immunohistochemistry (IHC) was done to determine the cell origin.

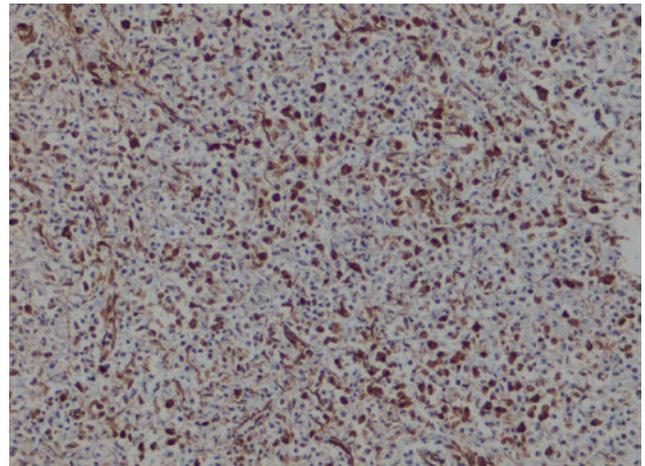
Immunohistochemical staining was performed on formalin-fixed, paraffin embedded sections. Neoplastic cells were positive for vimentin (monoclonal mouse anti-Vimentin clone Vim 3B4, M7020, Agilent, Santa Clara, United States) (Figure 3), but negative for cytokeratin (monoclonal mouse anti-human Cytokeratin clone AE1/AE3, M3515, Agilent, Santa Clara, United States), desmin (monoclonal mouse anti-human desmin clone D33, M0760, Agilent, Santa Clara, United States), neurofilament (monoclonal mouse anti-human neurofilament protein clone 2F11, M0762, Agilent, Santa Clara, United States), CD3 (polyclonal rabbit anti-human T-cell, A0452, Agilent, Santa Clara, United States), CD20 (polyclonal rabbit anti-CD20, RB-9013-P, Thermo Scientific, Waltham,



**Figure 1.** Hemorrhagic, firm perirenal mass of 25x15 cm surrounding the entire left kidney.



**Figure 2.** Neoplastic cells with indistinct cell borders, a round to polygonal, basophilic nucleus with coarse chromatin and clear eosinophilic cytoplasm. Note moderate anisokaryosis and anisocytosis.



**Figure 3.** Most of the neoplastic cells show immunopositivity for vimentin immunohistochemical staining.

United States) and Von Willebrand Factor (polyclonal rabbit anti-human Von Willebrand Factor (A0082, Agilent, Santa Clara, United States). Mesotheliomas may have an epithelioid or sarcomatous appearance and mesothelial cells may express both cytokeratin and vimentin. Immunostainings for calretinin, keratin-5 and Wilms' tumor protein used in humans for identifying mesotheliomas are not suitable for diagnostic purposes in animals (Sato et al., 2005; Geninet et al., 2003; Bacci et al., 2006). According to the histologic pattern and the immunohistochemical findings, the tumor was identified as a fibrosarcoma. On histology, the kidney was not attached to or infiltrated by the mass. No significant changes were found.

The liver showed mild at random necrosis. Hepatocytes in this area were brightly eosinophilic and shrunken with marked karyorrhexis and -lysis (lytic necrosis). Necrotic areas were moderately infiltrated by degenerate neutrophils. There was marked accumulation of yellow to green pigment within the bile ducts and bile canaliculi (bile stasis). Within the portal areas, there was mild infiltration of mononuclear cells and mild proliferation of fibroblasts with production of collagen (fibrosis).

The thyroid gland showed marked congestion of the parenchyma with normal colloid producing follicles, lined by normal cuboidal to columnar follicular cells and separated by a network of interfollicular stroma, capillaries and normal parafollicular cells.

## DISCUSSION

In case of a perirenal mass in bovine species, the differential diagnosis is wide. The following types of tumors have to be considered: congenital infiltrative lipoma or retroperitoneal lipoma, fibrochondrolipoma, malignant lymphoma, mesothelioma, heman-

giosarcoma and nephroblastoma. Perirenal lipomas, nephroblastomas and mixed tumors often become quite large and can cause obstruction of the ureter. This results in hydronephrosis or causes dystocia due to ascites. Abdominal mesotheliomas usually cause large amounts of abdominal fluid, and therefore dystocia (Agerholm et al., 2016; Misdorp, 2002a). Malignant lymphoma and nephroblastoma have been reported quite frequently in both calves and children. In contrast to children, mesotheliomas are regularly reported in calves. Because neonatal tumors in children and animals such as calves have a similar pathological spectrum, a developmental origin has been suggested (Misdorp, 2002ab; Moore et al., 2013). Furthermore, since the fetal period is short compared to the total life span of the animal, it is expected that genetic factors rather than environmental factors play a role in the development of such tumors (Misdorp, 2002b; Moore, 2013; Sickinger et al., 2009). Nevertheless, environmental factors can influence the fetus. A study by Ortega-Garcia et al. (2012) in humans showed a causative relation between prenatal exposure to petroleum derivatives and the occurrence of congenital fibrosarcomas in infants.

Given the relatively small size of the tumor and the absence of abdominal distention, it is unlikely that dystocia was the cause of death in the present case. The mass was hemorrhagic but no hemoabdomen was present, which also makes exsanguination an unlikely cause of death. Nevertheless, hemorrhagic diathesis has been reported in congenital infantile fibrosarcoma with anemia and thrombocytopenia, even in absence of overt bleeding (Mayssaa et al., 2013). More likely, the calf in the present case succumbed as a result of the random lytic necrosis that was present in the liver. This pattern is typical of many infectious agents including viruses and bacteria (Cullen and Brown, 2012). Bovine herpesvirus 1, an abortogenic herpes

virus, which can be transmitted by transplacental route, may have caused the random necrosis in the present case (Crook et al., 2012). However, following an eradication programme recognized by Europe, the herd was free from IBR since 2008 and had not experienced any clinical episodes of the disease. Unfortunately, fetal material was no longer available to test for IBR. Although bacterial examination of the liver was negative, bacterial septicemia or toxinemia (possibly intrauterine) and damage by bacteria originating from the gut should be taken into account as differential diagnosis for this type of necrosis. Toxic agents more likely cause midzonal or periportal necrosis, or in case of copper intoxication, the necrosis is rather centrilobular (Cullen and Brown, 2012). Intoxication seems less likely considering the pattern of necrosis and the age of the animal.

The increased volume of the thyroid gland in the present case was indicative for a congenital goiter. In lambs and cattle, congenital goiter is caused by iodine deficiency in utero (Leipold et al., 1990) and is commonly associated with abortion, stillbirth and birth of weak offspring (Capen, 1995; Seimya et al., 1991). In this case, a colloid or hyperplastic goiter could not be confirmed on histopathological examination.

Although rare, congenital fibrosarcoma should be considered as a differential when confronted with hemorrhagic masses in aborted fetuses and newborn calves. In this study, the importance of immunohistochemical staining for diagnosis was demonstrated.

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