Congenital Tumours and Tumour-Like Lesions in Calves: a Review

NEOPLASTIC DISEASE

Review

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Running head: J Gonçalves Pontes Jacinto *et al*

Congenital Tumours and Tumour-Like Lesions in Calves: a Review

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Summary

Congenital tumours and tumour-like lesions represent a group of rare disorders in both veterinary and human medicine that arise from tissue remnants and are detected during pregnancy or within the first 2 to 3 months of age. Different forms of congenital tumours and congenital tumour-like lesions have been reported in calves and their development is poorly understood. They often pose a diagnostic challenge and the referring nomenclature occasionally may be equivocal. Previous reports regarding tumour-like lesions, soft tissue, vascular, round cells tumours, and neoplasms of nervous, peritoneum and urogenital systems are summarized in this review and the role of genetic factors in the development of these conditions is discussed.

***Keywords*:** bovine; congenital tumours; malformations; tumour like-lesions

Introduction

Congenital tumours and tumour-like lesions arise from tissue remnants and are detected during pregnancy or within the first 2 to 3 months of life (Dorland, 1988; Smith and Philips, 2001; Alamo *et al*, 2011). As the term tumour (from the Latin word *tumor* meaning swelling) is commonly used as a synonym for neoplasm, this review encompasses tumours and tumour-like lesions which are often malformations and can mimic neoplasms. Limited numbers of congenital tumours have been recognized in human beings and animals, including calves. The purpose of this paper is to review the pathological features of congenital tumours and tumour-like lesions in calves as described in previous reports. The development of the lesions is discussed.

Congenital Tumour-Like Lesions

Hamartomas

Hamartomas are congenital tumour like-lesions characterized by an overgrowth of disorganized mature cells and tissues indigenous to the organ involved (Robinson and Robinson, 2016). They are relatively common in calves and vascular, fibrous, nasal and pulmonary forms have been reported. Vascular hamartomas are the most common and have been recognized in the gingiva (Sheahan and Donnelly, 1981; Stanton *et al*, 1984; Wilson, 1990;; Yeruham *et al*, 2004; Tsuka *et al*, 2016), heart (Sugiyama *et al*, 2007; Brisville *et al*, 2012), lung (Roth and Bradley, 1991), and cutaneous tissue (Madewell and Theilen, 1987; Yeruham *et al*, 1999; Veiga *et al*, 2017).

Gingiva vascular hamartomas appeared as reddish flat masses (2–7 × 1.5 cm diameter) and were usually located in the rostral mandibular gingival. Cardiac vascular hamartomas were located in the right atrial myocardium and were round and poorly delimited. Pulmonary vascular hamartomas appeared as spongy, non-cystic, uniformly soft, pale pink masses with a distinct lobulated patterns,

while cutaneous vascular hamartomas were oval, non-encapsulated or well-circumscribed, lobulated, exophytic and alopecic.

Vascular hamartomas were of similar histological appearance with thin-walled vascular channels lined by plump endothelial cells in a loose collagenous stroma. The vascular channels were collapsed or empty, some contained blood, and others, particularly near the surface, were thrombosed.

A fibrous hamartoma in the vagina of a calf was described by Lafond *et al* (2008). The tumour was composed of multiple pendulous vaginal masses, 5 to 15 cm long, that protruded through the vulva and often ended as cystic structures that were filled with translucent liquid and shared a common origin on a pedunculated base dotted with smaller papillary lumps. Histologically, the pendulous masses were composed of well-vascularized fibrous tissue lined by stratified squamous epithelium. The tissue was similar in appearance to the vaginal wall.

A single nasal tissue-derived hamartoma appeared as a horn-like, 1.5 × 3.5 cm mass in the maxillary gingiva (Tsuka *et al*, 2016). The mass was composed of cartilage-like and tubular structures lined by ciliated columnar epithelial cells. The mass and gingival mucosa were of similar colouration and the appearance of the cartilage and epithelial cells resembled those of the nasal chambers. A pulmonary hamartoma appeared as a 36 × 22 × 22 cm, spongy, pale pink mass with a distinct lobulated pattern (Roth and Bradley, 1991). Histologically, the mass was composed of bronchiolar and alveolar structures arranged in haphazard patterns. Ascites, localized subcutaneous oedema and chronic passive congestion of the liver were additional findings.

Choristomas and Dermoids

Choristomas are tumour-like lesions composed of histologically normal mature tissue in abnormal anatomical locations (Kusewitt and Rush, 2007). Pulmonary choristomas represent the most commonly reported form in calves (Chauvet *et al*, 1994; Medeiros de Oliveira *et al*, 2009; Bassi *et al*, 2010; Caswell and Williams, 2016). They appear as solitary, non-functioning, pale pink masses of

pulmonary tissue that lack communication with the tracheobronchial tree and receive an arterial blood supply from the systemic circulation. The histological appearance is of foetal pulmonary architecture, characterized by alveoli filled with a purulent inflammatory exudate. A previously unreported pulmonary choristoma from the archives of the Department of Veterinary Medical Sciences, University of Bologna is illustrated (Fig. 1 A, B and C).

Other choristomas in calves have been located in the abdominal cavity (Chauvet *et al*, 1994; Medeiros de Oliveira *et al*, 2009; Bassi *et al*, 2010; Binanti *et al*, 2013). A choristoma located in the perineal region of a calf was composed of mature adipose and fibrous tissue with nephrogenic rests, fragments of trabecular bone, cartilage, bone marrow, mixed with mature adipose and fibrous tissue, striated muscle, nerves and vessels (Binanti *et al*, 2013). Mature teratoma was not discussed as a differential diagnosis (Binanti *et al*, 2013). A nasal choristoma appeared as a broad-based, haired mass composed of normal nasal tissue on the nasolabial planum (Brudenall *et al*, 2008).

Choristomatous malformations in the ocular region are referred to as dermoids. Most occur unilaterally on the eyelids, conjunctiva, membrana nictitans and cornea and appear as fleshy masses with abortive hair follicle development (Brudenall *et al*, 2008).

Congenital Soft Tissue Tumours

Desmoid Fibromatosis

Fibromatoses represent a group of benign but locally aggressive pseudotumours arising from fasciae, aponeuroses or supporting connective tissue of skeletal muscle. Histopathologically, fibromatoses are characterized by infiltrative, aggressive proliferation of well-differentiated fibroblasts. Various subgroups have been identified based on anatomical, biological and epidemiological features (Fletcher, 2000; Cooper and Valentine, 2017; Alamo *et al*, 2011). Desmoid fibromatosis represents

one of these subgroups and is characterized by proliferation of uniform spindle-shaped cells resembling myofibroblasts, with an abundant collagenous stroma and vascular network.

A single case of congenital desmoid fibromatosis has been reported in a calf (Drolet *et al*, 2008). A whitish pink, moderately soft, fibrous-like mass extended from the base of the ear to the lateral canthus of the eye. The mass was poorly circumscribed and there was local infiltration of adjacent tissues. Sheets and bundles of mature, well-vascularized fibrous connective tissue had low to moderate cellularity. The tumour-like cells were strongly immunopositive for vimentin and negative for desmin, smooth muscle actin and S-100 antigens.

Lipocytic Tumours

Lipocytic tumours are grouped into pure and mixed cell forms. Simple lipomas and fibrolipomas have been described in calves.

A congenital simple lipoma in a calf appeared as retroperitoneal and perirenal deposits resembling normal fat tissue (Agerholm *et al*, 2016). Adjacent tissues were compressed with no evidence of local infiltration. Uniform populations of mature lipocytes with single large cytoplasmic vacuoles were located in sparse connective tissue stroma.

Five cases of congenital infiltrative lipoma, a benign, locally invasive tumour, have been reported in calves (Di Giancamillo *et al*, 2002; Sickinger *et al*, 2009; Militerno *et al*, 2011; Hobbenaghi *et al*, 2015; Agerholm *et al*, 2016). The tumours were localized subcutaneously in the face, neck, tail and thoracic wall and were white to yellowish, non-encapsulated and firm. Sheets of well-differentiated adipocytes, that infiltrated surrounding structures including muscle tissue, were associated with fibrosis and muscle atrophy (Agerholm *et al*, 2016). No evidence of metastasis was detected.

A congenital fibrolipoma located in the retroperitoneal area of a calf was soft, whitish and encapsulated (Marino *et al*, 2006). Well-differentiated adipocytes, with large fat vacuoles and flat

nuclei pushed to the periphery of the cells, were located in a rich network of connective tissue stroma. The stroma was lobulated and extended to the capsular surface.

Embryonal Rhabdomyosarcoma

Congenital embryonal rhabdomyosarcomas originate in embryonic mesenchyme with potential differentiation into skeletal muscle. A single case reported in a female Holstein calf appeared as a spherical, expansile, encapsulated, subcutaneous mass on the lateral side of the head (Ulrich *et al*, 2014). The highly cellular mass was composed of a reticular meshwork of moderately pleomorphic, small, spindle-shaped to round cells in a fibrovascular to myxoid stroma. Large, blunt, multinucleated myotube-like cells (strap cells) were immunopositive for desmin. The small spindle-shaped cells were positive for vimentin. Cytoplasmic bundles of myofilaments and Z bands were demonstrated within the strap cells by electron microscopy.

Myxoma

Myxomas are benign tumours composed of fibroblastic or multipotential mesenchymal cells with abundant myxoid stroma rich in glycosaminoglycans (Mauldin and Kennedy, 2016). A congenital myxoma in a calf was identified as an infiltrative intramuscular lingual myxoma (Hobbenaghi *et al*, 2014). The tumour was located on the dorsum of the lingual body and appeared as an 8 × 6 × 2.5 cm diameter, flabby mass. The cut surface of the mass was lobulated, pink and gelatinous. Histologically, stellate, spindle-shaped and elliptical cells were loosely scattered in abundant basophilic, periodic acid Schiff (PAS)-positive mucinous stroma. The tumour cells had small hyperchromatic nuclei and were locally invasive. Nuclear polymorphism and mitotic figures were not observed.

Congenital Vascular Tumours

Haemangioma

Congenital capillary haemangioma is frequently reported in calves and have been located in the skin (Kirkbride *et al*, 1973; Priestnall *et al*, 2010), gingiva (Tontis, 1994; Misdorp, 2002a), mandible (Tontis, 1994), lymph node medulla (Herzog and Geishauer, 1991) and spinal cord (Cho *et al*, 1979). The tumours occurred as single or multiple, ovoid, red–black masses that ranged from 0.5 to 7 cm in diameter (Kirkbride *et al*, 1973; Cho *et al*, 1979; Tontis, 1994; Misdorp, 2002a; Priestnall *et al*, 2010). Some oozed blood when cut and some regressed to leave a small ulcerated scar. Histologically, the masses were composed of blood-filled vascular spaces lined by a single layer of well-differentiated endothelium and separated by variable amounts of connective tissue stroma. Some of the blood vessels were thrombosed. The endothelial cells were positive for von Willebrand factor and were surrounded by small spindyloid cells positive for alpha smooth muscle actin (Priestnall *et al*, 2010).

Disseminated cavernous haemangioma has been reported in calves but details are sparse (Robinson and Robinson, 2016).

Lymphangioma

Congenital lymphangiomas are benign tumours characterized by abnormal proliferation of lymphatic vessels (Mauldin and Kennedy, 2016; Hendrick, 2017). They tend to occur in the subcutis along the ventral midline and limbs and appear as poorly demarcated, dermal masses that are soft and spongy to the touch. Clear, serous to milky, fluid exudation has been reported. A single case has been reported on the lower forelimb of a 6-month-old foetal calf (Misdorp, 2002a). Vascular spaces lined by endothelial cells were separated by loose oedematous stroma containing aggregates of lymphoid cells. The endothelial cells were immunopositive for von Willebrand factor, which is expressed by both vascular and lymphatic endothelium.

Haemangiosarcoma

A single case of congenital haemangiosarcoma has been reported in a stillborn calf (Badylak, 1983). Reddish-brown, 1.5 to 3.5 cm in diameter, smooth, firm nodular masses were located in the skin, skeletal muscles, bones, kidneys, spleen, mesentery, liver, lungs and heart. The cut surfaces were dark brown with blood-filled cystic spaces that caused compression of the normal adjacent tissue. Histologically, the vascular spaces were lined by pleomorphic spindle-shaped cells with local tissue invasion. The mitotic index of the tumour cells was low (<1 per high-power field).

Congenital Round Cell Tumours

Multicentric Lymphoma

Bovine malignant lymphoid tumours are well-characterized and include enzootic leukosis, caused by bovine leukemia virus (BLV), and sporadic forms, namely congenital multicentric lymphoma (CML), juvenile multicentric lymphoma, cutaneous lymphoma and thymic lymphoma. CML is one of the most commonly recorded tumours in calves (Cotchin, 1960; Overgoor, 1963; Misdorp and Dodd, 1968; Herzog and Geishauer, 1991; Yeruham *et al*, 1999; Misdorp 2002a; Yamamoto *et al*, 2007; Beytut and Özba, 2012). Although BLV is known to infect bovine foetuses and new-born calves, most cases of CML are sporadic and occur independently of BLV infection. Multiple lymph nodes usually are affected with thoracic and abdominal cavity involvement. Skin and brain lesions have been described and skeletal muscle involvement is rare.

The immunohistochemical assessment of bovine lymphomas is well documented and the predominant type is diffuse large B-cell lymphoma (Vernau *et al*, 1997; Beytut and Özba, 2012). Primitive B-lymphocytes and plasma cells may lack surface immunoglobulins and demonstration of cytoplasmic immunoglobulins may be helpful in the identification of the tumour cell lineage in newborn calves.

224

225 *Cutaneous Mast Cell Tumour*

226 Congenital cutaneous mast cell tumours have been described as randomly distributed nodular masses
227 that were sometimes ulcerated (Yeruham *et al*, 1999; Smith and Phillips, 2001; Palyada *et al*, 2008).
228 The skin of one affected calf was thickened and wrinkled because of diffuse tumour cell infiltration
229 and resembled that of a Chinese Sharpei dog. Hair loss was absent and peripheral lymph nodes were
230 not enlarged (Palyada *et al*, 2008). Poorly-defined aggregates of neoplastic mast cells in the lung,
231 spleen and skeletal muscles of one calf with cutaneous mast cell tumours represent the only report of
232 metastasis (Smith and Phillips, 2001). A previously unreported mast cell tumour from the archives of
233 the Department of Veterinary Medical Sciences, University of Bologna is illustrated (Fig. 1 D, E and
234 F).

235

236 **Congential Tumours of the Nervous System**

237

238 *Schwannosis*

239 Schwannosis is a benign peripheral nerve sheath tumour characterized by spontaneous invasion and
240 proliferation of aberrant Schwann cells into the central nervous system with peripheral myelination of
241 central axons. Typical cases in humans lack obvious gross tumour formation (Adelman and Aronson,
242 1972; Perry, 2010). A single case, in which no noticeable mass was detected, has been reported in a
243 calf with hydrocephalus (Miranda *et al*, 2019). Lesions were bilaterally located in the dorsal and
244 ventral roots at all levels of the spinal cord and the dorsal spinocerebellar tract in the medulla
245 oblongata. Plaques of proliferated spindle cells, admixed with myelinated axons, extended into the
246 dorsal, ventral, and lateral funiculi and grey matter. Proliferated spindle cells expressed myelin protein
247 zero and periaxin, proteins that are absent in the central myelin (Miranda *et al*, 2019).

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Medulloblastoma

The term medulloblastoma is conventionally limited to embryonal tumours that originate in the cerebellum. Tumours of similar histological appearance in other sites in the brain are referred to as primitive neuroectodermal tumours (Cantile and Youssef, 2016). Medulloblastomas are of uncertain origin and thought to arise from neuronal progenitor cells beneath the pia mater of the cerebellum (Jolly and Alley, 1969; Fankhauser *et al*, 1982; Cantile and Youssef, 2016). The molecular mechanisms governing neuronal progenitor cell neurogenesis are poorly elucidated. The tumours are usually located in the cerebellar vermis, grow rapidly and are highly malignant with a symptomatic duration of only a few months.

Medulloblastomas in calves appear as round, well-circumscribed, soft, grey to red infiltrating masses with necrosis and haemorrhage in the cerebellum and hindbrain (Fankhauser *et al*, 1982; Ciorba and Avalos-Umanzor, 1987; Guarda and Biolatti, 1987; Bianchi *et al*, 2015). The tumour cells are rounded, pyriform or elongated and arranged in clumps or palisades with complete or incomplete Homer Wright rosette formation. Mitotic figures are frequent. Positive immunolabelling occurred for several neuronal markers including neuron specific enolase and synaptophysin (Cantile and Youssef, 2016). The occurrence of the tumour in twin calves, reported by Fankhauser *et al* (1982), is suggestive of genetic involvement. A previously unreported medulloblastoma from the archives of the Department of Veterinary Medical Sciences, University of Bologna is illustrated (Fig. 2 A and B).

Congenital Tumours of the Peritoneum and Urogenital Systems

Mesothelioma

Congenital mesotheliomas are relatively frequent in calves and have been reported in the abdominal cavity (Baskerville, 1967; Misdorp, 2002a and b), pleural cavity (Schamber *et al*, 1982; Baskerville, 1967), pericardial cavity (Takasu *et al*, 2006) and tunica vaginalis of the testis (Peli *et al*, 2018). The

tumours appear as multiple, firm, variably-sized, sessile or pedunculated nodules and are usually accompanied by copious, yellowish–red effusion. Serosal surfaces were thickened in these cases with villous projections of cuboidal, squamous or columnar epithelial cells and sclerosis. Giant cells and necrosis were present, the tumour cells seemed less differentiated than those seen in mesothelioma in adult animals (Misdorp, 2002a) and were immunopositive for cytokeratin and vimentin. A previously unreported mesothelioma from the archives of the Department of Medical Veterinary Sciences, University of Bologna, is illustrated (Fig. 2 C and D).

Nephroblastoma

Nephroblastomas, also known as Wilms tumours, originate in the primitive metanephric blastema in the retroperitoneum. Reports of cases in the bovine foetus are lacking in detail (Misdorp 2002b; Cianciolo and Mohr, 2016). Nephroblastomas are usually unilateral and appear as multiple expansile masses in the affected kidney. Cut surfaces are lobulated, greyish–white, soft and myxomatous and larger tumours have extensive haemorrhagic necrosis. Reflecting the biological potential of the metanephric blastema, the tumours contain a variety of epithelial and mesenchymal components, including some not typically associated with the kidney. A typical pattern is one of islands of epithelial cells undergoing differentiation into tubules or glomerulus-like structures, surrounded by peripheral zones of stroma. Neoplastic mesenchymal elements including fibrous, myxoid, lipoid, myoid, chondroid and osteoid forms dominate in some tumours and may occur singly or in varying combinations and proportions (Nielsen *et al*, 1976). The immunoreactivity of bovine nephroblastoma is not reported. Consistent expression of cytokeratin 19 has been reported in tubular structures in porcine nephroblastomas (Grieco *et al*, 2006).

Sertoli Cell Tumour of the Testis

Sertoli cell tumours, also known as sustentacular cell tumours, arise from the supporting cells of the seminiferous tubules (Agnew and MacLachlan, 2017). Three cases have been described in calves, one in a neonatal German Holstein calf (Vissiennon *et al*, 2016) and two in newborn calves, both sired by the same Shorhorn bull (Palmer *et al*, 1980). Each of the latter two calves had only one testis. Affected testes were enlarged, soft and reddish purple with small greyish areas divided into lobules by light fibrous bands. Densely cellular tumours showed well-formed tubules lined by polygonal cells with round to elongated nuclei and scant eosinophilic cytoplasm. Less densely cellular tumours were composed of groups of vacuolated cells divided into small lobules by vascular connective tissue stroma (Palmer *et al*, 1980, Vissiennon *et al*, 2016). The tumour cells were immunopositive for α-oestrogen receptor, α-inhibin, vimentin and S-100 antigens.

Interstitial (Leydig) Cell Tumour of the Testis

Interstitial cell tumours of the testis arise from the interstitial (Leydig) cells. A congenital interstitial cell tumour has been described in a 1-month-old calf (Lopez *et al*, 1994) in which both testicles were undescended. The left testicle was notably enlarged, dark red and soft with scattered areas of necrosis. Histologically, monomorphic populations of polyhedral cells, with distinct cytoplasmic borders and abundant eosinophilic cytoplasm, were supported by well-vascularized bands of connective tissue stroma. Antibodies against luteinizing hormone and 3-beta-hydroxysteroid dehydrogenase represent useful markers for accurate identification of interstitial cell tumours as shown in the dog (Peters *et al*, 2002).

Teratomas

Teratomas arise from pluripotential cells that undergo neoplastic transformation into two or more germ cell types. They occur most often in the gonads and contain tissue that is foreign to the site (Mahour, 1988; Ibrahim and Ali, 2018). A single case has been reported in a calf and appeared as a large 5.5 kg

mass in the abdominal cavity (Hjärre, 1924). The mass was composed of multiple different fully differentiated tissues including adipose tissue, nervous tissue and epithelium. However, Binanti *et al* (2013) have reported a case of choristoma that resembled a mature teratoma.

Yolk Sac Tumours

Yolk sac tumours are primitive germ cell tumours derived from the embryonic yolk sac, allantois, or extra-embryonic mesenchyme. Most cases in humans develop in the testes or ovaries.

Four cases of yolk sac tumours have been reported in calves (Kagawa *et al*, 1998; Sasaki *et al*, 2012; Sakaguchi *et al*, 2013; Schindewolffs *et al*, 2015). Three of these cases involved the testes and one the abdominal cavity. Nodular masses were reddish–white, cystic and gelatinous. The tumour cells were arranged in different histological patterns including myxomatous, reticular, polyvesicular vitelline and endodermal sinus, and were immunopositive for alpha-fetoprotein. Variable findings were obtained using other immunohistochemical markers and were related to the histological patterns.

Embryonal Carcinoma

Embryonal carcinomas are derived from poorly differentiated embryonal epithelium. The histological appearance is of poorly differentiated epithelial cells forming solid, papillary, cyst-like and tubular patterns of growth embedded in abundant fibrous stroma (Agnew and MacLachlan, 2017).

A single case of embryonal carcinoma has been reported in a calf (Aihara *et al*, 2011). Multiple variable-sized, yellowish–white nodules were closely spaced on the lining of the abdominal cavity and the serosal surfaces of abdominal organs. The tumour cells were characterized by indistinct cell borders, eosinophilic granular PAS-positive cytoplasm and nuclear anisokaryosis. Mitotic figures, including atypical forms, were frequent and multinucleated cells and vascular invasion were prominent. The tumour cells were positive for alpha-fetoprotein, carcinoembryonic antigen and cytokeratin.

Congenital Tumours and Genetics

Damage to the cellular genome or altered expression of genes is common in virtually all neoplasms. Knowledge of these genetic aberrations is well advanced in humans and has been made possible by technological advances in DNA sequencing and other methods that permit genome-wide analysis of tumour cells. Similar studies in veterinary medicine, and especially in cattle, are limited. A syndromic disorder in Belgian Blue cattle, characterized by osteoporosis and gingival hamartomas, has been associated with a missense mutation in the *CLCN7* gene localized on the bovine chromosome 25 (Sartelet *et al*, 2014). Affected animals are stillborn or slightly premature, have small body size and ascites, an abnormal skull shape, inferior brachygnathism, blindness, protruding tongue and gingival hamartomas of variable sizes (up to 15 cm diameter) located on the lower jaw. The liver and kidneys are hypertrophied. A congenital Sertoli cell tumour in cattle associated with the autosomal sex determining gene *SOX9* has been reported (Schindewolffs *et al*, 2015). Genetic, transcriptomic and direct reprogramming experiments suggest that differentiation of supporting cell progenitors into male-specific Sertoli cells or female-specific granulosa cells is controlled by the presence or absence of *SOX9* and aberrant *SOX9* may be at the basis of tumour development (Ramoun *et al*, 2017). Another hypothesis has been advanced by Palmer *et al* (1980), who observed that two Shorthorn calves with Sertoli cell tumours were roan in colour with ample white areas. Interference with oestrogen receptivity in Shorthorns carrying the *W* gene for white coat in single or double copy was suggested.

A hereditary predisposition for bovine peripheral nerve sheath tumours (PNSTs) has been described in Danish Holstein cattle (Grossi *et al*, 2014). A preliminary genome-wide association study was completed on DNA isolated from 28 affected and 28 non-affected Holsteins to identify loci in the

bovine genome involved in the development of PNSTs. A single nucleotide polymorphism on chromosome 27 reached genome-wide significance.

Mast cell tumours in cattle comprise less than 1% of all bovine neoplasms and statistical evidence of breed predisposition is not recorded (Tamlin *et al*, 2020). Despite well-documented differences in the clinical presentation and biological behaviour of mast cell tumours in different species, mutations in the *Kit* proto-oncogene are regularly identified in neoplastic mast cells of dogs, cats and humans and contribute to mast cell carcinogenesis. That the *KIT* gene is also likely to be implicated in the development of mast cell tumours in other species is indicated by aberrant cytoplasmic KIT protein immunolabelling in ferrets, horses and cattle (Tamlin *et al*, 2020).

Conclusions

A multiplicity of different congenital tumours and tumour-like lesions have been described in calves. Much has yet to be learned about the development of these conditions and information on possible genetic associations is limited. Calves represent a valuable resource for further studies in this area.

Legends of the figures

Fig. 1. 15-day-old female Holstein-Friesian calf, congenital pulmonary choristoma (A) Well-circumscribed mass in ventral cervical region not covered by skin and had doubled in size in the previous 14 days. Bar, 10 cm. (B) Cross-section of the mass showing lobulated lung-like tissue with purulent foci. Bar, 10 cm. (C) The tissue in the mass is fibrosed and bronchiolar-like structures are inflammed (arrows). HE. Bar, 200 µm. Male Holstein Friesian calf, congenital cutaneous mast cell

tumour (D–F). (D) Thickened areas of skin on the face and muzzle at 5 months of age. Bar, 10 cm. (E) Periocular and muzzle lesions are less prominent at 1 year of age and skin lesions elsewhere on the body vary in size and some are ulcerated. Bar, 40 cm. (F) Neoplastic mast cells intermingled with eosinophils. HE. Bar, 100 µm. Inset: metachromatic granules in cytoplasm of neoplastic mast cells. Toluidine blue.

Fig. 2. 10-day-old female Holstein Friesian calf, congenital medulloblastoma (A and B). (A) Tumour has a soft gelatinous appearance. Bar, 10 cm. (B) Densely cellular neoplasm composed of elongated and ovoid cells, with scant cytoplasm and hyperchromatic nuclei. HE. Bar, 200 µm. (Courtesy of Dr Gianfranco Militerno, University of Bologna, Italy). (C) Widely disseminated nodular lesions on peritoneal serosa of a 1-month-old male Belgian Blue–Holstein Friesian crossbred calf, congenital mesothelioma. Bar, 20 cm. (D) Lobular proliferation of epithelioid cells with occasional rosette-like structures in lesions shown in Fig. 2D. HE. Bar, 200 µm. (Courtesy of Dr Gianfranco Militerno, University of Bologna, Italy).

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