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Case Report

Lipoblastoma in a Dog: Clinical, Histochemical and Immunohistochemical Features

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Abstract

Lipoblastoma is a rare benign tumor arising from embryonic white fat and occurs exclusively in infants and children. This neoplasia has an excellent prognosis but its growth rate can be rapid and reach a large size. In veterinary literature lipoblastoma has been reported only in a new born (2 day old) male calf. This case report describes the clinical, histochemical and immunohistochemical features of a lipoblastoma in a dog. The dog was followed up for 20 months after surgery and found to be healthy with no signs of recurrence.

Key Words: Lipoblastoma, fat tissue, soft tissue tumor, dog

Description

A 10 year old, intact female, mixed breed dog of 16 Kg was examined for a 3 months of progressive abdomen enlargement, weakness, anorexia and recurrent vomiting. The owner reported loss of appetite and increased body weight.

Physical examination revealed a large abdominal mass, polypnea and pale mucous membranes. Complete blood count (CBC) and complete biochemical profile revealed high leukocytosis (neutrophylia, monocytosis and lymphopenia), severe normocytic and normocromic anemia, low iron serum concentration (60.6 mg/dL, range 90-180 mg/dL), mild hypoglycemia (65 mg/dL, range 80-120 mg/dL) and severe increase of alkaline phosphatase (ALKP) (1477.2 U/L, range 77-200 U/L). Coagulation profile and urinalysis were otherwise unremarkable. Abdominal ultrasound showed a complex mass lesion occupying most of the abdominal cavity, initial hydronephrosis of the right kidney and ipsilateral ureteral dilatation due to mass compression.

Eco-guided fine needle aspiration of the lesion was performed: cytology revealed a large amount of naked nuclei, lipid vacuoles, spindle and multinucleated cells with intra-cytoplasm round vacuoles, mild anisokaryosis and prominent nucleoli. A fat tissue tumor was suspected.

Contrasted computer tomography was performed (CT) showing a large, well defined multilocular mass characterized by fat density, with enhancing septa occupying most of the abdomen and displacing organs and mesentery (Fig. 1). The lesion had no contrast enhancement showing a low blood perfusion and no metastases were detected.

Explorative laparotomy was performed removing a white 5kg mass originating from the suspensor ligament of the ovary. The mass was adherent to the right kidney and nephrectomy was necessary. Postoperative the dog rapidly improved, and after a month the haematology and biochemical profile were within the range of normality.

The surgical specimen was fixed in a 10% formalin solution before being processed in paraffin.

Microscopically, mature adipocytes characterized by dimensional pleomorphism were detected and no marked signs of cellular atypia were observed. Large clear vacuoles replaced the cytoplasm, with peripheralization and compression of nuclei. Many vascular elements were observed within the connective tissue and islands of extramedullary hematopoiesis (EH) were detected with no evidence of myelopoiesis or megakaryopoiesis. At high magnification lipoblasts, surrounded by a thin stroma, were recognized (Fig. 2A). A histopathological diagnosis of congenital lipoblastoma was performed.

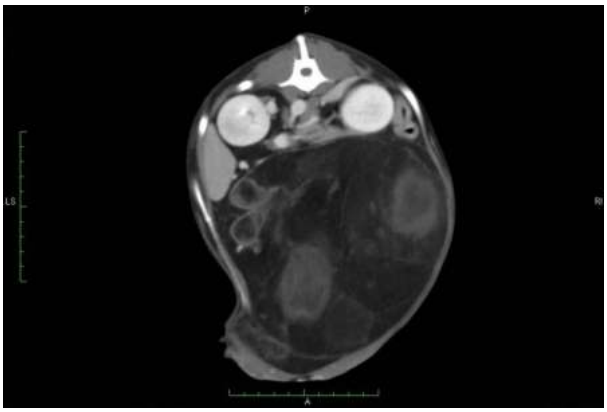

Figure 1. Lipoblastoma in a dog. CT scan show a large fat density mass occupying most of the abdominal cavity and displacing abdominal organs and mesentery.

In veterinary literature lipoblastoma is described only in a new born (2 day old) male calf [10] and in human medicine it represents a rare childhood tumor, described in approximately 200 cases which may present a diagnostic dilemma within soft tissue tumor neoplasias. This tumor is virtually indistinguishable from a lipoma and liposarcoma clinically [7], and a myxoid liposarcoma histopathologically [3]: for these reasons a histochemical (HC) and immunohistochemical (IHC) comparison with a canine myxoid liposarcoma and lipoma was considered.

For HC all the specimens were stained with Masson Trichrome, Van Gieson and Alcian Blu pH 2,5 (Bio-Optica, Milano, Italy).

IHC analysis was performed with streptavidin-biotin peroxidase method and Anti-Vimentin clone V9, anti-Ki67 clone MIB-1, anti-CD31 clone JC70A (DAKO, Carpinteria, CA, USA), anti-Epo-R rabbit polyclonal (Santa Cruz Biotechnology, Santa Cruz, CA, USA), were selected as primary antibodies. A negative control sample was included by omitting the primary antibody with a non-immune serum, and canine normal tissues were selected as positive controls: tonsil (mucosal associated lymphoid tissue) for CD31 and Vimentin, normal skin for Ki67, bone marrow for Epo-R.

At HC analysis lipoblastoma was surrounded by a reticulinic and myxoid stroma (Alcian Blu) and irregularly separated by filaments of collagen (Masson Trichrome, Van Gieson) (Fig. 2D, G, J). Comparing to the lipoma, myxoid liposarcoma showed an abundance of mucopolysaccharides (Alcian Blu) (Fig. 2K, L). Lipoma and liposarcoma showed occasional presence of collagen, organized in isolated fibers (Masson Trichrome, Van Gieson) (Fig. 2E, F, H, I).

At IHC analysis lipoblastoma was characterized by a rich vascular plexiform pattern (CD 31) and showed a cell proliferation index < 5% (Ki-67, 1-2/10 HPF) (Fig. 3G, J). EH was confirmed by Epo-R positivity (Fig. 3A). Myxoid liposarcoma showed a rich vascular plexiform pattern (CD31), with a proliferation index > 10% (Ki-67, 5-6/10 HPF) and no EH (Fig.3H, K, B). Lipoma showed small vessels (CD31), with no EH (Epo-R) and undetectable proliferation index (Fig. 3I, C, L).

Lipoblastoma is a rare, benign and encapsulated tumor arising from embryonic white fat, which occurs almost exclusively in infants and children [12, 6]. Published reports showed that 80–90% of cases occur before 3 years of age, and the 40% before 1 year [2]. The term lipoblastoma was first used by Jaffe in 1926 to describe a benign tumor of immature fat cells [5]. Since then, approximately 200 cases have been reported in the literature [1, 8]. Lipoblastoma has an excellent prognosis and does not behave aggressively or metastasize but, usually, its growth rate is rapid and can reach a large size. In addition, it is known to recur locally in the 9–25% of cases [6, 1] and the treatment of choice is a complete but conservative excision [2].

A final diagnosis of lipoblastoma was formulated in an aged dog differently from what usually described in human medicine in which juvenile patients are more frequently affected. In our opinion the large size of the mass and the low proliferation index correlate with the chronic symptoms of the patient, characterized by a slow decrease of BCS, weakness and progressive anorexia, and the laboratory findings of a chronic disease, like mild anemia and hyposideremia.

The development of a lipoblastoma in an aged patient could be hypothesized through activation and a subsequent neoplastic transformation of adipose-derived mesenchymal stem cells, physiologically present in the canine adipose tissue [11]. Although these cells are characterized by low proliferation ability and are normally refractory to adipogenic and osteogenic differentiation. Some authors demonstrated that, due to the presence of different factors like the action of the transforming growth factor beta (TGF-beta), this differentiation can be achieved [9].

Extramedullary haematopoiesis rarely occur in soft tissue tumors both in human and in veterinary medicine. Within the group of fat tumors, EH is reported in myelolipoma, a tipical adrenal tumor characterized by a mixture of mature adipocytes and various bone marrow elements, in hepatic angiomyolipoma and in a spindle cell lipoma [11], but in our knowledge it was never described before in a lipoblastoma. Although EH is rare in adipose tissue tumors some authors recently demonstrated that adipose tissue is an extramedullary reservoir for functional hematopoietic stem cells [4].

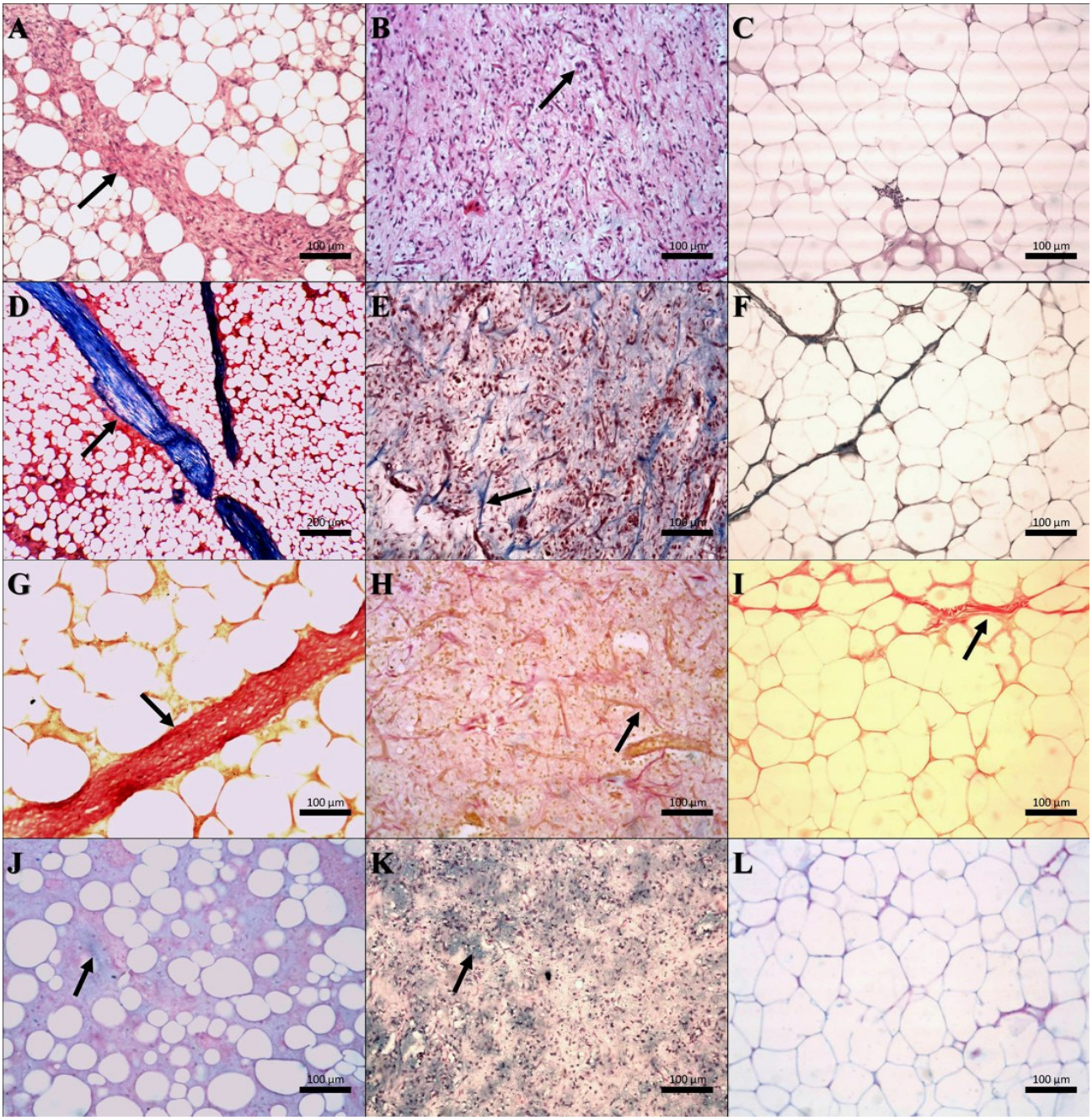

Figure 2. Histopathological and histochemical comparative analysis among the lipoblastoma, a myxoid liposarcoma and a lipoma. **A**, lipoblastoma: adipocytes characterized by dimensional pleomorphism without nuclear atipia,lipoblats scattered in the thin stroma and abundant presence of fibrous septa (arrow) (HE, 10X). **B**, myxoid liposarcoma: all cells, embedded in abundant mixoyd stroma, are morphologically atypical and many lipoblasts are present in the field (arrow) (HE, 10X). **C**, lipoma: mature adipocytes without atypia (HE, 10X). **D**, lipoblastoma: bundles of compact collagen in blue (arrow), thin stroma in red which delineates the size of mature adipocytes pleomorphism and focal areas of mucopolysaccharides in blue (Masson Trichrome, 5X). **E**, myxoid liposarcoma: thin and fragmented branches of collagene in blue (arrow) and mixoid stroma with abundant component of mucopolysaccharides in blue and lipoblasti in red (Masson Trichrome, 10X). **F**, lipoma: thin branches of collagene in blue, no presence of mucopolysaccharides nor lipoblasti (Masson Trichrome, 10X). **G**, lipoblastoma: abundant filaments of collagen stained in red (arrow) (Van Gieson, 10X). **H**, **I**, liposarcoma & lipoma: occasional presence of collagen (arrow) (Van Gieson, 10X). **J**, lipoblastoma: focal presence of mucopolysaccharides in the stroma (arrows) (Alcian Blu, 10X). **K**, myxoid liposarcoma: abundant and widespread presence of mucopolysaccharides (arrow) (Alcian Blu, 10X). **L**, lipoma: no presence of mucopolysaccharides (Alcian Blu, 10x).

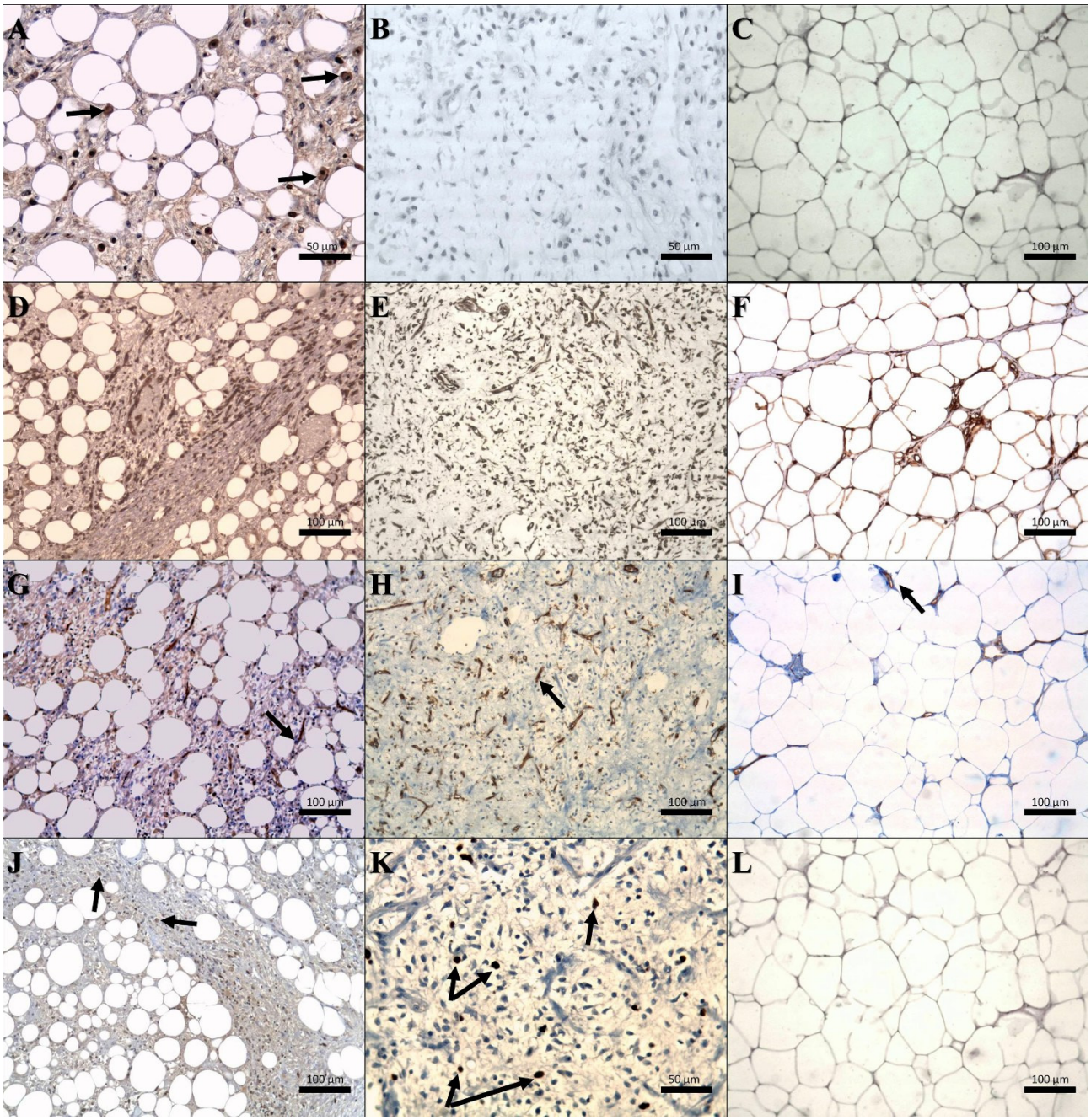

Figure 3. Immunohistochemical comparative analysis among the lipoblastoma, a myxoid liposarcoma and a lipoma. **A**, lipoblastoma: Epo-R focal positivity in foci of extramedullary erythropoiesis (arrows) (IHC, 20X). **B**, **C**, myxoid liposarcoma and lipoma: negativity of Epo-R immunostaining confirmed the absence of extramedullary erythropoiesis (IHC, 20X). **D - F**, Lipoblastoma, myxoid liposarcoma and lipoma: a diffuse cytoplasmatic positivity for Vimentin confirmed the mesenchymal origin of the lesions (IHC, 10X). **G**, Lipoblastoma: vascular plexiform pattern confirmed through endothelial cells membrane positivity for CD31 (arrow) (IHC, 10X). **H**, myxoid liposarcoma: CD31 immunostaining showed a rich vascular pattern surrounded by myxoid stroma (arrow) (IHC, 10X). **I**, lipoma: CD31 immunostaining revealed some vessels located near collagen fibers (arrow) (IHC, 10X). **J**, lipoblastoma: Ki-67 immunostaining revealed a cell proliferation index < 5% (1-2/10 HPF) (arrow) (IHC, 10X). **K**, myxoid liposarcoma: Ki-67 immunostaining revealed proliferation index > 10% (5-6/10 HPF) (arrows) (IHC, 20X). **L**, lipoma: Ki-67 immunostaining revealed an undetectable proliferation index (IHC, 10x).

The complete recovery of physical conditions in postoperative, and a 20 month negative follow-up for the metastasis development or local tumor recurrence, support the benign behavior of the lesion and the effectiveness of the surgery treatment in our patient. This case demonstrates that lipoblastoma should be considered in the differential diagnosis of soft tissue tumor in dogs.

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