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PATHOLOGY

Myolipoma associated with hyperadrenocorticism and diabetes mellitus in a female poodle

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ABSTRACT: *This report provides an unpublished account of an intra-abdominal myolipoma in a 11-year-old female Poodle with hyperadrenocorticism and diabetes mellitus. The patient was well controlled for both endocrine diseases; however, was suffering for severe abdominal discomfort. Ultrasound scan revealed a huge abdominal mass. At necropsy a pinkish mass (35cm x 28cm x 12cm) of elastic consistency attached to the broad ligament of the left uterine horn was reported. Histologically, this mass was constituted of a mixed population of well-differentiated adipocytes and of spindle-shaped mesenchymal cells. Both tumor cells were positive for vimentin at immunohistochemistry, while the spindle-shaped cells were positive for desmin and actin, compatible with smooth muscle cells. Immunohistochemistry was crucial for myolipoma characterization.*
Key words: *dog, abdominal tumors, Cushing's syndrome, immunohistochemistry.*

Miolipoma associado a hiperadrenocorticismo e diabetes mellitus em uma poodle fêmea

RESUMO: *Este relato apresenta um caso inédito de miolipoma intra-abdominal em um poodle fêmea de 11 anos de idade com hiperadrenocorticismo e diabetes mellitus concomitante. A paciente apresentava um bom controle das doenças endócrinas, porém, grande desconforto abdominal. Ao ultrassom abdominal evidenciou-se uma massa de grandes proporções. Na necropsia uma massa rosácea (35cm x 28cm x 12cm) de consistência elástica unida ao ligamento largo do corno uterino esquerdo foi identificada. Histologicamente esta massa era constituída de uma população mista de adipócitos bem diferenciados e células fusiformes mesenquimais. Ambos tipos celulares foram positivos para vimentina na imuno-histoquímica, enquanto as células fusiformes foram positivas também para desmina e actina, compatível com músculo liso. A imuno-histoquímica foi crucial para o diagnóstico do miolipoma.*
Palavras-chave: *cão, tumores abdominais, síndrome de Cushing, imuno-histoquímica.*

Myolipoma is an extremely rare benign tumor described in humans, formed by variable amounts of mature adipose tissue and smooth muscle. Also known as soft tissue myolipoma, it occurs mainly in adult women as a single large mass often located in the abdominal and retroperitoneal cavities, without any involvement of parenchymatous organs (KIM et al., 2013). When it occurs in the uterus, this type of neoplasm is called lipoleiomyoma and it has already been described in dogs (MANJUNATHA et al., 2010; SYCAMORE & JULIAN, 2011; WOLDEMESKEL, 2008). The aim of this case report was to provide an unpublished account of a large myolipoma in the broad ligament of the uterus in a bitch with diabetes mellitus (DM) and hyperadrenocorticism (HAC).

An 11-year-old female poodle weighing 8.5kg was brought in for veterinary care due to progressive abdominal enlargement over the past year, hyporexia, and bilateral hair loss. The patient showed exercise intolerance and inability to climb stairs and obstacles. Anestrus for at least 2 years was reported. The animal had been diagnosed with DM 3 years ago, being treated with 3IU every 12h with human neutral protamine Hagedorn (NPH) insulin (Novolin®, Novo Nordisk, Brazil), combined with commercial food for diabetic dogs (Diabetic®, Royal Canin, Brazil). The insulin therapy administered by the tutors was appropriate. Besides that, body condition score of 3 (1-9), in sharp contrast to a pronounced abdominal bulge firm on palpation, with a muscle mass score of 1 (0-3) was documented (Figure 1A). Based on

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clinical presentation the patient was tested for HAC by means of a low-dose dexamethasone suppression test (LDDST). Cortisol levels were measured by radioimmunoassay, showing 4.8µg/mL at baseline and 3.68µg/mL 8 hours after the IV administration of 0.01mg/kg (cortisol 8h after dexamethasone >1.4µg/dL consistent with HAC). Another LDDST was requested by tutors to confirm the diagnosis, whose results indicated a 2.22µg/dL cortisol level 8h post-dexamethasone; therefore, being considered positive for pituitary-dependent form by means of ultrasound scan results.

The abdominal ultrasound indicated hyperechoic and irregular lesions distributed throughout the abdominal cavity and displacement of abdominal viscera. Moreover, a small amount of free fluid in the cavity, suggesting adipose tissue/omental/peritoneal neoplasm. The adrenal glands had slightly irregular borders with preservation of their shape and size (right: 1.86cm x 0.63cm and left: 1.89cm x 0.65cm). An ultrasound-guided fine-needle aspiration of the abdominal mass was performed, revealing well-differentiated and loosely arranged adipocytes and liposomes.

After HAC initial treatment with mitotane (Lisodren®, Bristol-Myers, Brazil) and subsequent insulin dose adjustments the tutors agreed on an exploratory laparotomy. A tumor mass that occupied the whole abdominal cavity and did not allow the visualization of other abdominal organs was detected during the procedure. Due to tumor´s inoperability and the dog´s poor life quality secondary to this large intrabdominal mass, the owner consent with euthanasia during surgical procedure, and the dead body was necropsied.

Pronounced abdominal dilatation, with thin skin and multiple comedones, was observed at necropsy. After dissection, a pinkish and slightly elastic mass that filled the whole cavity and displaced abdominal organs was detected (Figure 1B). The mass measured 35cm x 28cm x 12cm and weighed 3.7kg (representing 37,8% of the bitch´s body weight). The mass was attached to the broad ligament of the left uterine horn (Figure 1C) and showed areas with a gelatin-like appearance upon its section.

Fragments of several tissues and of the abdominal tumor were fixed in 10% buffered formalin and processed for histological analysis. The sections were stained with hematoxylin and eosin, and Masson's trichrome. The abdominal tumor specimens were submitted to immunohistochemical tests using peroxidase-labeled streptavidin-biotin. The following primary antibodies were used for these tests: vimentin (Zymed®, Invitrogen, USA), desmin (Dako®, Denmark), and actin (Dako®, Denmark). The secondary reagent consisted of biotinylated anti-rabbit antibody (LSAB + System-HRP; Dako®, Denmark), followed by streptavidin peroxidase (LSAB + System-HRP, Dako®, Denmark). The reaction was developed with 3´3-diaminobenzine (DAB, Dako®, Denmark) chromogen, and the slides were counterstained with Harris hematoxylin. Fragments of skin and of the small intestine from healthy dogs were used as positive controls. Simultaneously, as negative control, sections of the tumor and of control tissues were incubated in phosphate-buffered saline, instead of primary antibody incubation.

Histologically, the abdominal tumor comprised a mixed population of well-differentiated adipocytes (60% of the lesion) and spindle-shaped mesenchymal cells (40% of the lesion), (Figure 1D). Spindle-shaped cells were arranged in tightly cohesive bundles, disposed in several directions, and were poorly pleomorphic. Masson's trichrome staining did not show collagen in spindle-shaped cells. In the immunohistochemical analysis, both tumor cells were positive for vimentin (Figure 1E); whereas, spindle-shaped cells were positive for desmin and actin (Figure 1F), being characterized as smooth muscle cells.

Myolipomas are rare benign tumors described in humans. Usually, they are characterized by large masses with clearly defined borders and without infiltrate in adjacent tissues, as observed in this case report (MENTZEL & FLECHER, 1995; KIM et al., 2013). The differential diagnosis should include other lipomatous tumors, such as liposarcomas, angiolipomas, spindle-cell lipomas, among others (MENTZEL & FLECHER, 1995; KIM et al., 2013). In the present case report, the diagnosis of myolipoma was based on histological findings, showing the presence of mature adipose tissue and well-differentiated spindle-shaped cells that were positively stained for desmin and actin, confirming its smooth muscle origin. In dogs, a similar tumor, made up of adipocytes and smooth muscle cells, known as lipoleiomyoma, has already been described in the reproductive tract (WOLDEMESKEL, 2008; SYCAMORE & JULIAN 2011). In humans, differentiation of lipoleiomyoma into myolipoma is basically related to location, as lipoleiomyoma occurs in the uterus and myolipoma is reported in soft tissues (MANJUNATHA et al., 2010; KIM et al., 2013).

Given the distribution of abdominal fat observed in HAC, the suspected presence of an

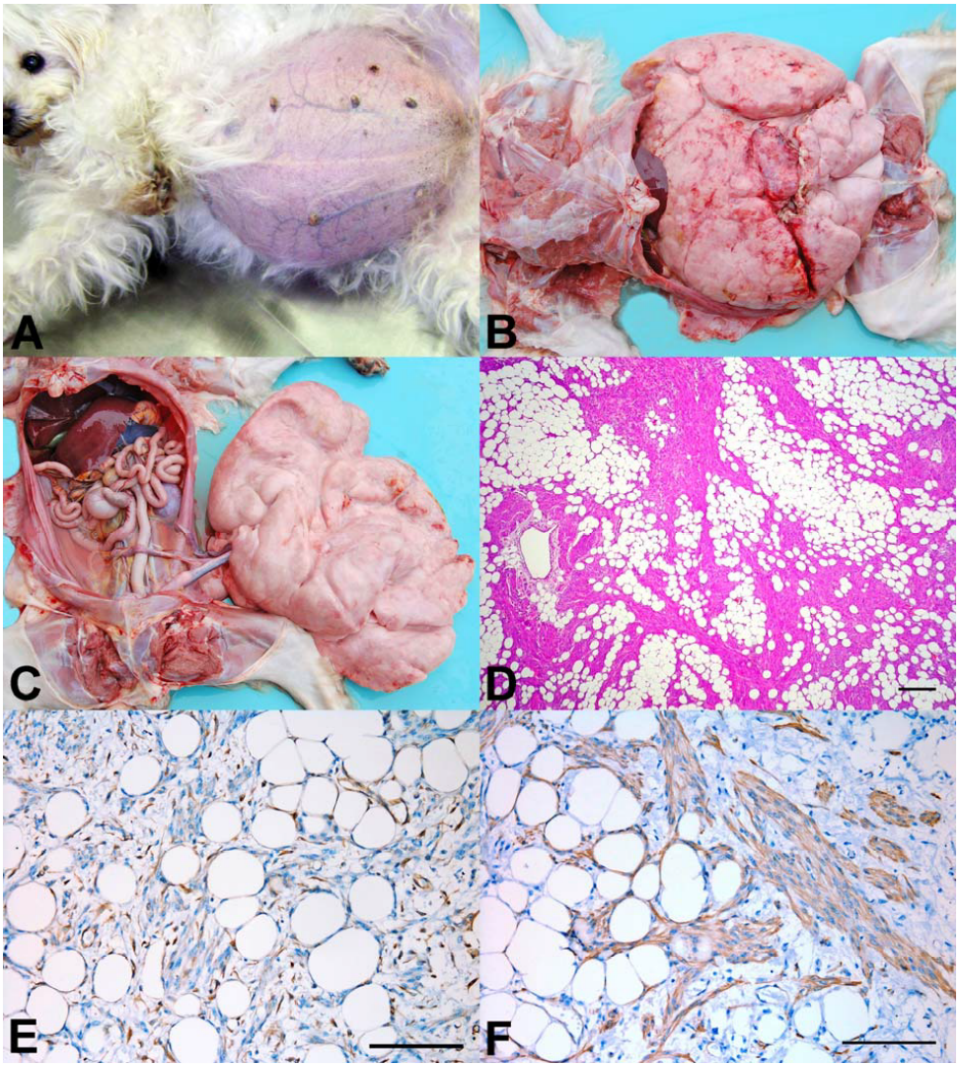

Figure 1 - Hyperadrenocorticism in a diabetic female Poodle with abdominal myolipoma. A. Pronounced abdominal bulging with hypotrichosis, comedones and telangiectasis. B and C. Tumoral lesion was attached to the broad ligament of the left uterine horn and occupied most of the abdominal cavity. D. Neoplasm comprised by a mixed population of well-differentiated adipocytes and spindle-shaped mesenchymal cells. Hematoxylin and eosin. Bar 300µm. E. Cytoplasmic immunostaining for vimentin in mesenchymal spindle-shaped cells and adipocytes. Chromogen DAB. Bar 180µm. F. Immunostaining for smooth muscle actin in the cytoplasm of mesenchymal spindle-shaped neoplastic cells. Chromogen DAB. Bar 180µm.

abdominal tumor initially led to some uncertainty over the origin of the abdominal bulge. One of the clinical features of HAC is the subcutaneous adipose tissue catabolism associated with larger deposition of visceral fat (BEHREND et al., 2012; MICELI et al., 2012). This effect results from hormone-sensitive lipase cortisol-induced activation, combined with lipoprotein lipase cortisol-induced inhibition on the subcutaneous tissue. In the visceral adipose tissue, cortisol induces the differentiation of pre-adipocytes and the increase in glyceroneogenesis, expanding fat deposition in the omental region (MICELI et al., 2012). Likewise, the large muscle catabolism observed in the patient, which could be explained by

the effect of hypercortisolism on the skeletal muscle tissue, or by diabetes catabolism (BEHREND et al., 2012; NELSON, 2015), was associated with tumor cachexia secondary to the large tumor. The good clinical response regarding diabetes treatment such as polyuria and polydipsia absence and body weight maintenance (NELSON, 2015) even with a low relative insulin doses, and plasma cortisol after adrenocorticotrophic hormone stimuli under the reference range (BEHREND et al., 2012) gives subside for tumor cachexia in this case.

This case report provides an interesting unpublished account of a huge intracavitary myolipoma in a patient with HAC and DM. Immunohistochemistry staining for vimentin, desmin, and actin were crucial for the characterization of myolipoma, underscoring the importance of using specific molecular markers in the histopathological diagnosis, especially of rare tumors, instead of aspiration cytology.

DECLARATION OF CONFLICTING OF INTERESTS

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

BIOETHICS AND BIOSSECURITY COMMITTEE APPROVAL

We authors of the article entitled "Myolipoma associated with hyperadrenocorticism and diabetes mellitus in a female poodle" declared, for all due purposes, the project that gave rise to the present data of the same has not been submitted for evaluation to the Comissão de Ética no Uso de Animais of the Universidade Federal do Rio Grande do Sul (CEUA/UFRGS), but we are aware of the content of the Brazilian resolutions of the National Council for Control of Animal Experimentation-CONCEA <http://www.mct.gov.br/index.php/content/view/310553.html> if it involves animals.

Thus, the authors assume full responsibility for the presented data and are available for possible questions, should they be required by the competent authorities.

AUTHORS' CONTRIBUTIONS

AGP, LMC and SPP contributed for the conception, writing and reviewing of the manuscript. AGP, CACB and AVDLF performed clinical and surgical procedures described in the manuscript. SPP performed postmortem analysis.

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