



## Metastatic melanoma in a Saanen goat: clinical, ultrasonographic and anatomopathological aspects – case report

[*Melanoma metastático em cabra Saanen: aspectos clínicos, ultrassonográficos e Anatomopatológicos – relato de caso*]

A.I. Conceição<sup>1</sup>, J.F.P. Cajueiro<sup>1</sup>, C.L. Mendonça<sup>1</sup>, M.I. Souza<sup>1</sup>, J.A.B. Afonso<sup>1</sup>,  
J.B.S. Oliveira<sup>2</sup>, R.L. Santos<sup>2</sup>, A. Arenales<sup>1\*</sup>

<sup>1</sup> Clínica de Bovinos – Universidade Federal Rural de Pernambuco – Garanhuns, PE

<sup>2</sup> Escola de Veterinária – Universidade Federal de Minas Gerais – UFMG – Belo Horizonte, MG

### ABSTRACT

This report describes clinical, ultrasonographic and anatomopathological findings in a case of metastatic melanoma in an adult Saanen goat. Clinically, the goat had apathy, an intra-abdominal palpable firm structure, and exophytic keratinized areas on the skin of the udder. Ultrasound revealed non-encapsulated oval structures, with heterogeneous echogenicity and marked central and peripheral vascularization, and hypoechoic hepatic multifocal to coalescent areas. In the udder, there were non-encapsulated oval structures with heterogeneous echogenicity and hyperechoic center surrounded by hypoechogenic tissue. Grossly, there were black multifocal to coalescent areas in the liver, as well as black nodules in mammary and mesenteric lymph nodes, uterus, spleen, and myocardium. Microscopically, multifocal melanocytic neoplastic proliferation was observed in the dermis and junction of the udder epidermis. Most of the neoplastic cells had cytoplasmic granules of melanin. In the liver there were areas of neoplastic tissue compressing the adjacent parenchyma, with central foci of necrosis, mild desmoplasia, and multifocal infiltration of malignant cells into the adjacent tissues. Similar findings were observed in the mammary and mesenteric lymph nodes, uterus, spleen, and myocardium, which characterized metastatic melanoma. Ultrasonography played a key role for establishing the diagnosis of a metastatic melanoma and helped establish a proper clinical management protocol.

Keywords: dairy goat, diagnostic imaging, metastasis

### RESUMO

*Este relato descreve os achados clínicos, ultrassonográficos e anatomopatológicos em um caso de melanoma metastático em uma cabra Saanen adulta. Clinicamente, a cabra apresentava apatia, estrutura firme palpável intra-abdominal e áreas exofíticas queratinizadas na pele do úbere. A ultrassonografia revelou estruturas ovais não encapsuladas, com ecogenicidade heterogênea e marcada vascularização central e periférica, além de áreas hepáticas multifocais a coalescentes hipoechoicas. No úbere, havia estruturas ovais não encapsuladas, com ecogenicidade heterogênea e centro hiperecogênico circundado por tecido hipoeecogênico. Macroscopicamente, havia áreas pretas multifocais a coalescentes no fígado, bem como nódulos pretos nos linfonodos mamários e mesentéricos, no útero, no baço e no miocárdio; microscopicamente, proliferação neoplásica melanocítica multifocal foi observada na derme e na junção da epiderme do úbere. A maioria das células neoplásicas apresentava grânulos citoplasmáticos de melanina. No fígado, havia áreas de tecido neoplásico comprimindo o parênquima adjacente, com focos centrais de necrose, desmoplasia leve e infiltração multifocal de células malignas nos tecidos adjacentes. Achados semelhantes foram observados nos nódulos linfáticos mamários e mesentéricos, no útero, no baço e no miocárdio, que caracterizaram o melanoma metastático. A ultrassonografia desempenhou um papel*

Recebido em 10 de fevereiro de 2021

Aceito em 18 de maio de 2021

\* Autor para correspondência (*corresponding author*)

E-mail: alexandre.arenales88@gmail.com

fundamental para estipular o diagnóstico de um melanoma metastático e ajudou a estabelecer um protocolo de manejo clínico adequado.

Palavras-chave: cabra leiteira, diagnóstico por imagem, metástase

## INTRODUCTION

Ultrasonography is a non-invasive diagnostic tool that allows evaluation of morphological changes in internal organs, which otherwise would be mostly done by exploratory laparotomy or necropsy (Braun and Steininger, 2011; Sousa and Teixeira, 2019). This technique has been applied to ruminant diagnostic medicine, including its application the diagnosis of neoplastic processes including hepatocellular adenoma (Braun et al., 2005), biliary carcinoma (Braun and Steininger, 2011), lymphoma (Braun et al., 2011), and leiomyoma (Sharma et al., 2012) in cattle; as well as a case of thymoma in a goat (Szaluś-Jordanow et al., 2019).

Melanoma is a malignant melanocytic neoplastic proliferation that is more common in the oral cavity of dogs when compared to other domestic animal species, whereas melanocytoma is the benign counterpart of melanocytic tumors (Goldschmidt and Goldschmidt, 2017). However, melanoma has been reported in goats, in which it is probably due prolonged UV exposition, hereditary factors, or exposure to carcinogens (Parsons et al., 1990; Mavangira et al., 2008; Fazili et al., 2013; El-Shafaey and Hamed, 2020). In goats, melanomas have been reported affecting the lips, nasal planum, horns, perineum, and mammary gland (Ramadan et al., 1988; Mavangira et al., 2008; Carvalho et al., 2014). Although caprine melanoma has been proposed as a suitable model for human melanocytic

neoplasms (Parsons et al., 1990), clinical data and anatomopathological data are scarce, and an ultrasonographic analysis has not been previously reported. Therefore, considering that an accurate diagnosis is critical for establishing the prognosis and to elect suitable therapeutic approaches (Goldschmidt and Goldschmidt, 2017), the aim of this report was to describe ultrasonographic and pathologic findings in a case of metastatic melanoma in a Saanen goat.

## CASUISTRY

An 8-year-old female Saanen goat was referred to the *Clínica de Bovinos de Garanhuns, Universidade Federal Rural de Pernambuco (CBG/UFRPE)* with a history of anorexia. Clinically, the goat had apathy, pale mucous membranes, moderate dehydration, and mild tachypnea. A firm structure at the caudal portion of the right 13th rib was detected by abdominal palpation. There was also bilateral enlargement of mammary lymph nodes, and multiple exophytic and keratinized foci on the skin adjacent to teats. Blood samples were collected for complete blood count, as well as for serum quantification of total proteins, albumin, globulin, creatinine, aspartate aminotransferase and the glutamyl transferase range (Harvey, 2012). The blood count revealed a normochromic normocytic anemia, neutrophilic leukocytosis of 16,250  $\mu$ L, with a left-hand regenerative shift. The biochemical findings are shown in Table 1.

Table 1. Biochemistry values in a Saanen goat with metastatic melanoma

Test	Values	Reference ranges <sup>a</sup>
Serum protein (mg/dL)	7,3	6,4 – 7
Albumin (mg/dL)	2,3	2,70 – 3,90
Globulin (mg/dL)	5	2,70 – 4,10
Albumin:Globulin ratio	0,46	0,63 – 1,26
Aspartate aminotransferase (U/L)	618,1	167 – 513
Gamma glutamyl transferase (U/L)	145,3	20 – 56
Creatinine (mg/dL)	0,84	1,0 – 1,8

<sup>a</sup>: Jain, 1993; Eckersall, 2008; Hoffman and Solter, 2008.

### *Metastatic melanoma...*

Ultrasonographic examination was performed with the goat in quadrupedal position without sedation (Z6Vet, Mindray®, convex probe, multifrequency model 3C5P at 5.0 MHz). In the right paralumbar fossa, corresponding to the hepatic region, there were multiple ovoid non-encapsulated structures with heterogeneous echogenicity, containing multifocal to coalescent hypoechoic areas with dimensions up to 12 x 11.65 cm in diameter (Fig.1A). In addition,

marked central and peripheral vascularization was demonstrated by Doppler ultrasound (Fig.1B). In the mammary parenchyma, there was a multilobulated non-encapsulated and round structure in the dorsal region of the mammary gland, with heterogeneous echogenicity and hyperechoic centers surrounded by hypoechoic tissue (Fig.1C). Euthanasia was performed due to the unfavorable prognosis.

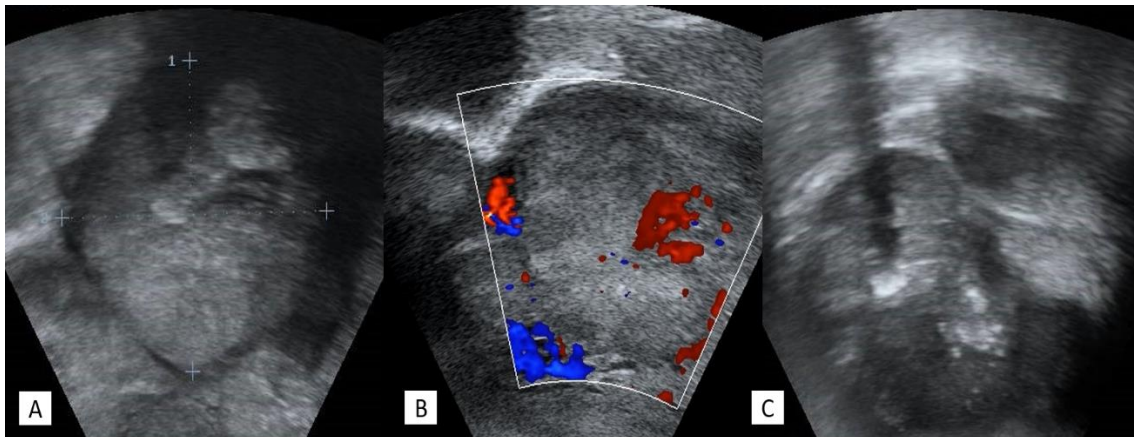


Figure 1. Ultrasound examination in a goat with metastatic melanoma. (A). In the hepatic parenchyma, there are multiple focally extensive and rounded areas of structures with heterogeneous echogenicity. (B). Doppler mode with intense central and peripheral vascularization of nodular structures observed in the liver. (C). Mammary parenchyma with rounded non-encapsulated structures of heterogeneous echogenicity, with a hyperechoic center and surrounded by hypoechoic tissue.

Grossly, there were bilateral focal symmetric areas of abundant and coalescent exophytic cutaneous cornification measuring about 3.0 cm in diameter on the udder adjacent to the teats (Fig.2A). The adjacent skin of the udder had multifocal to coalescent, well circumscribed, and plane pigmented foci, with 0.3 to 0.5 cm in diameter. On the cut surface, there was a focal and multilobulated black pigmented well demarcated nodule measuring approximately 5.0 cm in diameter in the mammary parenchyma (Fig.2B). There were multifocal to coalescent firm black poorly demarcated neoplastic masses occupying approximately two thirds of the hepatic

parenchyma, commonly with a central cavity (Figs.2C and 2D). Multiple mesenteric lymph nodes had a diffuse parenchymal blackish discoloration. A focal nodular blackish area measuring 1.0 cm in diameter was observed in the endometrium of the uterine body. There was also a well circumscribed nodule in the splenic parenchyma measuring 1.5 cm in diameter, and a nodule with 0.3 cm in diameter in the myocardium of the right auricle. Tissue samples were fixed in 10% neutral buffered formalin, processed for paraffin embedding, sectioned in a microtome (3  $\mu$ m-thick sections), and stained with hematoxylin and eosin.

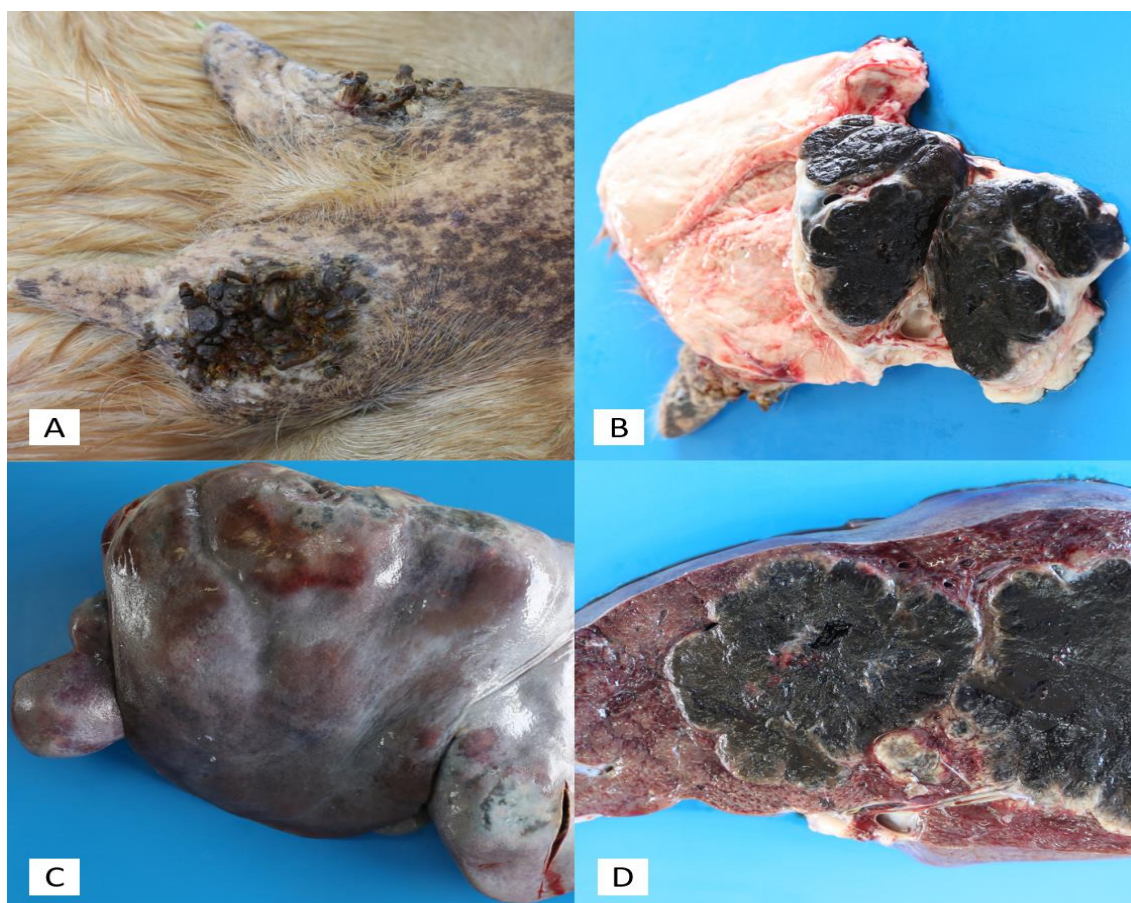


Figure 2. Macroscopic findings in a goat with metastatic melanoma. (A) Abundant cornification in the skin adjacent to both teats. (B) Udder cut surface with a blackish area. (C and D). Majority of hepatic parenchyma is effaced by large multifocal to coalescent and cavity areas.

Microscopically, multifocal to coalescent small aggregates of a neoplastic proliferation at the dermis and dermal-epidermal junction in the skin of the udder. Neoplastic cells were poorly demarcated and loosely aggregated, forming loose nests. The cytoplasm of neoplastic cells was mildly eosinophilic and homogeneous; with a small, round and central nucleus containing fine coarse chromatin and one nucleolus. Within, there are occasional aggregates of cells with heavily pigmented cytoplasm due to accumulation of black to brown granules of melanin. Overall, there were moderate anisocytosis and anisokaryosis, and 4 mitotic figures in 10 per high-power field. Multiple small aggregates of neoplastic cells with variable degrees of pigmentation were observed within the epidermal layer (intraepidermal nests), associated with a moderate multifocal to coalescent lymphocytic inflammatory infiltrate. There was marked keratocyte proliferation

forming exophytic epidermal projections, with severe and diffuse orthokeratosis hyperkeratosis.

In the liver, there were similar neoplastic cells compressing the adjacent parenchyma, with multiple central foci of necrosis, mild desmoplasia and multiple foci of neoplastic infiltration in adjacent tissue (Fig.3). Similarly, there was melanocytic neoplastic proliferation in the uterus, spleen, and heart. Finally, the mammary lymph node was markedly enlarged due to metastatic melanoma.

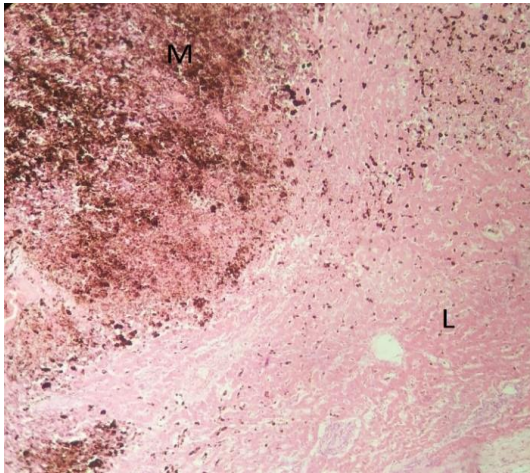


Figure 3. Hepatic microscopic findings in a goat with metastatic malignant melanoma. There is a metastatic foci (M) characterized by abundant blackish pigmented round cells; with expanding growing in the liver parenchyma (L). 10x. H&E.

### DISCUSSION

This report describes an uncommon presentation of a metastatic melanoma in a goat, with ultrasonography playing major role in the diagnosis. In this case, the primary tumor site was not clinically recognizable mainly because the udder skin is commonly pigmented. In fact, the bilateral papillomatous lesions on the udder skin were the cause for skin tissue samples at necropsy and further microscopic evaluation so it is possible that without it, no primary skin tumor would be detected in the present case. Interestingly, two cases lacking primary skin tumors have been previously described in metastatic malignant melanomas in goats (Aydogan *et al.*, 2013; Oryan *et al.*, 2018).

Hematological findings observed here are frequently described in neoplasia studies (Fazili *et al.*, 2013; Rizzo *et al.*, 2019), and may be related to iron homeostasis, abnormal proliferation of erythroid cells, alteration in the production of erythropoietin, reduction red blood cell lifetime and chronic disease, which maintain the acute inflammatory stimulus active (Jain, 1993). The elevated serum levels of GGT and AST observed are compatible with liver injury (Hoffman and Solter, 2008). Increase in total proteins in this case is justified by hyperglobulinemia, consequent to chronic inflammation; and hypoalbuminemia may be associated with synthesis failure, which is

exclusively hepatic. Also, as a consequence of the increase in the concentration of globulin and the decrease in albumin, there is a reduction in Albumin/Globulin ratio (Eckersall, 2008); Similar biochemical changes were found by Rizzo *et al.* (2019).

In healthy animals, liver parenchyma is homogeneous and hypoechoic (Streeter and Step, 2007; Imran *et al.*, 2011; Sousa and Teixeira, 2019), but when it is affected by tumors may change in size, shape and echogenicity. Therefore, pathological changes may result in hypoechoic, hyperechoic or heterogeneous ultrasonographic appearances, varying due to vascularity, tissue infiltration and increased cellularity often associated with neoplasms (Nyman *et al.*, 2004; Braun *et al.*, 2005; Braun, 2009).

In this case, there were structures with heterogeneous echogenicity and hypoechoic areas in the hepatic parenchyma. This appearance was similar to previous descriptions in cases of lymphoma in cattle (Braun *et al.*, 2011; Buczinski *et al.*, 2011) and in the uterus of a cow with leiomyoma (Sharma *et al.*, 2012). Therefore, changes in echogenicity of parenchymal organs are interpreted as ultrasound parameters for possible tumor metastasis or primary tumors (Braun *et al.*, 2005; Buczinski *et al.*, 2011). Furthermore, in this study we were able to demonstrate intense vascularization at center and periphery of neoplastic nodules by using the Doppler mode. Importantly, Doppler analysis have not been previously used in other cases with ultrasonography tumoral detection in cows (Braun *et al.*, 2011; Buczinski *et al.*, 2011; Sharma *et al.*, 2012).

In this case, junctional melanocytic proliferation was associated with severe dermatitis with abundant papillomatous proliferation and hyperkeratosis. Nevertheless, one series of cases of melanoma in goats describes junctional melanocytic proliferation in four animals out of 62 (Ramadan *et al.*, 1988), without any mention of dermatitis, papillomatous lesions or hyperkeratosis. Junctional melanocytic neoplastic proliferation at the dermal-epidermal junction is considered a poor prognostic marker in canine digit and lips melanomas, however it has uncertain prognostic value for cutaneous melanomas (Goldschmidt and Goldschmidt, 2017 Smedley *et al.*, 2011); in addition, multiple and

large intraepidermal nests of neoplastic cells were observed, but it also has not been associated with prognosis in dogs (Smedley et al., 2011). This change likely stimulated papillomatous epidermal proliferation in this case.

### CONCLUSION

Melanoma has an unfavorable prognosis and should be included as a differential diagnosis of metastatic neoplasms in goats. The ultrasound examination was invaluable in this case for tumoral identification and prognostic assessment.

### REFERENCES

- AYDOGAN, A.; HALIGUR, M.; OZMEN, O. Hepatic malignant melanoma in a goat, primary or metastatic? *Isr. J. Vet. Med.*, v.68, p.124-127, 2013.
- BRAUN, U. Ultrasonography of the liver in cattle. *Vet. Clin. N. Am. Food A.*, v.25, p.591-609, 2009.
- BRAUN, U.; NUSS, K.; SOLDATI, G.; OSSENT, P. Clinical and ultrasonographic findings in four cows with liver tumours. *Vet. Rec.*, v.157, p.482-484, 2005.
- BRAUN, U.; SCHNETZLER, C.; DETTWILER, M. et al. Ultrasonographic findings in a cow with abomasal lymphosarcoma: case report. *BMC Vet. Res.*, v.7, 4p., 2011.
- BRAUN, U.; STEININGER, K. Ultrasonographic characterization of the liver, caudal vena cava, portal vein, and gallbladder in goats. *Am. J. Vet. Res.*, v.72, p.219-225, 2011.
- BUCZINSKI, S.; BÉLANGER, A.M.; FRANCOZ, D. Ultrasonographic appearance of lymphomatous infiltration of the abomasum in cows with lymphoma. *J. Am. Vet. Med.*, v.238, p.1044-1047, 2011.
- CARVALHO, F.K.L.; DANTAS, A.F.M.; RIET-CORREA, F. et al. Estudo retrospectivo das neoplasias em ruminantes e equídeos no semiárido do Nordeste Brasileiro. *Pesqui. Vet. Bras.*, v.34, p.211-216, 2014.
- ECKERSALL, P.D. Proteins, proteomics, and the dysproteinemia, In: KANEKO. J.J.; HARVEY J.W.; BRUSS M.L. *Clinical biochemistry of domestic animals*, 6.ed. Amsterdam: Academic Press, 2008. p.117-155.
- EL-SHAFAEY, E.; HAMED, M.F. Uveal melanoma in an Aradi Goat (*Capra aegagrus hircus*). *J. Comp. Pathol.*, v.177, p.5-9, 2020.
- FAZILI, M.R.; DARZI, M.M.; BUCHOO, B.A. et al. Melanoma of foot in two local goats of Kashmir - a case report. *Vet. Arh.*, v.83, p.105-113, 2013.
- GOLDSCHMIDT, M.H.; GOLDSCHMIDT, K.H. Epithelial and melanocytic tumors of the Skin. In: MEUTEN, D.J. *Tumors in domestic animals*. 5.ed. Iowa: John Wiley & Sons; 2017. p.88-142.
- HARVEY, J.W. Hematology procedures. In: HARVEY, J.W. (Eds.). *Veterinary hematology. A diagnostic guide and color atlas*. St. Louis: Elsevier, 2012. p.11-32.
- HOFFMAN, W.E.; SOLTER, P.F. Diagnostic enzymology of domestic animals. In: KANEKO. J.J.; HARVEY J.W.; BRUSS M.L. *Clinical biochemistry of domestic animals*. 6.ed. Amsterdam: Academic Press, 2008. p.351-378.
- IMRAN, S.; TYAGI, S.P.; KUMAR, A. et al. Comparative ultrasonographic imaging of spleen and liver in healthy crossbred cows. *ISRN Vet Sci.* p.1-7. 2011.
- JAIN, N. C. *Essentials of veterinary hematology*. Philadelphia: Lea & Febinger, 1993, 417p.
- MAVANGIRA, V.; HUGHES, J.M.; MIDDLETON, J.R. et al. Malignant melanoma of the horn base in a Pygora goat. *J. Vet. Diagn. Invest.*, v.20, p.104-107, 2008.
- NYMAN, H.T.; KRISTENSEN, A.T.; FLAQSTAD, A.; McEVOY, F.J. A review of the sonographic assessment of tumor metastases in liver and superficial lymph nodes. *Vet. Radiol Ultrasound*, v.45, p.438-448, 2004.
- ORYAN, A.; GHANE, M.; AHMADI, N.; DANESHBOD, Y. Melanoma of unknown primary origin metastasizing to visceral organs in a sheep. *Braz. J. Vet. Pathol.*, v.11, p.24-27, 2018.
- PARSONS, P.G.; TAKAHASHI, H.; CANDY, J. et al. Histopathology of melanocytic lesions in goats and the establishment of a melanoma cell line: a potential model for human melanoma. *Pigment Cell Res.*, v.3, p.297-305, 1990.
- RAMADAN, R.O.; EL HASSAN, A.M.; EL DEEN, T.M.H. Malignant melanoma in goats: a

*Metastatic melanoma...*

clinico-pathological study. *J. Comp. Pathol.*, v.98, p.237-241, 1988.

RIZZO, H.; ARAÚJO, C.A.S.C.; SILVA, B.H.S.; OLIVEIRA, R.A.S. *et al.* Melanoma em cabra leiteira. *Acta Sci.*, v.47, Supl.1, p.1-7, 2019.

SHARMA, A.; KUMAR, A.; IMRAN, S. *et al.* Ultrasonographic, surgical, and histopathological findings of a uterine leiomyoma in a cow. *Case rep. Vet. Med.*, p.1-4, 2012.

SMEDLEY, R.C.; SPANGLER, W.L.; ESPLIN, D.G. *et al.* Prognostic markers for canine melanocytic neoplasms: a comparative review of

the literature and goals for future investigation. *Vet. Pathol.*, v.48, p.54-72, 2011.

SOUSA, F.C.; TEIXEIRA, D.I.A. Ultrassonografia esplênica, hepática, biliar e renal em caprinos: uma revisão. *Med. Vet.*, v.13, p.506-513, 2019.

STREETER, R.N.; STEP, D.L. Diagnostic ultrasonography in ruminants. *Vet. Clin. North Am. Food Anim. Pract.*, v.23, p.541-574, 2007.

SZALUŚ-JORDANOW, O.; CZOPOWICZ, M.; WITKOWSKI, L. *et al.* Malignant thymoma – the most common neoplasm in goats. *Pol. J. Vet. Sci.*, v.22, p.475-480, 2019.