Abdominal wall mass in a dog

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Specimen

Abdominal wall mass aspirates and biopsy specimen touch imprints.

Signalment

11yo, neutered female, Golden Retriever.

History

The dog was admitted due to the presence of a slowly progressive growing mass detected three months before initial presentation on the ventral abdomen.

Clinical findings

The presence of a 3 cm nodule initially described as subcutaneous was confirmed during the physical examination. No other abnormalities were found on the physical examination. The lesion was located

on the rectus abdominis muscle, slightly to the right of the midline, and it was characterized by being hard in consistency and to be adhered to surrounding tissues.

Diagnostic procedures

Complete blood count (CBC) and biochemistry showed no abnormalities. A fine needle aspirate (FNA) of the sample was performed and sent for cytological evaluation (Figure 1,3).

Based on the cytological findings a complete work-up including thoracic radiographs, abdominal ultrasound, and computed tomography (CT), was performed prior to an en bloc surgical resection. Imprint touch slides from the biopsy specimen were prepared right after surgical resection (Figure 2,4).

- **Mass and abdominal ultrasound:**

Abdominal ultrasound and thoracic radiographs were unremarkable.

The mass was hypoechoic, slightly heterogeneous, and had well-defined margins. It was circumscribed between the muscular layers of the ventral abdominal wall and measured about 2cm in diameter.

- **Computed tomography**:

A soft tissue-attenuating nodule of 2cm in diameter was identified at the level of L3, in the rectus abdominis muscle, affecting both internal and external layers. The lesion showed moderate heterogeneous contrast enhancement and did not extend the peritoneal cavity (figures 5-6).

In the thoracic cavity, a rounded soft tissue-attenuating lesion of 5mm diameter and moderate contrast enhancement was observed in the right cranial lung lobe. Differential diagnoses included metastatic nodule, granuloma, or fibrotic lesion. Follow-up CT was recommended to characterize this lesion better.

Questions

1.- Describe the cytological findings of both aspirate and touch imprints

2.- Based on the cytological findings, list the most likely differential diagnosis

Interpretation/Diagnosis

The cytological interpretation was consistent with a proliferation of hepatocytes with mild to moderate atypia and a cytologic diagnosis of a well-differentiated hepatocellular carcinoma (WD-HCC) was made.

Additional information

On cytology, an abundant number of sheets of polygonal to rounded epithelial cells with a moderate nucleus to cytoplasm ratio were detected. Most of the cells displayed a perivascular arrangement and some acinar structures were also visualized. Nuclei were round, centrally placed, with coarsely stippled chromatin and one to multiple prominent nucleoli. The cytoplasm was amphophilic with distinct borders. Occasional intracytoplasmic clear vacuoles were present. Mild to moderate anisocytosis and anisokaryosis were observed. Also seen were frequent binucleated and multinucleated cells, macrokaryosis, and atypical mitotic figures (Figures 1-4).

Right after surgical resection of the mass, it was sent for histopathological evaluation. Sections of the nodule were stained with haematoxylin and eosin (HE). It consisted of a partially encapsulated, moderately cellular, lobulated neoplastic growth that expanded adjacent muscle fibers and adipose tissue. It was composed of irregular trabeculae with a moderate amount of fibrous desmoplasia and multifocally random distributed areas of coagulative necrosis and hemorrhage. Neoplastic cells show a cuboidal morphology with well-defined cell borders, a moderate amount of deep eosinophilic cytoplasm and single rounded nuclei. Anisocytosis and anisocariosis were mild to moderate and the mitotic index low (2-3 mitotic figures/HPF) with occasionally aberrant mitotic figures (Figure 7). Immunostaining for Ki 67 was performed and showed a high cellular proliferative activity (21.1 positive nuclei/HPF) (Figure 8). Well-differentiated trabecular hepatocellular carcinoma was diagnosed.

Previous history, follow up and clinical outcome

One year and a half before presentation due to the presence of the slowly growing ventral abdominal muscular mass, the dog was admitted for the investigation of a markedly increased in liver enzymes

activities. A 10 x 6 cm heterogeneous pedunculated liver mass, affecting the left liver lobe, in the mid-abdomen was detected via abdominal ultrasound. An ultrasound-guided core-needle biopsy of the mass was performed using a semiautomatic core-needle biopsy of 14-gauge (ARGON Medical Devices®, USA). The histological examination showed a diffuse mild inflammatory process mainly composed of macrophages and scarce neutrophils, hepatic trabeculae were regular in thickness and hepatocytes resembled normal hepatocytes. The absence of portal triads and the small sample size made it impossible to establish whether the lobular architecture of the liver was intact. The dog was reevaluated three months after the initial presentation. The owners described episodes of tachypnea interpreted as episodes of pain. Physical examination was normal. CBC, biochemistry, thoracic radiographs, and abdominal ultrasound were performed. Due to a persistent marked increase in hepatic enzymes and a mild increase in the size of the liver mass, a partial hepatectomy was performed (Figure 9).

Sections of the liver mass were stained with hematoxylin and eosin (HE) and immunohistochemistry for Ki 67 proliferation marker was performed. The histopathologic examination of the mass showed a non-encapsulated, moderately cellular, neoplastic epithelial proliferation that was clearly demarcated and well-differentiated from the adjacent normal liver. Neoplastic cells arranged forming regular trabeculae of 2-3 cells thick separated by sinusoids. They showed a cuboidal morphology with a moderate to a high amount of deeply eosinophilic cytoplasm, occasionally microvacuolated (glycogen storage), and well-defined cytoplasmic borders. Nuclei were rounded with stripped chromatin and single nucleoli. Anisocytosis and anisocaryosis were mild and the mitotic index was minimum (0-1 mitotic figures/HPF). Within the neoplastic proliferation and in a multifocal to generalized pattern there was moderate ductal proliferation surrounded by scarce mature fibrous tissue. Multifocally and randomly distributed, a few hepatic sinusoids appeared distended and filled with blood (interpreted as telangiectasias) (Figure 10). Immunostaining for Ki 67 protein of cellular proliferation showed a slight positivity (2.9 positive nuclei/HPF) (Figure 11). The non-affected liver parenchyma showed a massive cytoplasmic rarefaction (glycogen storage). The diagnosis of a hepatocellular adenoma was made. After surgical resection of the abdominal wall mass, the dog recovered without any complication, and, at the time of writing, the dog was free of disease.

Discussion

Hepatic neoplasia is a rare condition in dogs accounting for between 0.6 to 1.3% of all canine neoplasms (1,2). Hepatocellular carcinoma (HCC) is the most frequent primary hepatic neoplasm, being the hepatocellular adenoma (HCA) an unusual condition. They usually appear in dogs older than 10 years and, there is not sex or breed (1,2). Dogs with hepatic neoplasia can show non-specific clinical signs including anorexia, weight loss, lethargy, polyuria/polydipsia, ascites, vomiting, diarrhea, and less frequently neurologic signs. Other more specific clinical signs such as hepatomegaly and icterus can also be present (1,2). However, up to 50% of dogs with hepatic tumors show no clinical signs and will be diagnosed during the investigation of increased liver enzyme activities (3). Although the physical examination is often unremarkable, a cranial abdominal mass can be detected in up to 75% of dogs with a liver tumor (2). Clinicopathological findings are non-specific, therefore, they cannot distinguish between neoplastic and nonneoplastic diseases of the liver. Nonregenerative anemia, leukocytosis, and increased liver enzymes (ALP, ALT, AST) are the most common laboratory findings (1,2).

Diagnostic differentials of hepatic masses in dogs include nodular hyperplasia, regenerative nodules, hepatocellular adenoma, hepatocellular carcinoma, bile duct carcinoma, hepatic carcinoids, abscesses, and metastatic neoplasia. Therefore, in veterinary medicine, morphologic evaluation of the liver remains necessary to establish a definitive diagnosis (4). However, in human medicine, diagnosis is mainly based on computed tomographic and magnetic resonance imaging findings, and biopsy is only used when the imaging pattern is not fully concordant with the diagnostic criteria (5). In this case, a first diagnostic attempt was carried out through an ultrasound-guided core-needle biopsy. The regularity of the trabeculae and the morphological features of the hepatocytes resemble normal liver parenchyma, but the absence of portal spaces made it impossible to establish whether it was a well-differentiated benign neoplastic growth (adenoma) or a hyperplastic nodule. A study in dogs comparing different methods of liver core-needle biopsies using different needle sizes with paired necropsy biopsies found a low accuracy between both core-needle and wedge biopsies (6). This observation was related to the small size of the samples obtained with core-needle biopsies and the presence of 3-12 portal triads and multiple biopsies were recommended to enhance the likelihood of a correct diagnosis (6).

In the present case, the histologic features of the surgically resected liver mass were consistent with hepatocellular adenoma. However, a year and a half after the core-needle biopsy, a slowly growing abdominal wall nodule appeared in the region of the needle tract. This mass was diagnosed as a well-differentiated hepatocellular carcinoma cytologically and histologically. Histologically, it presented characteristics of malignancy such as multiple areas of necrosis, irregular trabeculae, moderate anisokaryosis and anisocytosis, and a highly increased proliferative activity (examined by Ki67 immunostaining) that confirmed the cytological diagnosis. Additionally, both histological specimens were later blinded reviewed by different anatomic pathologists confirming both diagnoses.

Malignant transformation of an HCA into an HCC is a rare but well-known complication in human medicine (7). Malignant transformation has been reported in 4.2% of human patients with HCA (7). However, to the authors' knowledge this is the first report suggesting a possible malignant transformation of HCA into HCC associated with a needle tract seeding. Although the natural history of this progression is not well defined, multiple risk factors have been associated with malignant transformation including male sex, tumor size > 5cm, oral contraceptive intake, and genetic mutations (7,8). In this case, the presence of a 10-fold increase in the expression of Ki 67 by the abdominal wall mass compared with the initial liver mass could support the hypothesis of a malignant transformation during the seeding process. The ability of the Ki 67 in differentiating HCA from HCC has been evaluated in human liver samples (9). Although most of the HCA had a low Ki 67 expression (less than 4%), up to 50% of the HCC cases had also a Ki 67 expression lower than 4%, limiting its usefulness (9).

The morphological features of a WD-HCC often overlap with those of benign neoplasm HCA and less frequently with benign proliferations such as nodular hyperplasia, and regenerative nodules, making them histopathological and cytologically difficult to distinguish (10). Therefore, an initial HCC classified as HCA due to its well-differentiated nature with its subsequent seeding cannot be completely ruled out.

Needle-tract seeding is a known complication associated with percutaneous needle biopsies. Although its incidence is rare in both human and animal patients, the development of needle tract metastases (NTM) following biopsies has been described for almost every type of human cancer (11). In veterinary medicine, has been described in transitional cell carcinoma (12–15), pancreatic carcinoma (16), pericardial mesothelioma (17), renal cell carcinoma (18), carcinomatosis (19) and pulmonary

adenocarcinoma (14,20). Seeding of HCC along the needle tract has been widely described in human medicine and, even though initially the incidence was thought to be high (up to 5% of cases depending on the study) (21), larger recent studies have described incidences of needle track seeding of HCC of 0.25% (22). The time needed for the development of seeded tumors is variable and it seems not to affect survival. Factors associated with a higher risk of implantation along the needle tract are several including multiple needle passes, use of larger-gauge needles and with cutting mechanism, degree of histologic differentiation (higher risk for patients with WD-HCC, due to a longer survival), and thickness of the liver parenchyma along the needle tract. Small size of the tumor has also been related to an increased risk of implantation, but this is explained since in human medicine imaging findings of small HCCs are non-specific and, therefore a higher number of small HCCs are biopsied than larger ones (23). In the present case, a biopsy with a 14-gauge needle and a single pass was performed, however, the large size, its superficial position and the well-differentiated nature of the tumor could be the reasons why the implanted tumor was detectable. Finally, although veterinarians should be aware of the risk of needle tract implantation after percutaneous biopsies, the frequency seems to be generally low, and the benefits outweigh the cons when compared with the valuable information obtained. Therefore, due to the low accuracy between core needle and wedge biopsies, a fine needle aspiration prior to a more invasive liver biopsy techniques, should always be pursued as a first step when dealing with hepatic masses and nodules.

In conclusion, this case report documents for the first time a needle-tract seeding of a liver epithelial tumor in a dog. In addition, this case also reflects for the first time in the veterinary literature a possible malignant transformation of HCA into HCC.

FIGURES

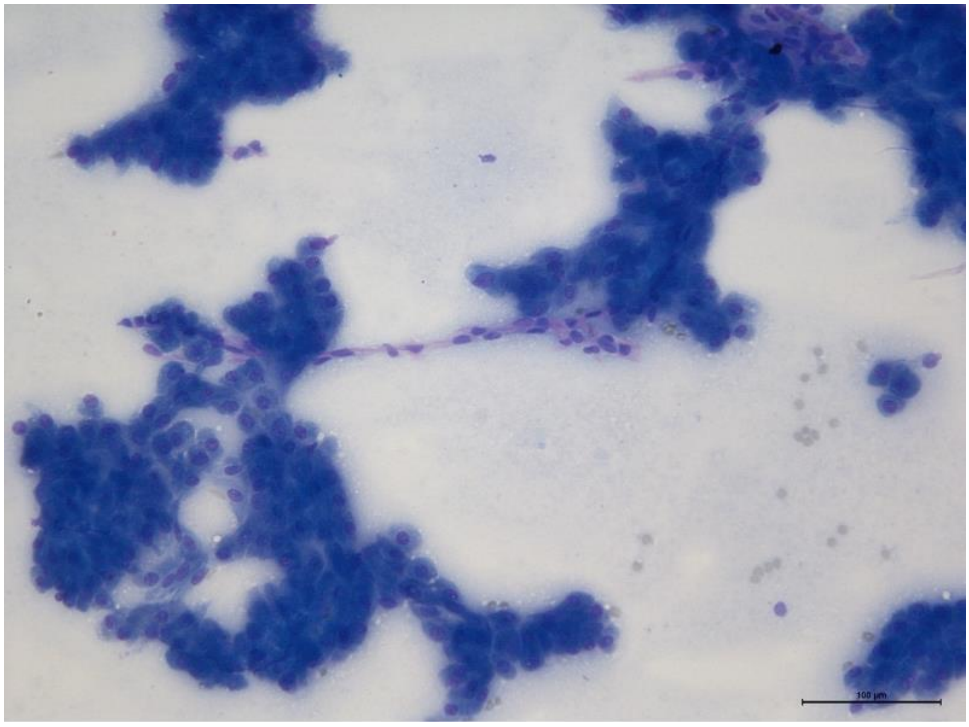

Figure 1.- **Abdominal wall mass FNA**; modified rapid Romanowsky-stain (Quick Panoptic®) (x200)

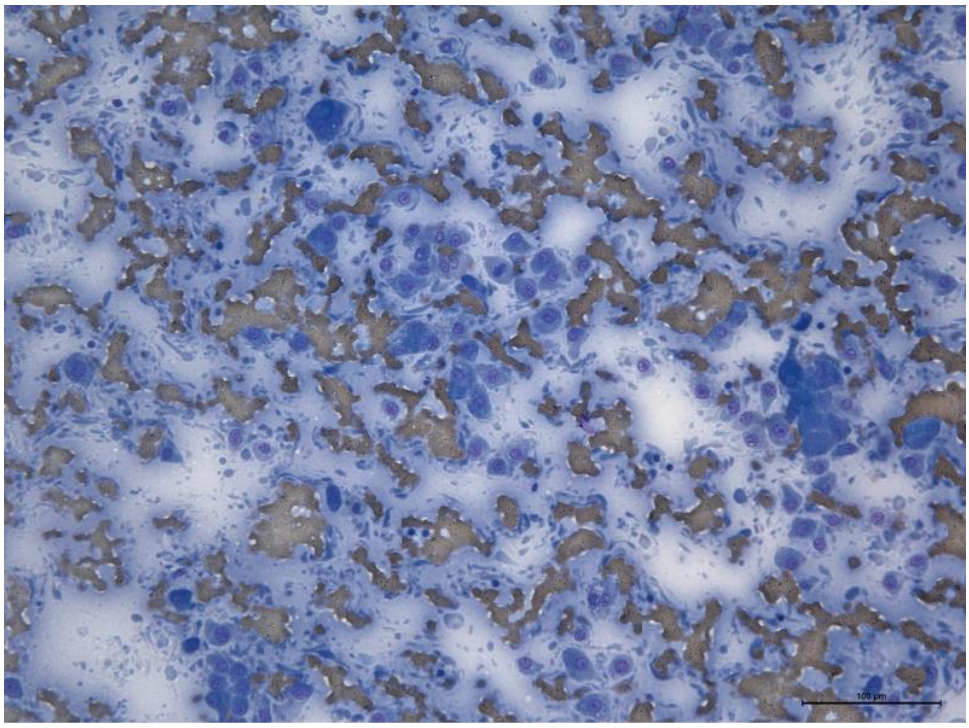

Figure 2.- **Abdominal wall mass touch imprint**; modified rapid Romanowsky-stain (Quick Panoptic®) (x200)

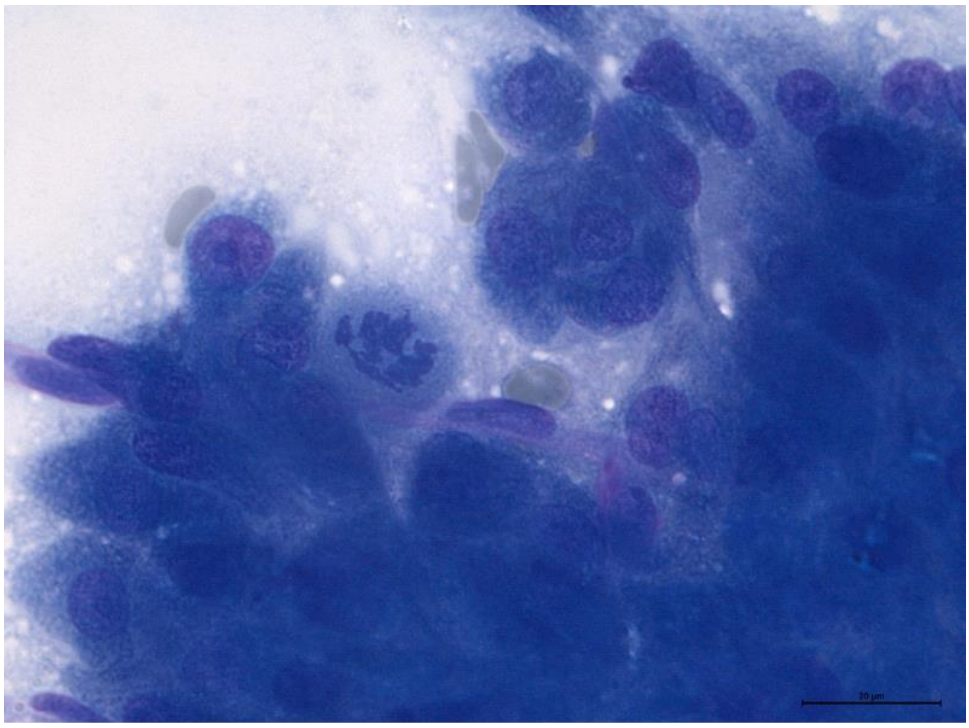

Figure 3.- **Abdominal wall mass FNA**; modified rapid Romanowsky-stain (Quick Panoptic®) (x1000)

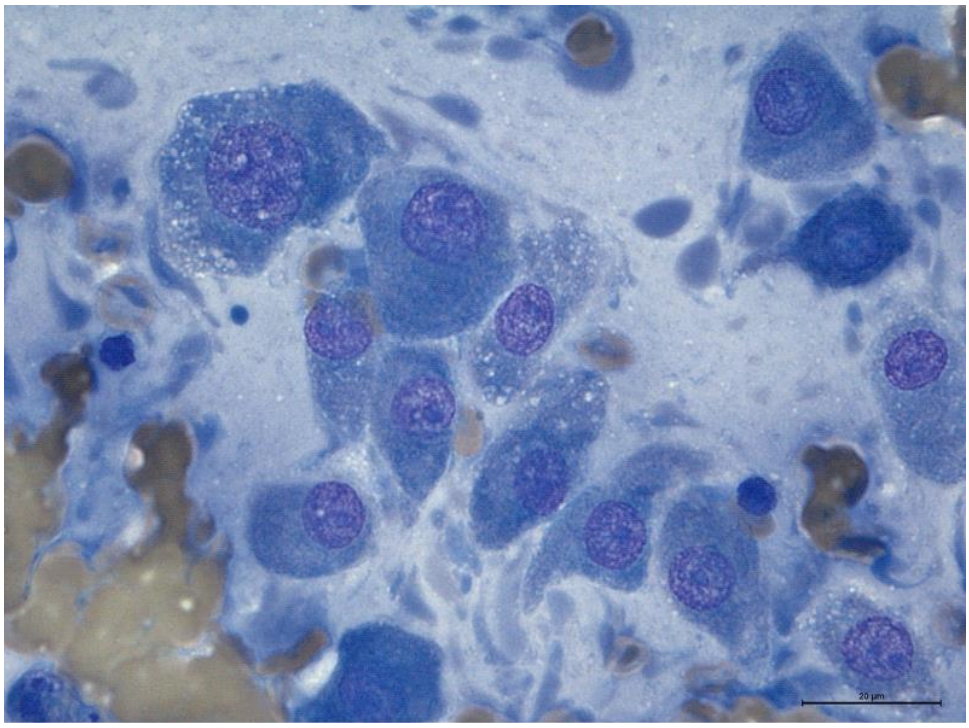

Figure 4.- **Abdominal wall mass touch imprint**; modified rapid Romanowsky-stain (Quick Panoptic®) (x1000)

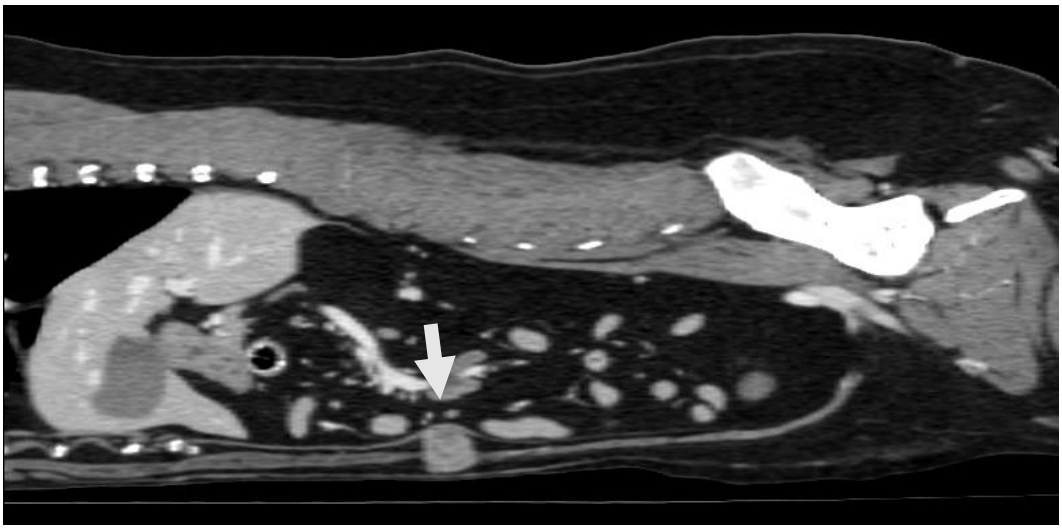

Figure 5.- **Post contrast sagittal CT reconstruction in soft tissue window.** The soft tissue-attenuating nodule (white arrow) was located around 8 centimeters caudal to the liver.

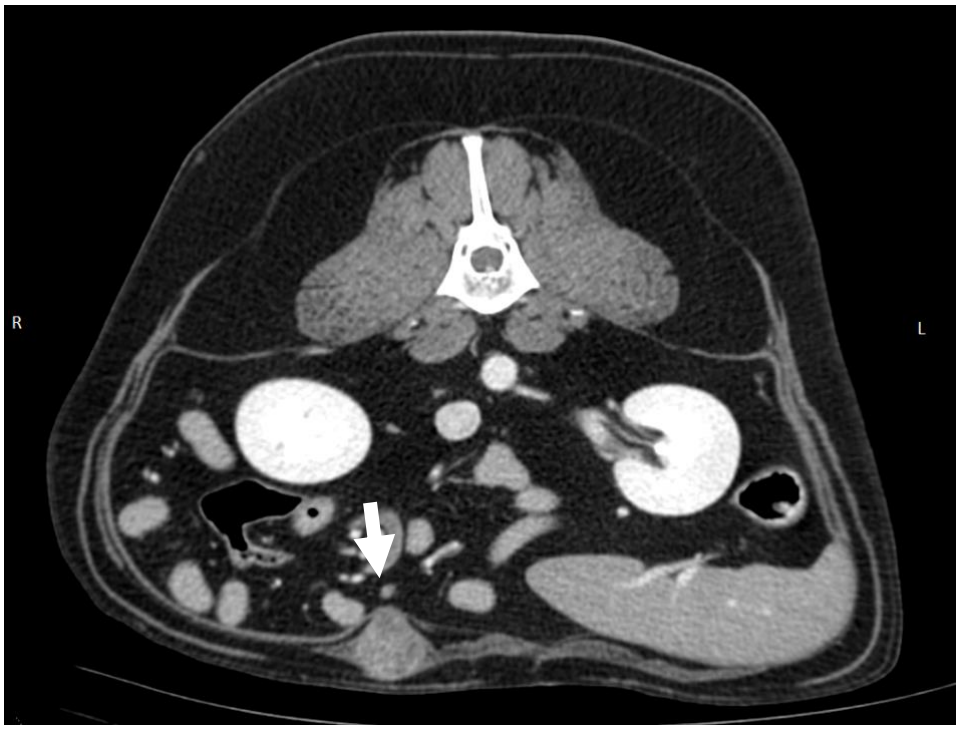

Figure 6.- **Post-contrast transverse CT image at the level of the kidneys**. The soft tissue-attenuating nodule (white arrow) was located between the internal and external layers of the rectus abdominis muscle without extending into the abdominal cavity.

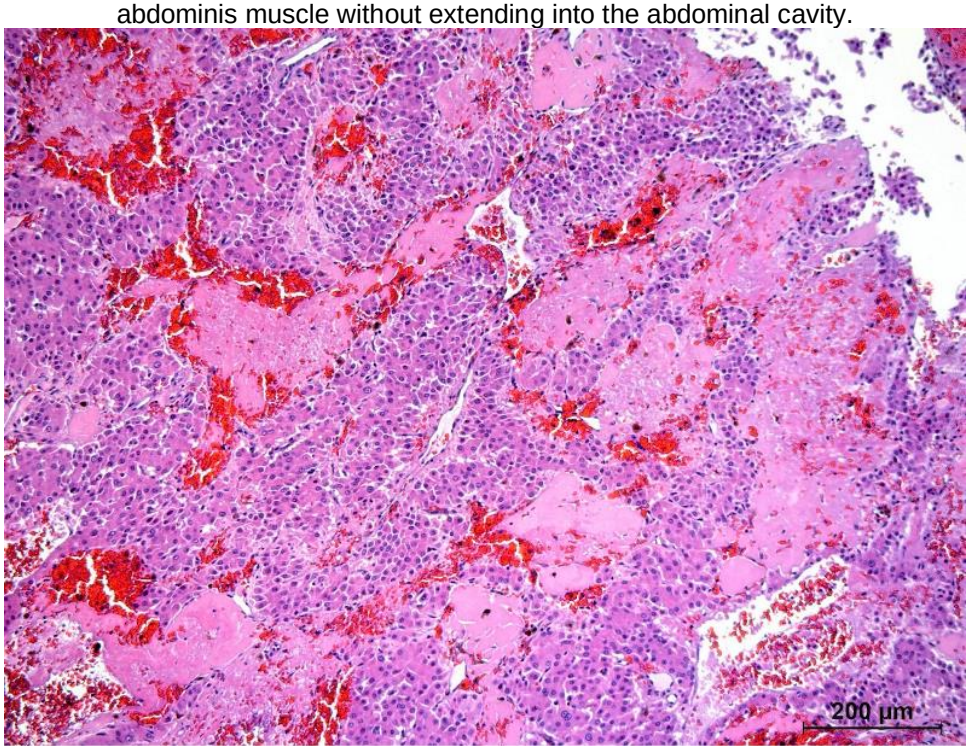

Figure 7.- **Abdominal wall mass histopathology;** HE stain (x20). Irregular trabeculae were observed admixed with multifocal randomly distributed areas of necrosis and hemorrhage.

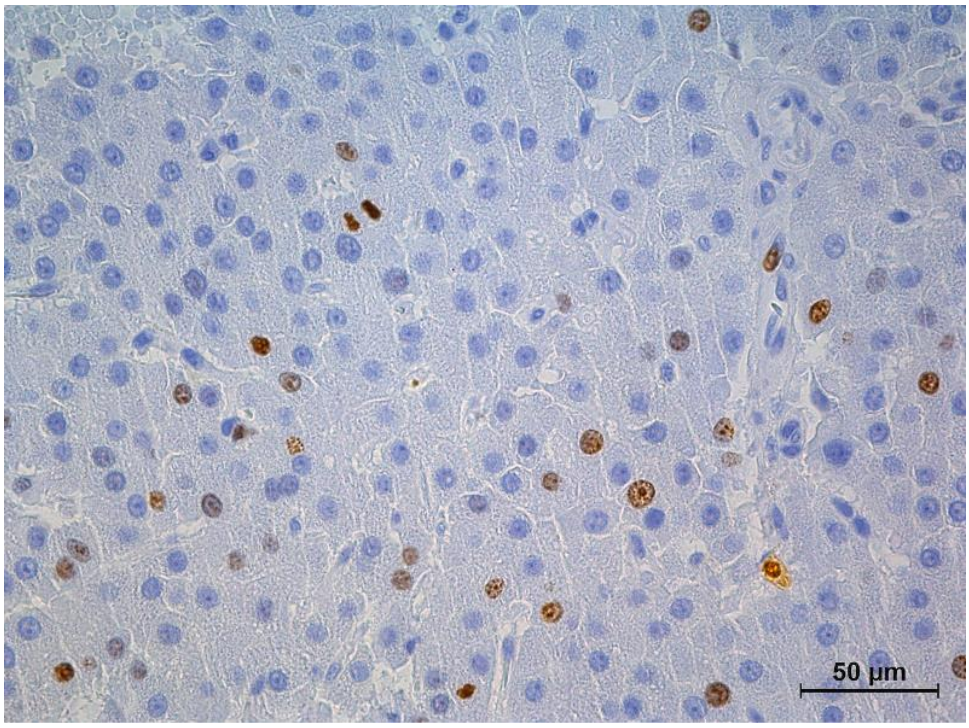

Figure 8.- **Abdominal wall mass immunohistochemistry**. Ki-67 stain (x40) shows a high cellular activity of an average of 21.1 positive nuclei/HPF.

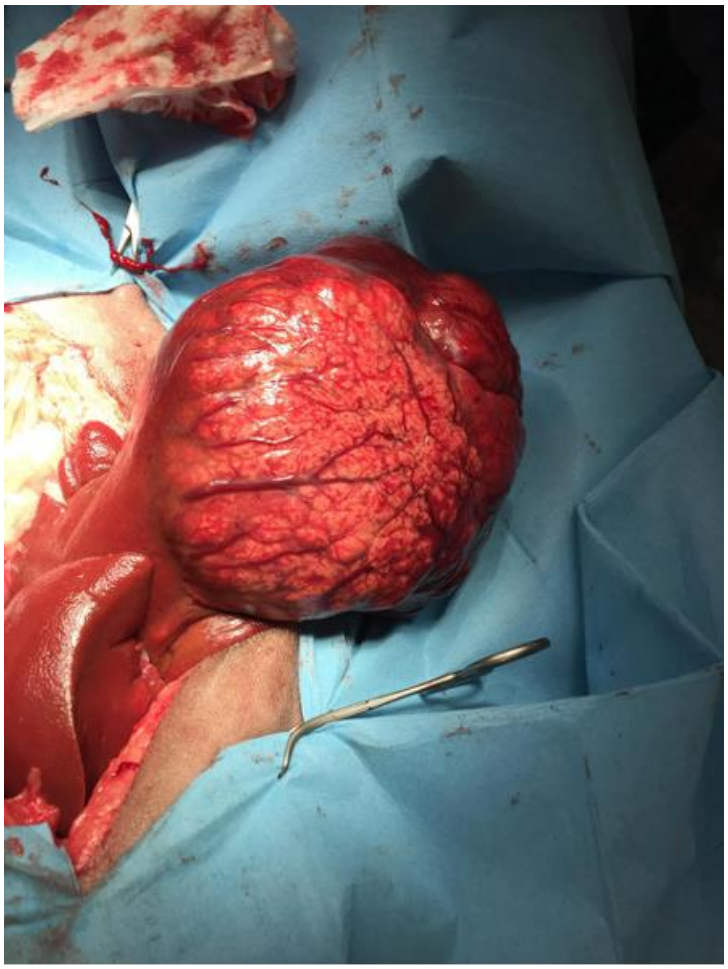

Figure 9.- Left hepatic lobe presented a pedunculated, well vascularized soft nodule of 10-12 cm in diameter that showed a distinct border with the surrounding and apparently normal liver.

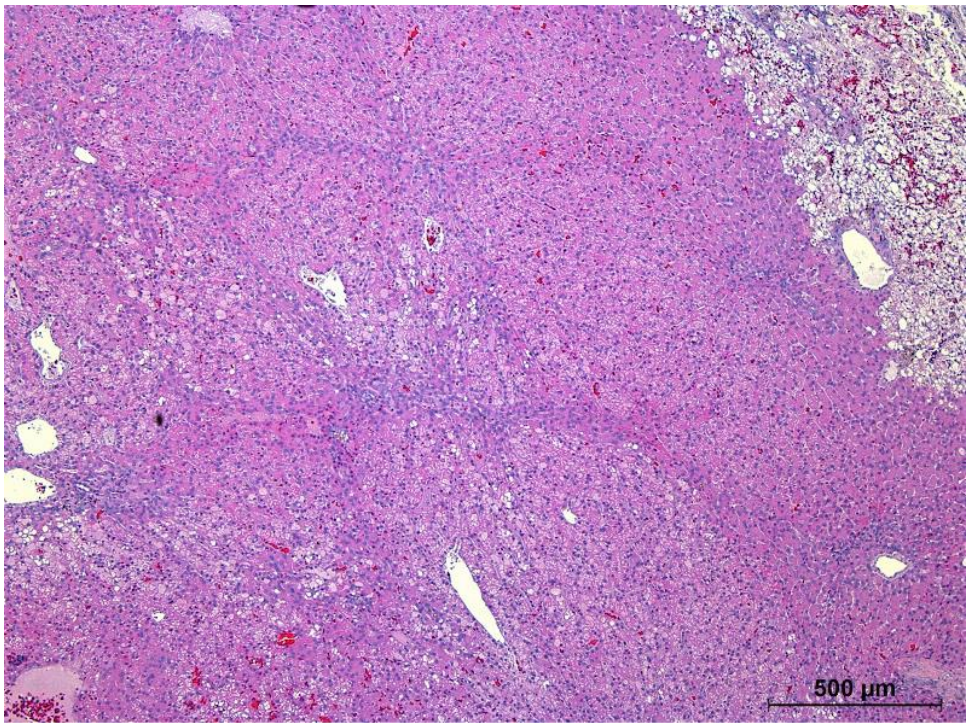

Figure 10.- **Liver mass histopathology**; HE stain (x10). Multiple hepatic pseudo lobules with an occasional centrolobulillar vein and regular thick trabecula.

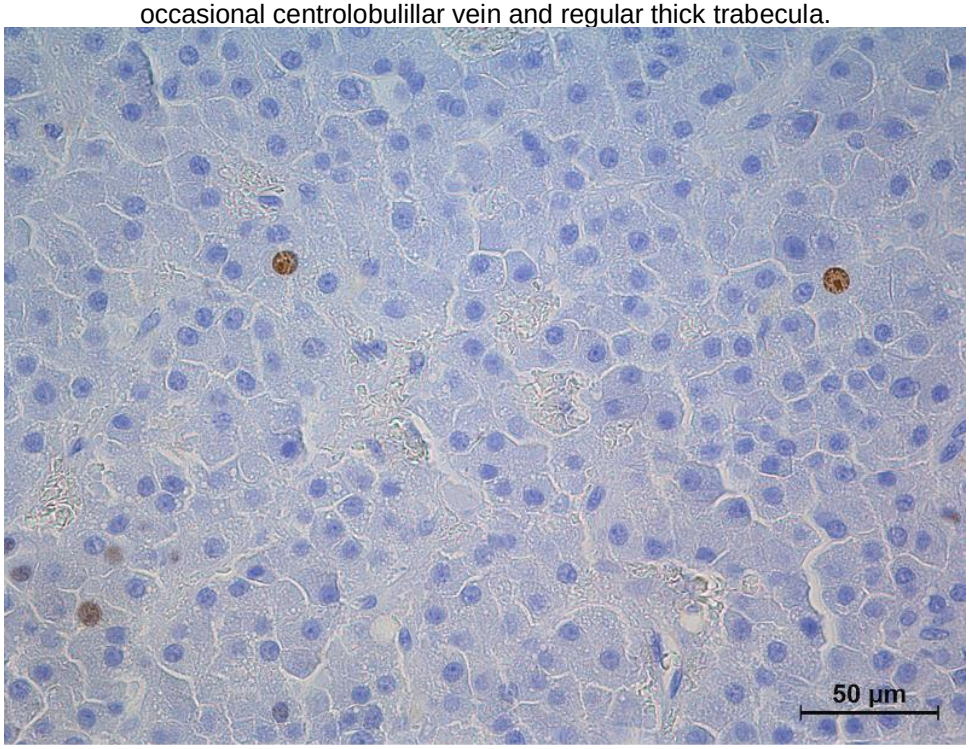

Figure 11.- **Liver mass immunohistochemistry**. Ki-67 stain (x40) shows a slight positivity of an average of 2.9 positive nuclei/HPF.

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