Case 4

Adrenocortical carcinoma in a dog

CYTOLOGIC DESCRIPTION

The preparations from the adrenal mass were highly cellular with good cell preservation. The smears contained large sheets of polygonal-shaped cohesive cells, occasionally associated with strands of wispy, fibrillar, magenta staining matrix. These cells exhibited moderate anisocytosis and anisokaryosis. They had abundant granular amphophilic cytoplasm which contained many small clear vacuoles. Cells had round and centrally placed nuclei with coarse chromatin and frequently a single prominent nucleolus. Occasional cells had increased nuclear-to-cytoplasmic ratio and occasional binucleated cells were seen.

The smears from the liver were of high cellularity with good cell preservation. These preparations contained sheets of well-differentiated hepatocytes, showing moderate to marked cytoplasmic rarefaction. There were also a few cells with an appearance similar to those observed in the aspirates from the adrenal mass.

The cytological interpretation for the adrenal gland was aspiration of adrenal cortical tissue, and given the features of atypia displayed by the epithelial cells, an adrenal cortex carcinoma was a differential. The hepatic aspirates were suggestive of metabolic hepatopathy and there was suspicion of metastasis of adrenal cortex carcinoma to the liver.

In light of these findings, a CT scan of the abdomen was performed.

ADDITIONAL TEST RESULTS

Imaging

A CT scan of the abdomen was performed and demonstrated a large, encapsulated mass associated with the right adrenal gland. This was in close proximity to the caudal vena cava. The left adrenal gland appeared to be normal. There were multiple hypo-attenuating nodules present throughout the liver and one was present within the spleen.

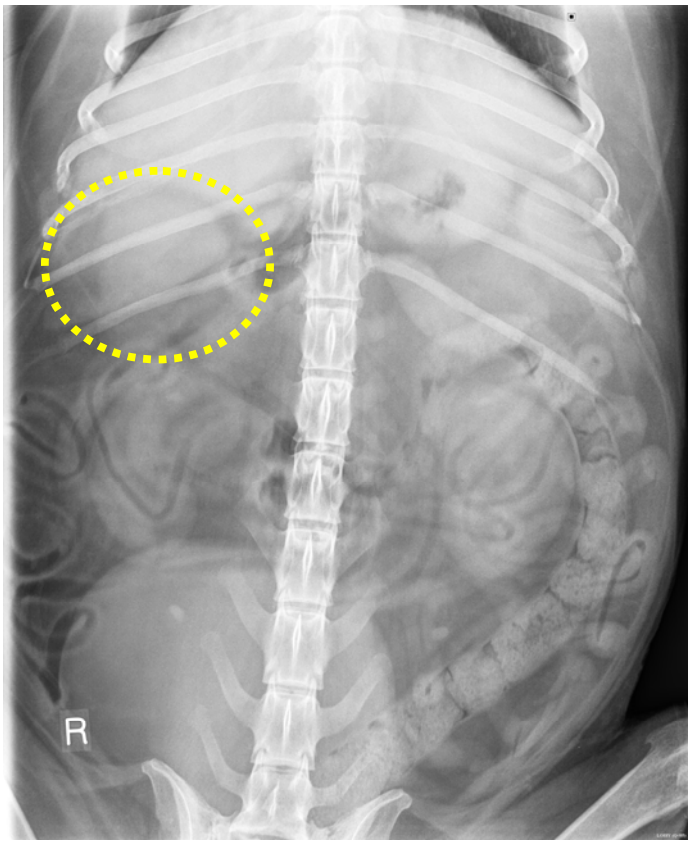


Figure 6. Abdominal radiography. Ventro-dorsal view.

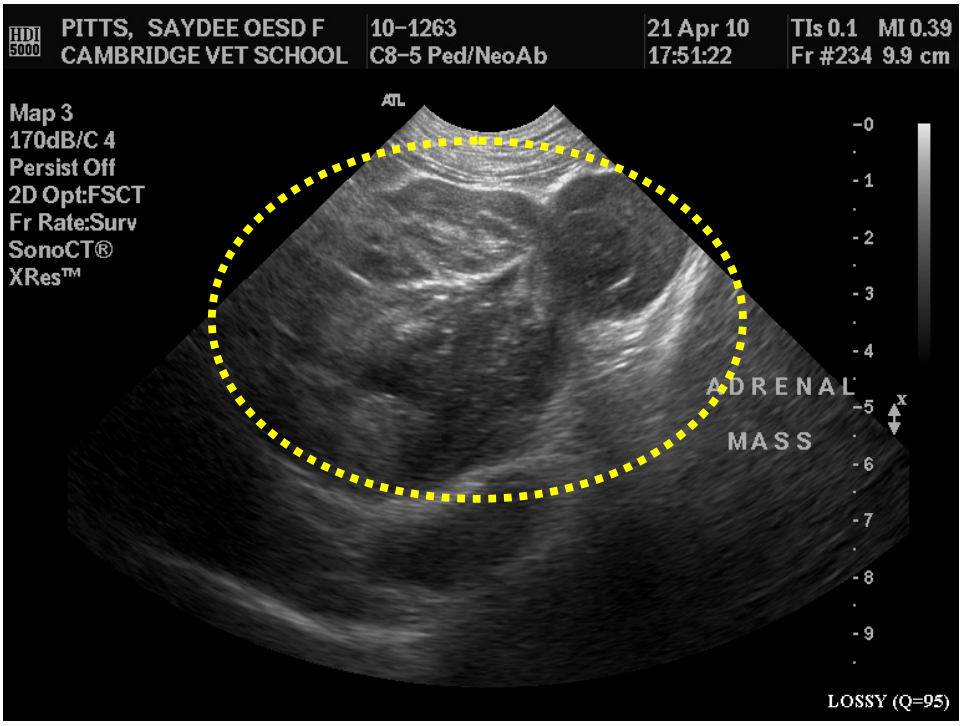


Figure 7. Abdominal ultrasonography. Right adrenal gland.

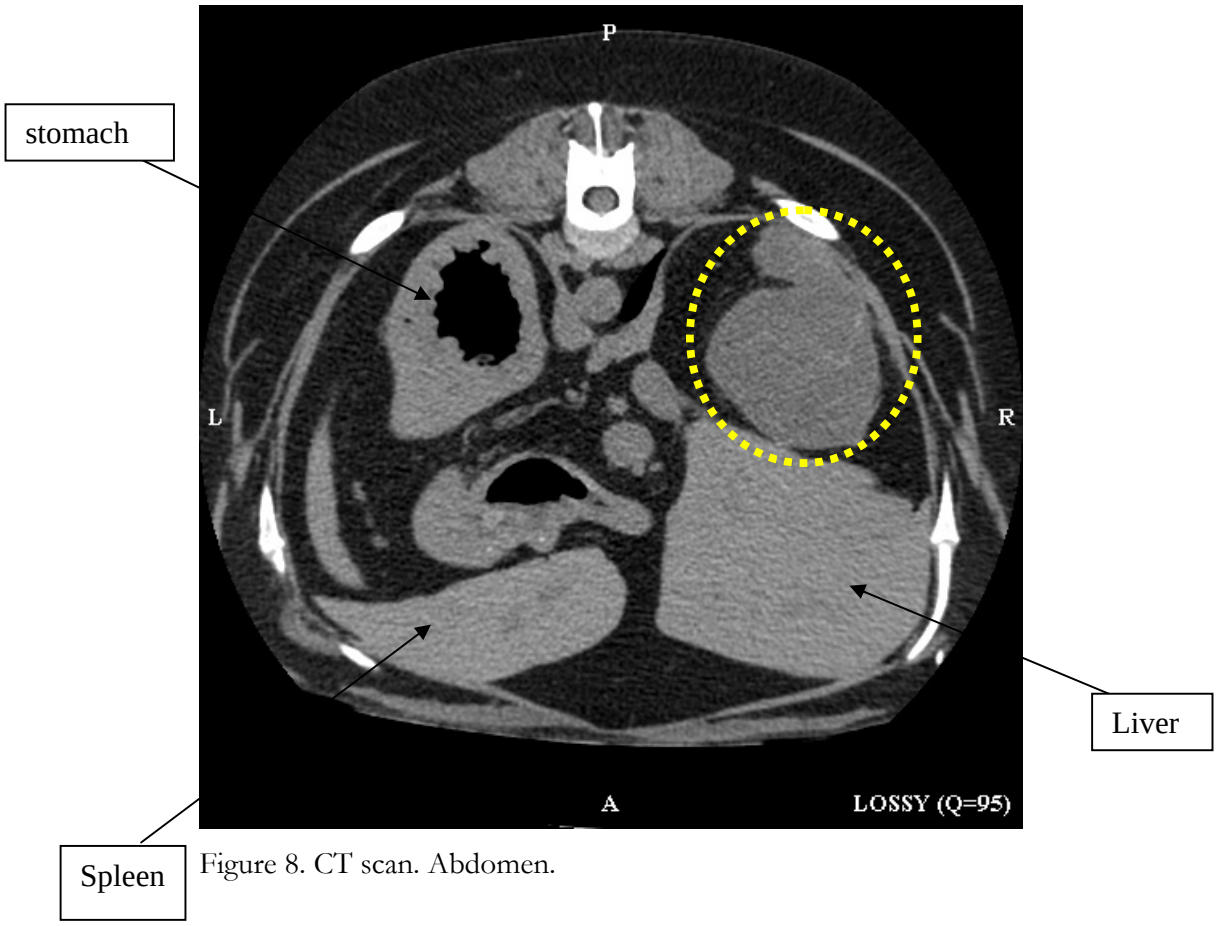


Figure 8. CT scan. Abdomen.

The owners agreed to surgery to remove the right adrenal gland and to obtain liver biopsies. Surgery proceeded without any complications. Saydee recovered well, although her blood pressure remained high.

Impression smears from the adrenal glands were submitted for cytological evaluation whilst awaiting the histopathological results. These smears contained a similar population of epithelial cells noted in the aspirates from the enlarged adrenal gland and from the nodules in the liver, and the cytological findings remained suspicious for a cortical adrenal neoplasm.

Histopathology

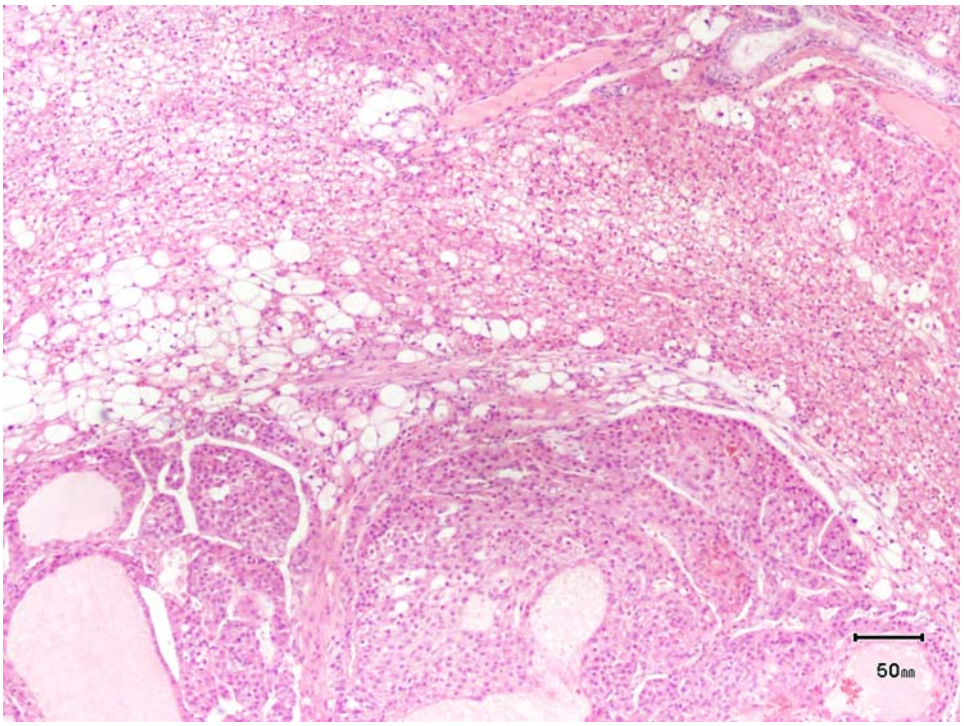
Both the adrenal gland and the liver biopsies were fixed in 10% buffered formalin and histopathological examinations were performed.

Histological sections of the adrenal gland showed that the adrenal gland was effaced by a large, densely cellular, partially encapsulated mass. The neoplastic epithelial cells were arranged in multiple lobules separated by moderately thick fibrous septa. The epithelial cells were large, polygonal to round, with moderate amounts of finely granular eosinophilic cytoplasm with indistinct cell borders. Nuclei were round with finely stippled chromatin and variably prominent one to 2 small nucleoli. Anisocytosis and anisokaryosis were moderate. Mitotic figures were 2 per 10 HPF (40X). Occasional binucleated and multinucleated neoplastic cells were seen. Moderate numbers of small, well defined, basophilic areas (mineralization) were scattered throughout the neoplastic tissue.

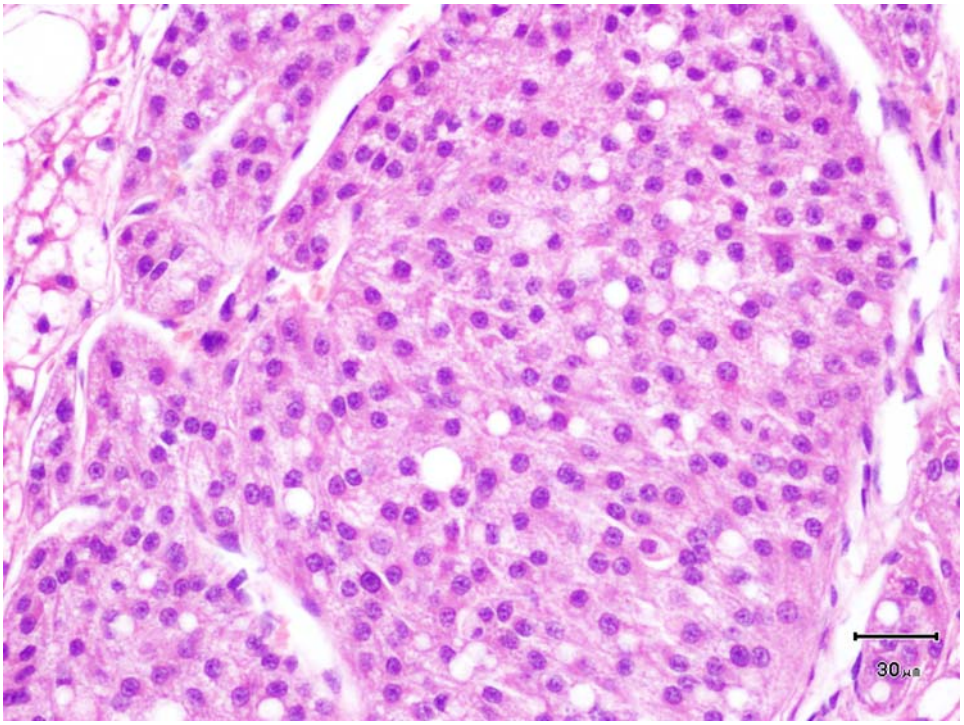
Histology of the liver biopsies revealed variably sized, well-defined, multifocal nodular foci composed of neoplastic epithelial cells, which were arranged in lobules and occasionally formed acini with small amounts of fibrous stroma. The neoplastic cells were polygonal with moderate amounts of vacuolated and slightly granular eosinophilic cytoplasm and indistinct cell borders. Nuclei were small, round, with stippled chromatin and one to two variably prominent nucleoli. Surrounding the metastatic foci, there were moderate numbers of hepatocytes showing moderate to severe hydropic cytoplasmic vacuolation.

Selected sections of the adrenal tumour were tested with a special stain to detect argentaffin granules (Schmorl's stain) and no immunolabeling was detected, excluding a diagnosis of pheochromocytoma.

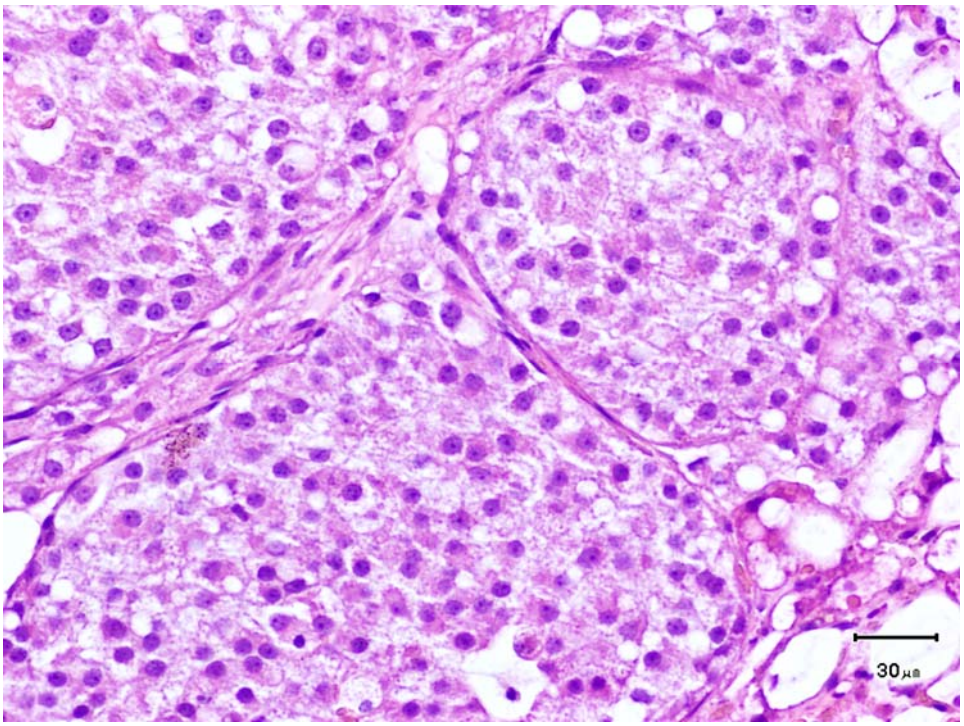
The histological diagnoses were adrenocortical carcinoma and metastasis of carcinoma to the liver with hepatopathy.



Liver – H&E.



Liver – H&E.



Adrenal mass – H&E

DISCUSSION

Adrenocortical carcinomas are reported to occur less frequently than adenomas ([1]). These appear to develop more frequently in old dogs ([2,3,4]) and one study observed that the majority of the affected dogs weighted over 20 kg ([5]). In this case report, the dog weighted 46 kg. There is no report of sex or breed prevalence, and the right and left adrenal glands appear to be affected with equal frequency ([6]). In this case the right gland was affected, although there was evidence in the abdominal ultrasonography also of mild focal enlargement of the left gland.

Canine adrenocortical adenomas and carcinomas can be functional and secrete excessive amount of glucocorticoids, resulting in hyperadrenocorticism. However, this is an infrequent finding, as functional primary adrenal cortical neoplasia has been diagnosed only in 15 to 20% of the cases of hyperadrenocorticism ([7]) . In the present case, an ACTH stimulation test was within normal limits, while a low dose dexamethasone suppression test (LDDS) showed a low resting cortisol, but lack of suppression at 8 hours post dexamethasone dose, which was suggestive of adrenal dependent hyperadrenocorticism. Reusch and Feldman ([5])

observed that approximately 60% of dogs with adrenocortical tumours have an excessive response to ACTH stimulation. In contrast, a LDDS test revealed escape from suppression and thus confirmed hyperadrenocorticism in all the dogs with adrenocortical neoplasia. The low basal cortisol noted in Saydee was difficult to interpret, but a study by Norman et al ([8]) demonstrated that dogs with adrenal tumours may have unexpectedly low circulating cortisol concentrations, and may be negative for hyperadrenocorticism by either ACTH stimulation testing or LDDS testing. The results are not clear cut in this case. Further testing with sex hormones (e.g. 17 hydroxyprogesterone) might have been helpful to exclude a sex hormone-secreting adrenal tumour. The electrolytes were within normal limits and the low basal aldosterone excluded a mineralcorticoid secreting tumour.

A peculiarity of this case was that the clinical sings of hypertension and progressive epistaxis were initially more suggestive of a tumour of the adrenal medulla, a pheochromocytoma, rather than a primary adrenocortical neoplasm. However, the reported polyuria and polydipsia, persistently elevated ALT and ALP, mature neutrophilia, distended abdomen on physical examination and the increased urinary cortisol:creatinine ratio, were findings compatible with hyperadrenocorticism.

The blood pressure had remained consistently around 160 mmHg (and sometimes up to 200 mmHg) most of the time Syadee was hospitalised, and stress of hospitalisation might have played a role on this. However, the hypertension might have been unrelated to the adrenal tumour. No more episodes of epistaxis have been observed.

The morphology of the cells in the fine needle aspirate of the adrenal gland were highly suggestive of adrenocortical carcinoma, and not consistent with a tumour arising from the adrenal medulla. Furthermore, these cells exhibited frequent atypical features such as anisocytosis and anisokaryosis and multinucleation. These findings were confirmed on histopathology and immunohistochemistry, as the latter failed to reveal a positive chromaffin reaction (which would have been expected in a pheochromocytoma).

The liver aspirates had shown the same epithelial cells noted in the adrenal gland aspirates, raising the suspicion of a metastatic focus and this was confirmed by the presence of nests of pleomorphic adrenocortical cells amidst the rafts of hepatocytes in the liver biopsies.

Carcinomas of the adrenal cortex are reported to metastasize primarily to the liver, kidney, and mesenteric lymph nodes ([1]). Moreover, these tumours have been observed to invade through the thin wall of the caudal vena cava. Also in this case, the tumour was in very close

proximity to the vena and the surgeons during the adrenalectomy noted that the caudal part of the adrenal gland was attached to the caudal vena cava.

This case demonstrates the efficacy of cytology in the diagnosis of adrenal cortex carcinomas and demonstrates the unpredictable secretory activity of these tumours.

Acknowledgments

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