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CASE REPORT

Pheochromocytoma in Dogs: A Report on Cytohistological Findings

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ABSTRACT

Pheochromocytoma is a tumor of the chromaffin cells of adrenal medulla or sympathetic paraganglia and rare tumor of middle or aged dogs which leads to thromboembolism. Adult castrated Doberman dog having anamnesis of weight loss and progressive edema on both limbs for 2 months. At necropsy, left adrenal showed 8×4×4 cm size tumoral nodule of tan to gray, soft. Two-thirds of lumen of the caudal vena cava was obstructed by the mass. Cytopathology showed high cellularity consisting of round intact cells. Marked anisokaryosis, many mitotic figures and high nuclear to cytoplasm ratio were also observed. Histopathologically neoplastic cells differ from adrenal medullary cells with characteristically divided into short cords and nests by a prominent fibrovascular stroma. Cells were cuboidal with moderate amount of eosinophilic cytoplasm and hyper chromatic round to oval nuclei. Marked anisokaryosis and anisocytosis were observed. A final diagnosis of Pheochromocytoma was made based on necropsy, cytopathology and histopathological findings.

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INTRODUCTION

Pheochromocytoma is a catecholamine-secreting tumor derived from the chromaffin cells of the adrenal medulla, appear to be rare, constituting only 0.17-0.76% of pet dogs representing 1-2% of all canine tumors. It is most commonly seen in the Boxer breed of dog, mostly observed in middle or old age dogs (Moulton, 1990). They are occasionally malignant with metastasis to distant organs (Reusch, 2006). Pheochromocytomas occasionally result in secondary conditions like thrombosis of the caudal vena cava and aortic thromboembolism, which occurs due to the endothelial damage, blood stasis and hyper coagulable states and sometimes accumulation serosanginous fluid in body cavity (Goncalves *et al.,* 2008). Diagnosis of pheochromocytoma is difficult due to the lack of specific clinical findings and low index of suspicion of the disease. General signs of weight loss, anorexia, panting, tachypnea, lethargy, depression and collapse are frequently reported in chromaffin cell tumor cases (Santamarina *et al.,* 2003). It may show arrhythmic crisis. Diagnosis is made as an incidental finding at necropsy and definitive diagnosis of pheochromocytoma can only be obtained through histopathology.

MATERIALS AND METHODS

Case history and observation

A case of 11year old male Doberman dog was presented to the Madras Veterinary Teaching Hospital with the history of weight loss, progressive edema of hind limbs and unable to bear weight on both the hind limbs for the past 2 months. Clinical examination revealed weakness, panting, tachycardia, lethargy, hind limb edema and pain on palpation in pelvic limbs. Whole blood and serum samples were collected for haematology and serum biochemical analysis. Electrocardiogram was done. Inspite of the critical care and management the dog was collapsed after two days. A complete necropsy was performed in the Department of Veterinary Pathology.

RESULTS

The complete blood count was within normal range except total leucocyte count which was moderately increased and platelet count was highly increased (Table 1). The liver enzyme levels were within normal range. However, Electrocardiograph showed “Q” deeping and tall peaked “T” wave. X-ray examination showed thoracic

Table 1: Altered hematological value

Laboratory test	On 1st day	After a week	Reference value
Total leucocyte count	19,800	20,000	6000-17,000
Platelet count	4,30,000	6,33,000	1,70,000-4,00,000

and lumbar spondylosis, metatarsal and peritoneal reaction.

Post mortem examination showed approximately 500mL serosanguinous fluid accumulated in the abdominal and thoracic cavity. Lung examination showed reddish-brown in color and edematous with multiple, multiple grey-white, hard spherical nodules of varying sizes in right apical lobe 1.2 cm in diameter where as right diaphragmatic lobe showed 3×1.5×1cm in size. This mass had a similar cytomorphologic appearance to the mass in the abdomen, consistent with metastatic malignancy. The liver showed hepatomegaly with multiple, non-raised gray-brown nodules of varying sizes, with enlarged rounded borders, with rib impression on all lobes. Moderate spleenomegaly with prominent gray-white areas. Both kidneys showed rough granular cortex with firm capsule and difficult to peeling off. Left adrenal gland showed 8×4×4cm, tan to gray, soft, well demarcated nodule. Two-thirds of the lumen of caudal vena cava was obstructed by the mass. The obstructed mass invaded in vena cava of size 6.5×3×3cm. It forms a thrombus leading to impaired venous return from posterior extremities (Fig. 1).

All mesenteric lymph node were enlarged, hard and gray-white appearance. On cytopathological smears showed high cellularity consisting of round intact cells. Marked anisokaryosis, many mitotic figures and high nuclear to cytoplasm ratio were observed (Fig. 2). On histological examination of formalin fixed Paraffin embedded tissue, the neoplastic cells of the tumor were characteristically divided into short cords and nests by a prominent fibro-vascular stroma. The tumor cells characteristically subdivided in to small lobules by a fine connective tissue septa and capillaries (Fig. 3).

Vascular sinusoids lined directly by polyhydral to spindle shaped tumor cells. Neoplastic cells were larger than those of adrenal medulla, cuboidal with moderate to abundant eosinophilic cytoplasm and finely granular. Nuclear pleomorphism is a conspicuous feature. Hyperchromatic round to oval nuclei with coarsely granular chromatin with high mitotic figures, which was diagnosed as malignant pheochromocytoma in adrenal. Cells formed densely packed sheets, dissected by thin fibrovascular stroma into variably sized cords and packets. The cells had round, ovoid, variably sized hyperchromatic nuclei with finely stippled chromatin and occasional nucleoli metastases was observed in the lung, liver, spleen and lymphnode. Marked anisokaryosis and anisocytosis were observed.

DISCUSSION

Pheochromocytoma is a rare disorder mostly seen in old aged dogs, horses and cattle (Moulton, 1990). Physical examination and clinical examination findings in animals with pheocromocytoma are usually non specific (Barthez *et al.,* 1997) and most of pheocromocytoma are

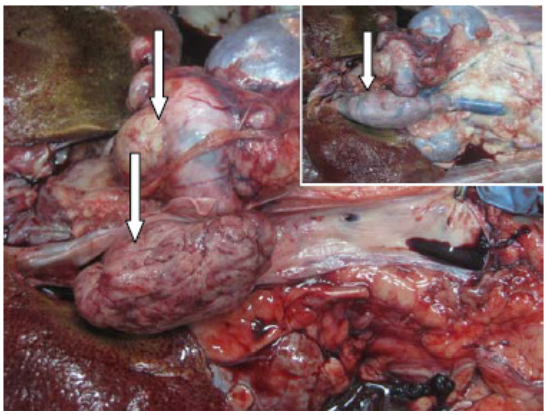

Fig. 1: Adrenal tumour (arrow) in the lumen of caudal venacava. **Insert**: Before openup of venacava.

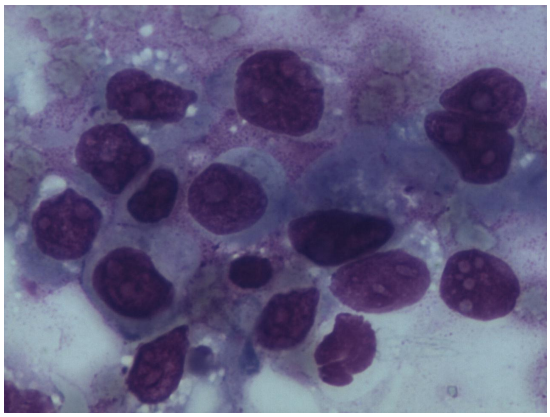

Fig. 2: Peochromocytoma- Cytology. MGGx400

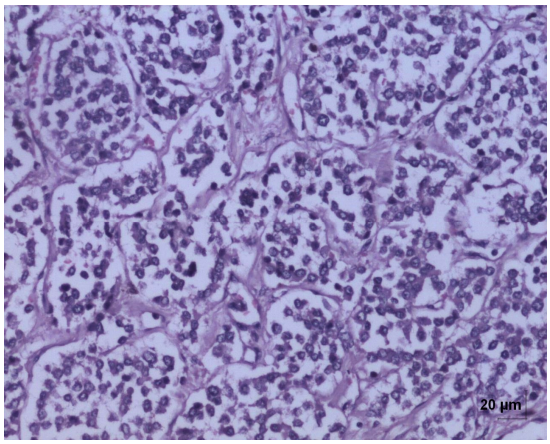

Fig. 3: Pheochromocytoma. Histopathology, H&E. Bar =20µm

endocrinologically silent as seen in this case (Galac *et al.,* 2010). Durant and Soloff reported that malignant pheochromocytoma it raely shows cardiac arrhythmia as it is reported in present case; deeping "Q" and tall peaked "T" wave. In present case the tumor were observed on left adrenal gland similar observation noted by scientist and reported that pheochromocytoma usually unilateral and infrequently bilateral (Meuton, 2002). They are often large and invade into the posterior vena cava forming an extensive tumor cells thrombus. The vena cava is greatly

distended and partially occluded by thrombus leading to impaired venous return from posterior extremities. Posterior vena cava may undergo extensive hemorrhages and form serosanginous fluid in thoracic and abdominal cavity. This disorder is rare in dogs and commonly a complication of another disease, including dirofilariasis, neoplasia, idiophatic thromboembolic disease, hyperadrenocorticism, disseminated intravascular coagulation, sepsis, autoimmune hemolytic anemia, arteriosclerosis, protein–losing enteropathies and nephropathies, bacterial endocarditis and cardiac disease (Good *et al*., 2003). Occlusion of the aortic trifurcation, as we seen in the present case, obstructs internal and external iliac arteries and the median sacral artery which cause muscle ischemic myopathy, axonal degeneration and ischemic muscle contracture. Abdominal ultrasonography may enable the detection of liver metastasis or invasion of the caudal vena cava in adrenal carcinomas as found in this case (Guillamont *et al*., 2012). The results of routine laboratory work, Including complete blood count, biochemical profile, and urinalysis, were non-specific. The scientists had reported that malignant tumors are more common in adrenal medulla as compared to cortex. Common sites of metastasis include the lung, liver, kidney, spleen, lymph nodes, and bone. Malignant pheocromocytoma invade through the adrenal capsule and adjacent structures and also metastasize in to distant site as it is reported in this case metastasis in the liver, lung, spleen and lymph node (Mexicano, 2005). Malignant pheocromocytoma cells larger and having frequent mitotic figures than benign pheochromocytoma. Besides this, any neoplasia can be a common cause of hypercoagulability with a multifactorial etiology, as platelet hyperaggregability and the inhibition of the fibrinolytic system (Good and Manning, 2003). These factors could contribute to the development of the thrombus as seen in this report. Radiographs of the abdomen can reveal a mass in perirenal area similar observation noted by scientists (McNeil and Twedt, 1998). Thoracic radiographs can reveal changes pulmonary congestion or oedema and also thoracic and lumbar spondyloisis as it is metatstized in to the lumbar vertebral body (L2) resulting in localized osteolysis and pregressive paraparesis. Large tumors may exert pressure on adjacent organs or vessels, and that regional invasion of the caudal vena cava may be seen in up to one third and distant metastases in up to half of afflicted dogs (Goncalves *et al.,* 2008). This invasive form cause a variety of extra-adrenal manifestations including venous distention, pain and hind limb paraparesis or paraplegia secondary to vascular compromise as well as primary neurological abnormalities. Pheochromocytomas can vary markedly in their histologic appearance.

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