

Diagnostic Exercise
From The Davis-Thompson Foundation*

Case #: 136 Month: January Year: 2020

Answer Sheet

Title: Pituitary mass in aged greyhound

Contributors: Emily Jones BVSc and Rachel Allavena BVSc (hons), BVBiol, GCHEd, GradDip (Anatomic pathology), MANZCVS (Pathobiology, Laboratory Animal Science), PhD, DACVP. The University of Queensland, Australia.



Figure 1. Forebrain and midbrain sections after fixation in 10% neutral buffered formalin.

Morphologic diagnosis: Brain (pituitary, thalamus): Pituitary adenoma with secondary thalamic compression

Differential Diagnoses: Pituitary carcinoma [when there is evidence of metastasi(e)s], meningioma, oligodendroglioma, astrocytoma, glioblastoma, metastatic neoplasm (e.g. carcinoma or melanoma), ependymoma.

Microscopic Findings: Compressing the right hypothalamus is a basophilic, densely cellular, well demarcated, unencapsulated, nodular mass with neoplastic cells forming sheets and palisading around scant fibrovascular stroma. Neoplastic cells are polygonal and 10-20 μm in diameter with distinct cell borders, moderate amounts of granular eosinophilic cytoplasm, round paracentral basophilic nucleus with open chromatin, and occasional eosinophilic nucleoli. There is minimal anisocytosis and anisokaryosis; mitotic figures and binucleate cells are rare. Towards the margin of the neoplasm are tens of brightly eosinophilic cells (remnant resident acidophils) and the mass is interspersed with occasional haemosiderin-laden macrophages.



Figure 2: Brain, right side at the level of the optic chiasm, with a basophilic, densely cellular, unencapsulated nodular mass visible at the ventral aspect. H&E, 1x digital magnification.

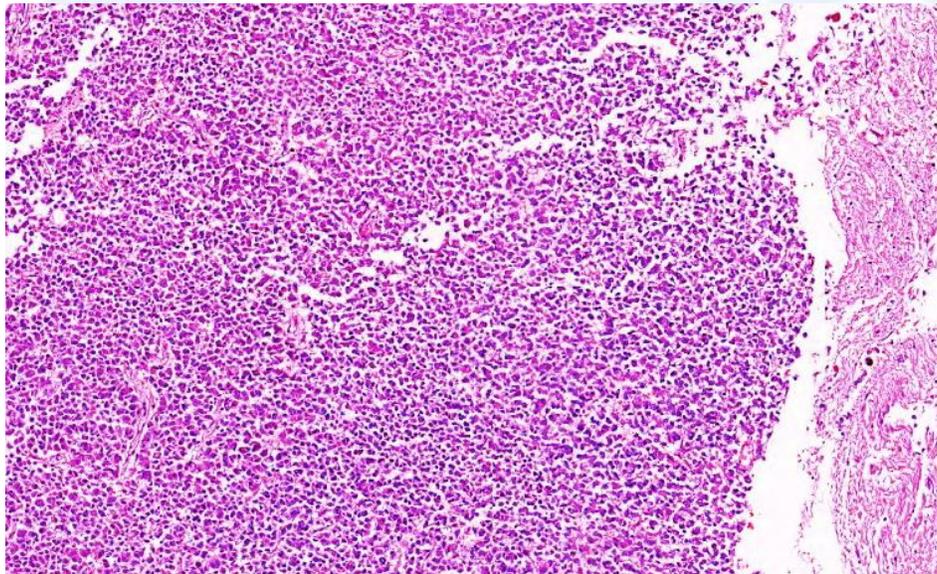


Figure 3: Lesional cells are forming sheets and are palisading around scant fibrovascular stroma. H&E, 4x digital magnification.

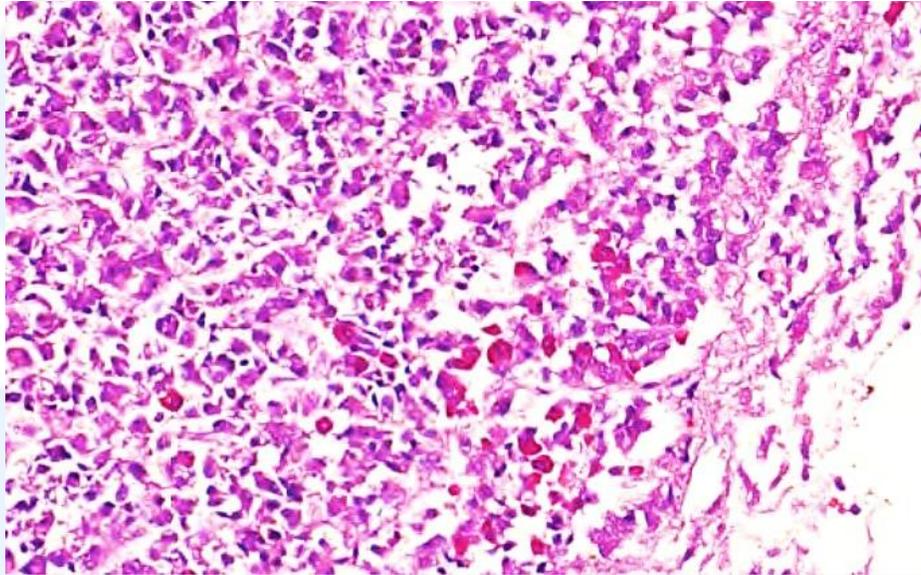


Figure 4: Towards the edge of the process are brightly eosinophilic cells. H&E, 10x digital magnification.

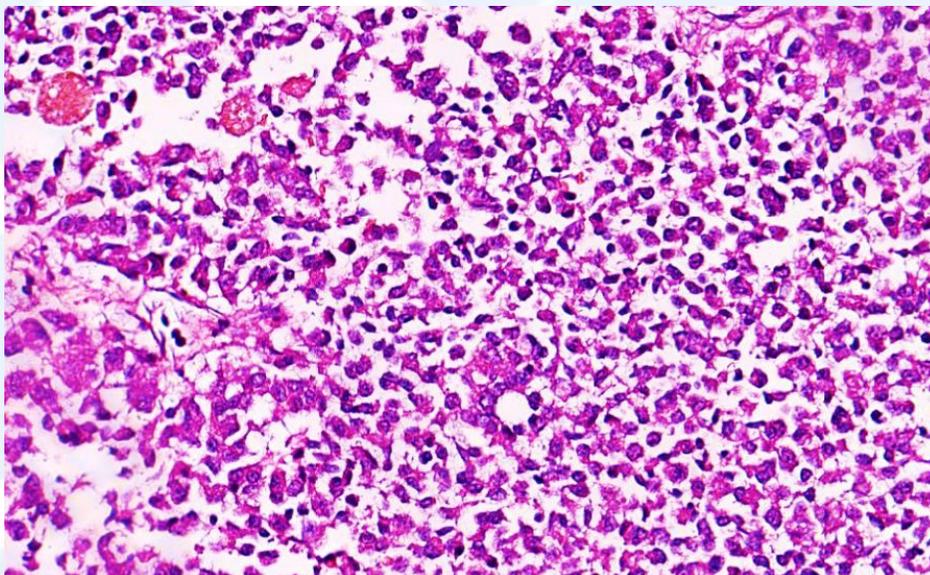


Figure 5: Polygonal lesional cells are predominantly arranged in sheets, interspersed with occasional haemosiderin-laden macrophages (top left). H&E, 15x digital magnification.

Final Diagnosis: Chromophobe pituitary adenoma of the pars distalis with associated pituitary cachexia.

Typical Gross Findings:

- Variable sized white to brown lesion in the ventral mid-brain
- Haemorrhage and necrosis progressing to mineralisation and liquefaction in larger neoplasms

- Compression or effacement of the hypothalamus and thalamus, sometimes dorsal expansion resulting in neurological signs
- Sometimes atrophied adrenal cortex

Typical Microscopic Findings:

- Sheets of well-differentiated, polygonal neoplastic cells
- Acidophils located towards the tumour margin
- Fine scant fibrovascular septa
- Presence of haemosiderin-laden macrophages
- Low mitotic rate
- Myelin degeneration downstream of compressed axons

Discussion: Pituitary adenomas are the most common type of pituitary neoplasms and result in space-occupying lesions that may compromise the function of cells of the pituitary, hypothalamus and thalamus (1). Most pituitary adenomas are chromophobic adenomas composed of cells from the pars distalis (1). Corticotroph-secreting neoplasms are the most common type of functional pituitary neoplasm in dogs, producing hyperadrenocorticism known as Cushing's disease (1). The lack of clinical signs of hyperadrenocorticism or other clinical signs in this case is consistent with a non-functional neoplasm.

Non-functional pituitary adenomas may interfere with normal secretion of hormones from the pituitary gland, with muscle atrophy and weight loss being common clinical findings due to decreased effect of growth hormone (GH), responsible for protein anabolism, a phenomenon commonly referred to as 'pituitary cachexia' (1). In addition to the decreased growth hormone effect, pituitary adenomas may cause headaches and therefore reduced appetite due to tumour expansion (2) and other signs that may occur include loss of coordination, depression and behavioural changes (1).

The hypertension and collapse in this dog may have been due to:

1. Mass effect from the pituitary neoplasm;
2. Hypothalamic inflammation secondary to compression by the neoplasm, which can lead to development of hypertension in people by disrupting signalling pathways in the central control of blood pressure (3);
3. In addition to the pituitary tumour, this dog was found to have a small thyroid mass, the exact diagnosis of which unfortunately could not be made due to tissue autolysis. Functional thyroid neoplasms are rare in dogs with only 10% of canine thyroid neoplasms being functional (4); however if this mass was functional, it may have contributed to the weight loss and hypertension observed in this dog.

This dog also had severe panleukopenia. Pancytopenia has been observed in rare human cases with pituitary adenoma (5) and in hypophysectomized rats (6). The relationship between pancytopenia and panhypopituitarism is poorly understood at this time (5).

The legal issues surrounding this case with respect to the very poor body condition are most likely 'neglect to treat' (when the guardian of the animal did not recognise and/or seek help when the animal became emaciated) rather than intentional neglect by failing to provide adequate food. This is based on the presence of a pituitary chromophobe adenoma that likely caused the muscle loss and weight loss; however, intentional neglect cannot be ruled out completely based on these findings. Notably the animal did have severe dental disease but did eat a small amount at the animal shelter before terminal collapse.

References:

1. Rosol TJ, Gröne A. Endocrine Glands. In: Maxie MG, editor. Jubb, Kennedy & Palmer's Pathology of Domestic Animals: Volume 3 (Sixth Edition): W.B. Saunders; 2016. p. 269-357.e1.
2. Gondim JA, de Almeida JPC, de Albuquerque LAF, Schops M, Gomes É, Ferraz T. Headache associated with pituitary tumors. The Journal of Headache and Pain. 2009;10(1):15-20.
3. Khor S, Cai D. Hypothalamic and inflammatory basis of hypertension. Clinical Science. 2017;131(3):211-23.
4. Lunn KF, Page RL. 25 - Tumors of the Endocrine System. In: Withrow SJ, Vail DM, Page RL, editors. Withrow and MacEwen's Small Animal Clinical Oncology (Fifth Edition). Saint Louis: W.B. Saunders; 2013. p. 504-31.
5. Lang D, Mead JS, Sykes DB. Hormones and the bone marrow: panhypopituitarism and pancytopenia in a man with a pituitary adenoma. Journal of General Internal Medicine. 2015;30(5):692-6.
6. Nagy E, Berczi I. Pituitary dependence of bone marrow function. British Journal of Haematology. 1989;71(4):457-62.

*The Diagnostic Exercises are an initiative of the **Latin Comparative Pathology Group (LCPG)**, the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (http://www.cldavis.org/diagnostic_exercises.html).

Associate Editor for this Diagnostic Exercise: Rachel Allavena
Editor-in-chief: Vinicius Carreira