

Latin Comparative Pathology Group

The Latin Subdivision of the CL Davis Foundation

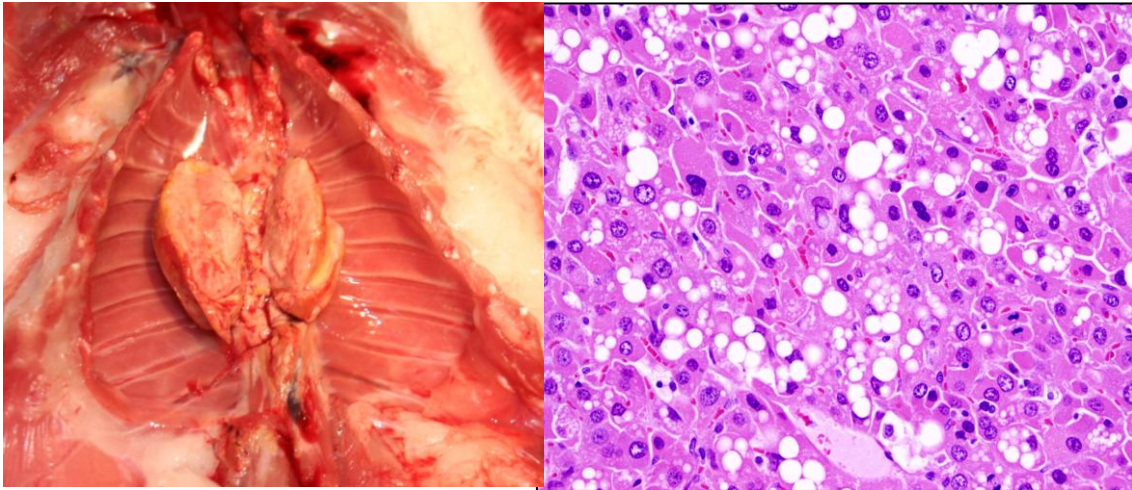
Diagnostic Exercise

Case #: 15 Month: November Year: 2011

Answer sheet

1. Morphologic diagnosis:

Brown adipose tissue: Hibernoma, benign



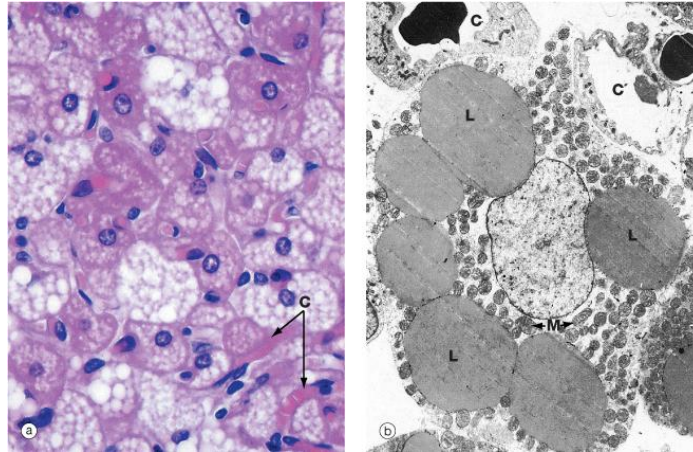
H&E, 20x

Arising from a section of brown adipose tissue adjacent to the aorta is an expansile pseudoencapsulated neoplasm (gross picture, left) comprised of sheets of round to polygonal mesenchymal cells supported by a fine fibrovascular stroma (photomicrograph, right). The neoplastic cells have indistinct margins and contain moderate to abundant amounts of foamy to multivacuolated eosinophilic cytoplasm which marginates the nucleus. Nuclei are round to oval with a finely stippled chromatin pattern. Randomly scattered individual neoplastic cells within the mass are necrotic. There is a moderate degree of anisocytosis and anisokaryosis, and occasional cells are multinucleated. The overall mitotic rate average is 1 per 5 HPF, with occasional bizarre mitotic figures present.

In practice, malignancy is based on the presence of metastases or clear invasion, both of which were lacking in this tumor; mitotic rate varies greatly between tumors and seems to be an unreliable indicator of malignancy.

2. **Immunohistochemical marker:** Uncoupled protein 1 (UCP-1, Thermogenin)

3. **Ultrastructural findings:**



Photomicrograph (left) and electron micrograph (right) of brown adipose tissue. Note the multilocular nature of stored lipid (L). The cytoplasm of brown adipocytes is crammed with mitochondria (M) which have numerous, closely packed cristae. These mitochondria are extremely rich in cytochromes, part of the electron transport chain involved in oxidative energy production; this accounts for the brown color of brown adipose tissue when examined macroscopically. Note the intimate association of capillaries (C) with the brown adipocyte in this micrograph.

Discussion:

The brown adipose tissue is mainly controlled by the sympathetic nervous system. It is abundant in rodents, cold-acclimated, and hibernating animals. In other animals is present in neonates and undergoes involution in the adults. Several xenobiotics target brown fat either directly or indirectly. A few examples include PPAR modulators (diabetes, atherosclerosis), adrenergic agonists and antagonists, and fat-soluble environmental chemicals such as DDT and PCBs.

Classically, at low magnification, two types of cell can be seen in brown adipose tissue. Many cells, and especially cells at the center of lobules, are eosinophilic due to cytoplasm packed with mitochondria. Other cells, and especially those at the periphery of lobules have a clear cytoplasm which is due to the presence of multiple vesicles containing lipid.

Background incidence generally accepted as being <0.1%. Reported incidence from 1977-1981 was 3 in 3200 (0.09%). Charles River Laboratory compiled data from 31 different carcasses 1989-2002 and found no hibernomas. The tables below contain historical control data from MPI Research.

Number of Studies	Number of Control Groups	Number of Control Animals	Lowest % Incidence	Highest % Incidence	Average % Incidence	Classification (Common/ Uncommon)	P-value for Increasing Trend
39	52	6229	0.00%	3.33%	0.29%	Uncommon	0.2344

1999	2000	2001	2002	2003	2004	2006	2007	2008	2009
0.00%	0.00%	0.00%	0.00%	0.63%	0.27%	0.67%	0.42%	0.23%	0.24%

Recommended literature:

Al Zubaidy AJ, Finn JP (1983) Brown fat tumours (hibernomas) in rats: histopathological and ultrastructural study. *Lab Anim* 17: 13-17

Bruner R, Novilla M, Picut C, Kirkpatrick J, O'Neill T, Scully K, Lawrence W, Goodman D, Saladino B, Peters D, Parker G; Spontaneous Hibernomas in Sprague-Dawley Rat, *Toxicologic Pathology*, June 2009; vol. 37, 4: pp. 547-552.

Elroy F. Sheldon (1924). "The so-called hibernating gland in mammals: A form of adipose tissue". *The Anatomical Record* (Department of Histology and Embryology, Stimson Hall, Cornell University, Ithaca, New York) 28 (5): 331-347.

Elwell MR, Stedham MA, Kovatch RM (1990) Skin and subcutis. In: Boorman GA, Eustis SL, Elwell MR, Montgomery CA, Jr, MacKenzie WF (eds) *Pathology of the Fischer rat. Reference and atlas*. Academic Press, San Diego New York London, pp 261-277.

Please send your comments/questions to the whole LCPG list by hitting "reply to all".
A final document containing this material with answers and a brief discussion will be posted on the C. L. Davis website by the end of the current month
(http://www.cldavis.org/lcpg_english.html).