

Latin Comparative Pathology Group

The Latin Subdivision of the CL Davis Foundation

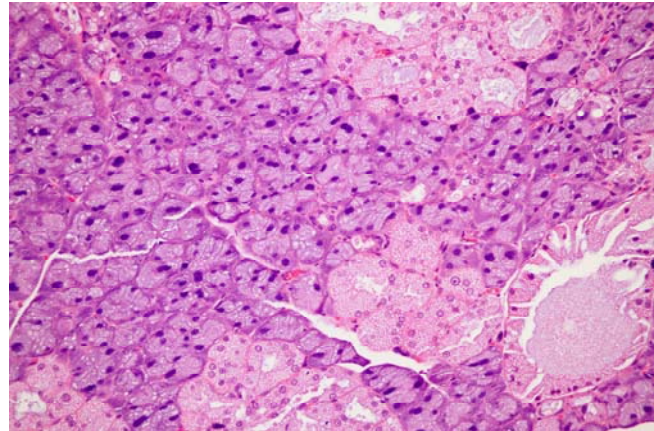
Diagnostic Exercise

Case #: 10 Month: June Year: 2011

Answer Sheet

Diagnosis:

Morphologic Diagnosis: Lacrimal gland,
harderization



Typical gross findings:

- “White spots”

H&E, 20x

Typical microscopic findings:

- Alveoli are composed of cuboidal to columnar cells with finely vacuolated cytoplasm
- Alveolar lumens are distinct

Discussion:

In addition to Harderian gland, which lies behind the eye in the orbit and partially encircles the optic nerve³, the rodent eye is also equipped with one intraorbital and one extraorbital lacrimal gland composed of serous glands, structurally similar to those found in the parotid gland¹. The intraorbital lacrimal gland is associated with the eyelid, and the large extraorbital lacrimal gland lies subcutaneously

at the base of the ear³. The extraorbital lacrimal gland has marked irregularity in size of nuclei and variation in mitochondrial content of the cytoplasm⁶. The lacrimal glands are lobulated and consist of serous acini with narrow lumens and branching duct system of intralobular ducts. Acinar cells are polyhedral or pyramidal with round to oval nuclei⁴. The extraorbital lacrimal gland has marked irregularity in size of nuclei and variation in mitochondrial content of the cytoplasm (cytomegaly and karyomegaly)⁶. These are more prominent in males than females and become more frequent with age⁴. The acini in males are generally larger than those in females⁴. The secretory granules of male extraorbital lacrimal gland are prevalently composed of sulphate substances, those of the female are composed of acid substances, and only a few cells positive to proteins have been seen in the acinar epithelium of the glands². Androgen and estrogen receptors are present in the rat extraorbital lacrimal gland of both sexes².

Harderization of the lacrimal gland (also known as harderianization⁵, Harderian gland alteration⁴ or ectopic Harderian glandular tissue³) consists of the appearance of lipid foci in the extraorbital lacrimal gland². It is not an uncommon finding in aging rats, starting as early as at three weeks of age⁵ and increases at six months of age in the male glands, while it is not detectable anymore in those of females². It is not certain if the cells have the metabolic and functional characteristics of Harderian gland cells and thus represent a metaplastic change or whether the change is simply a degenerative one⁴. It appears that the Harderian gland cells develop from undifferentiated basal cells of the acini and the intercalated ducts in the extraorbital lacrimal gland at age 2-6 months⁵. Then, at age 22 months, they also probably developed from those of the excretory ducts of the extraorbital lacrimal gland⁵. It has been suggested that estrogen plays a role in the harderization process². The estradiol present in older female rats may prevent the further lipid degeneration of the female extraorbital lacrimal gland at six months of life, while the disappearance of estrogen receptor in the male gland promotes the development of harderization².

References and Recommended literature:

1. Greaves P. Histopathology of Preclinical Toxicity Studies, pp. 885-886. . Academic Press, New York, 2007.
2. Ferrara D, Monteforte R, Baccari GC, Minucci S, Chieffi G. Androgen and estrogen receptors expression in the rat exorbital lacrimal gland in relation to "harderianization". J. Exp. Zool. **301A**: 297–306, 2004.
3. Frith CH, Ward JM. Color Atlas of Neoplastic and Non-neoplastic Lesions in Aging Mice. Charles Louis Davis DVM Foundation, Gurnee, IL.
4. Yoshitomi K, Brown HR. Ear and Pinna. *In*: Pathology of the Fischer Rat, ed. Boorman GA, Eustis SL, Elwell MR, Montgomery Jr CA, and Mackenzie WF. pp. 239-256. Academic Press, San Diego, CA, 1990.
5. Sashima M, Hatakeyama S, Satoh M, Suzuki A. Harderianization is another sexual dimorphism of rat exorbital lacrimal gland. Acta Anat (Basel). **135**(4):303-6, 1989.
6. Snell KC. Spontaneous lesions of the rat. *In*: The Pathology of the Laboratory Animals, ed. Ribelin WE and McCoy JR. pp. 241-243. Charles C. Thomas, Springfield, IL, 1965.

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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).