



NTP Nonneoplastic Lesion Atlas

Liver, Hepatocyte – Cytoplasmic inclusions

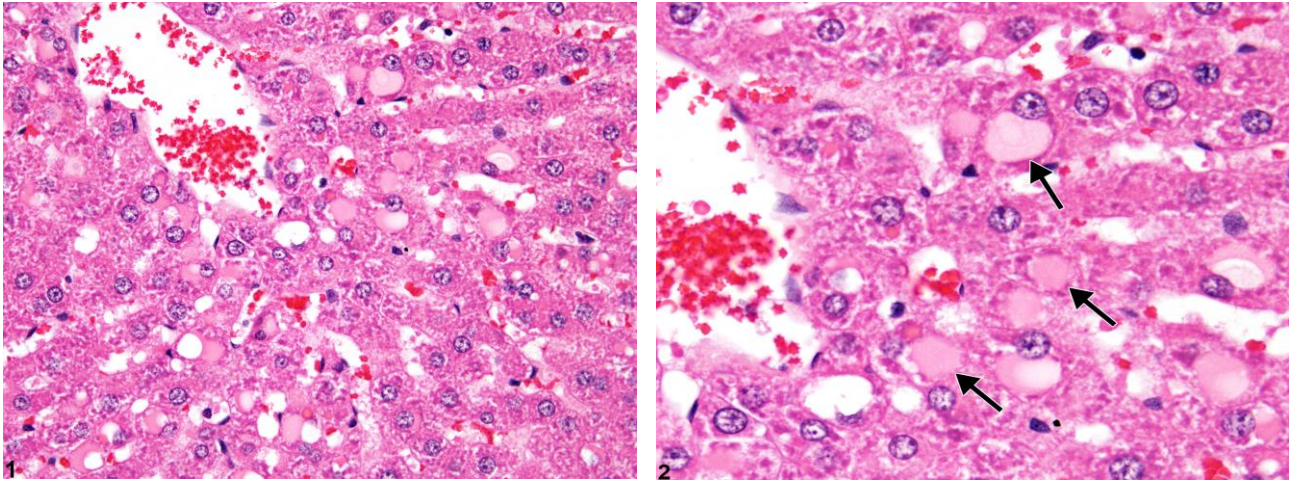


Figure Legend: **Figure 1** Cytoplasmic inclusions in a male F344/N rat from a subchronic study. **Figure 2** Cytoplasmic inclusions (arrows) in a male F344/N rat from a subchronic study.

Comment: Eosinophilic or cytoplasmic inclusions or material (Figure 2, arrows) can be found in control as well as treated rodents. These hyalinized inclusions are also seen in hepatocellular neoplasms. The examples in Figure 1 and Figure 2 represent a postmortem, time-dependent artifact especially common in male rats that are not completely exsanguinated at necropsy. The cytoplasmic vacuoles contain plasma that has entered the hepatocyte cytoplasm (plasma influx) of affected hepatocytes (Li et al. 2003). Similar but more discrete eosinophilic hyalinized inclusions, which may represent protein present in lysosomes, can be seen in control and treated rodents and are also seen in hepatocellular neoplasms.

Recommendation: Hyaline intracytoplasmic inclusions are relatively uncommon and thus should be documented and given a severity grade that is based on the frequency of affected hepatocytes. If there is reason to believe that they are a time-dependent artifact associated with incomplete exsanguination at necropsy, this should be discussed in the pathology narrative. Cytoplasmic inclusions need not be documented when present in neoplastic hepatocytes.



NTP Nonneoplastic Lesion Atlas

Liver, Hepatocyte – Cytoplasmic inclusions

References:

Eustis SL, Boorman GA, Harada T, Popp JA. 1990. Liver. In: Pathology of the Fischer Rat (Boorman GA, Eustis SL, Elwell MR, Montgomery CA, MacKenzie WF, eds). Academic Press, San Diego, 71–94.

Abstract: <http://www.ncbi.nlm.nih.gov/nlmcatalog/9002563>

Greaves P. 2007. Histopathology of Preclinical Toxicity Studies: Interpretation and Relevance in Drug Safety Evaluation, 3rd ed. Elsevier, Amsterdam.

Abstract: <http://www.sciencedirect.com/science/book/9780444527714>

Harada T, Enomoto A, Boorman GA, Maronpot RR. 1999. Liver and gallbladder. In: Pathology of the Mouse: Reference and Atlas (Maronpot RR, Boorman GA, Gaul BW, eds). Cache River Press, Vienna, IL, 119–183.

Abstract: <http://www.cacheriverpress.com/books/pathmouse.htm>

Li X, Elwell MR, Ryan AM, Ochoa R. 2003. Morphogenesis of postmortem hepatocyte vacuolation and liver weight increases in Sprague-Dawley rats. Toxicol Pathol 31:682–688.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/14585737>

Thoolen B, Maronpot RR, Harada T, Nyska A, Rousseaux C, Nolte T, Malarkey D, Kaufmann W, Kutter K, Deschl U, Nakae D, Gregson R, Winlove M, Brix A, Singl B, Belpoggi F, Ward JM. 2010. Hepatobiliary lesion nomenclature and diagnostic criteria for lesions in rats and mice (INHAND). Toxicol Pathol 38:5S–81S.

Full-text: http://tpx.sagepub.com/content/38/7_suppl/5S.full

Author:

Robert R. Maronpot, DVM, MS, MPH, DACVP, DABT, FIATP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC