Phospholipidosis: Histologic finding or histopathology?

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Phospholipidosis is an unusual intracellular accumulation of phospholipids associated with a variety of diseases such as inborn errors of metabolism and exposure to toxic xenobiotics. Characterized by intracellular inclusions called lamellar bodies, phospholipidosis is also a common finding in nonclinical toxicology studies designed to enable clinical trials and marketing applications for new drugs. When observed, there is uncertainty concerning the safety implications of the finding. Phospholipidosis is a finding usually associated with what are generally referred to as cationic amphiphilic drugs (CADS). CADs have a distinct structure: they contain both hydrophobic and hydrophilic domains, which enables transit through cellular membranes and intracellular concentration. This chemical property may be desirable for drugs that act on intracellular targets and in some circumstances phospholipidosis could be related to pharmacodynamic activity and drug efficacy. However, there are many examples of phospholipidosis associated with pathology. Thus, there is a dilemma in assessing the safety implication of phospholipidosis. Many factors should be considered in evaluating phospholipidosis: structural relationship to chemicals known to cause pathology, tissues affected, and histopathology associated with lamellar bodies. This is a very complex subject and requires assessment of many parameters in order to determine if demonstration of phospholipidosis is a cause for concern.