Zoo/Exotic Pathology Service

Histopathology Report

November 20th, 2009 Pathologist ROBERT E. SCHMIDT, DVM, PhD Diplomate, American College of Veterinary Pathologists

RES: br

All American Pharmaceutical and Natural Foods Corporation Study ID IDEXX Reference Laboratories, Inc. Accession Number

INTRODUCTION

Submitted were formalin-fixed tissues from 18 rats in three different groups. These tissues were processed by standard histopathologic methods, embedded in paraffin, trimmed, placed on slides, and stained by hematoxylin eosin. The slides were examined histologically, and the lesions are given in the individual animal reports.

RESULTS/DISCUSSION

The cause of the lesions noted in the heart is not determined. Some rats have myocardial degeneration as an aging change although usually without an intense inflammatory reaction. This type of reaction, however, could be a stage in that process. The possibility of some sort of inflammation secondary to infection would have to be considered, but no organisms were noted. Since the lesions only occurred in the 1X test group, I believe they are probably incidental. The finding myocardial mineralization in one animal is also incidental. Extramedullary hematopoiesis in the liver is a common incidental finding in rats. One animal in the 10X group had a congested liver, and its exact cause was not determined. Animals in all groups had variable changes in the kidney. These lesions are considered to be most likely associated with chronic progressive nephropathy, a common condition in rats, particularly in male rats of certain strains. The exact cause of this lesion is not determined; however, it becomes worse with age and may be diet-related, particularly with high-protein diets. These changes are not considered to be associated with any treatment effect. Mineralization is also a common incidental finding in the kidneys of rats. The congestive lesions noted were, as with one liver, only seen in animals in the 10X group. Changes in the small intestine were only noted in two of the animals in the 10X group and were minimal. Although they could indicate some sort of treatment effect, they certainly are not definitive. The lesions were comprised of minimal multifocal degeneration in one animal and villar congestion in two animals. What appeared to be a minimal amount of hemorrhage was noted in the animal with the degenerative changes. Since there was some autolysis noted in the small intestinal sections, the lesions must be interpreted with care.

In general, the only lesions that may have represented a treatment effect included the minimal changes noted in two of the small intestines. The status of the heart lesions, as mentioned above, is indeterminate, but I believe they probably represent incidental findings. The kidney lesions are consistent with chronic progressive nephropathy of rats, and I do not believe they represent any treatment-related effect. No lesion was seen in the liver that would be considered any sort of a toxic insult. In terms of the clinical status of the animals and the report of minimal amounts of blood from the nose, since that material was not analyzed in the laboratory, I believe it very well may have been perforin rather than blood. Although it could indicate that there was some sort of lacrimal or harderian gland problem in these rats, it certainly is not an unusual finding. Since those particular organs were not examined histologically, no further determination can be made.

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Individual Animal Histopathology Report

CONTROL GROUP

<u>Animal ID – Male #7:</u>

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Male #8:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Male #7:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: Glomerulonephritis, focal, minimal to mild;

Proteinuria, multifocal, minimal to mild.

Small intestine: No lesion recognized.

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Animal ID – Female #7:

Heart: No lesion recognized.

Liver: Extramedullary hematopoiesis, focal, minimal.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Female #8:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Female #9:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

TEST GROUP (1X)

Animal ID – Male #4:

Heart: No lesion recognized.

Liver: Extramedullary hematopoiesis, multifocal, minimal.

Kidney: Mineralization, multifocal, minimal.

Small intestine: No lesion recognized.

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Animal ID – Male #5:

Heart: Epicarditis/myocarditis, multifocal, mild to moderate.

Liver: Extramedullary hematopoiesis, focal, minimal.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Male #6:

Heart: Epicarditis/myocarditis, multifocal, mild to moderate.

Liver: No lesion recognized.

Kidney: Glomerulonephritis, multifocal, minimal to mild;

Proteinuria, multifocal, mild.

Small intestine: No lesion recognized.

Animal ID – Female #4:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Female #5:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

Animal ID – Female #6:

IDEXX Reference Laboratories, Inc. Accession Number

Heart: Mineralization, focal, minimal.

Liver: No lesion recognized.

Kidney: Proteinuria, focal, minimal.

Small intestine: No lesion recognized.

TEST GROUP (10X)

Animal ID – Male #1:

Heart: No lesion recognized.

Liver: Congestion, diffuse, minimal to mild.

Kidney: Congestion, diffuse, mild.

Small intestine: Villar hemorrhage/degeneration, multifocal, moderate.

Animal ID – Male #2:

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: Congestion, diffuse, mild.

Small intestine: Villar congestion, multifocal, minimal.

Animal ID – Male #3:

Heart: No lesion recognized.

Liver: Extramedullary hematopoiesis, multifocal, minimal.

Kidney: Proteinuria, multifocal, mild to moderate.

Small intestine: No lesion recognized.

Animal ID – Female #1:

IDEXX Reference Laboratories, Inc. Accession Number

Heart: No lesion recognized.

Liver: Extramedullary hematopoiesis, focal, minimal.

Kidney: No lesion recognized.

Small intestine: No lesion recognized.

<u>Animal ID – Female #2:</u>

Heart: No lesion recognized.

Liver: Extramedullary hematopoiesis, focal, minimal.

Kidney: Glomerulonephritis, multifocal, minimal to mild;

Proteinuria, multifocal, mild to moderate;

Nephrosis/tubular necrosis, multifocal, minimal to mild.

Small intestine: No lesion recognized.

<u>Animal ID – Female #3:</u>

Heart: No lesion recognized.

Liver: No lesion recognized.

Kidney: Glomerulonephritis, focal, mild;

Proteinuria, multifocal, minimal to mild.

Small intestine: No lesion recognized.