Radiation-Induced Renal Changes in the Göttingen Minipig

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ABSTRACT

Introduction/Objectives: During the development of a hemi-body shielded model of radiation-induced gastrointestinal injury (GI-ARS) in Göttingen mini-pigs, unique morphologic effects were identified within the kidneys, including necrosis and regeneration of the collecting tubules, which have not been previously described.

Experimental Design: Male and female Göttingen mini-pigs were hemi-body shielded and exposed to a single uniform total body dose of gamma irradiation at dose levels of 14 to 16 Gy. Animals were necropsied at several intervals ranging from Study Day 10 to 60. Methods: At the time of necropsy, tissues were placed into 10% neutral-buffered formalin (NBF), routinely processed and embedded in paraffin. Sections were stained with hematoxylin and eosin (H&E) and evaluated for light microscopy.

RESULTS

At the time of necropsy, tissues were placed into 10% neutral-buffered formalin (NBF), routinely processed and embedded in paraffin. Sections were stained with hematoxylin and eosin (H&E) and evaluated for light microscopy.

Figure 1. Renal cortex from mini-pig exposed to 14 Gy radiation and necropsied on Study Day 15. Scattered tubules in the medulla and corticomedullary junction are lined by basophilic cells with prominent nuclei, characteristic of tubular regeneration (arrows).

Figure 2. Grade of severity of tubular necrosis/regeneration by day of death.

Figure 3. Renal cortex from mini-pig exposed to 16 Gy radiation and necropsied on Study Day 32. The medullary rays within the cortex are composed of basophilic tubules with prominent profiles and an irregular appearance. Nephropathology of 3a. Tubular epithelial cells within the medullary rays have more basophilic cytoplasm and enlarged, prominent nuclei, characteristic of regeneration.

Figure 4. Kidney, including renal pelvis, of mini-pig exposed to 16 Gy radiation and necropsied on Study Day 38. There is diffuse interstitial fibrosis present, with widespread loss of tubular profiles.

Figure 5. Kidney, including renal pelvis, of mini-pig exposed to 16 Gy radiation and necropsied on Study Day 7. The renal pelvis is expanded by edema and the lining epithelium is thin to non-existent.

Figure 6. Kidney of a mini-pig exposed to 16 Gy radiation and necropsied on Study Day 11. There is an increased amount of amorphous tissue within the glomeruli, with loss of glomerular capillary profiles.

CONCLUSIONS

The kidney is a common target of radiation toxicity, with renal disease most commonly developing as a delayed effect. Most publications on radiation toxicity describe glomerular changes or lesions consistent with ischemia-reperfusion injury (particularly proximal tubular necrosis) as the renal changes observed.1,2,3 Glomerulonephritis was observed in most animals from this study, including animals that died early and those that survived to the scheduled necropsies. However, proximal tubular necrosis was not a striking feature in any of the animals. Tubular necrosis and regeneration in this study was almost completely limited to the collecting tubules within the medulla and medullary rays, and this pattern was observed in almost all of the animals examined. This may represent a species-specific radiation-induced effect in the mini-pig kidney. A previous report on radiation nephropathy in the pig described glomerulonephritis as well as tubular necrosis and regeneration.4 However, the tubular necrosis and regeneration was observed in the subcapsular regions rather than in the medulla and medullary rays. The reason for this discrepancy between our study and the previous report was uncertain. Interestingly, renal changes in this study were observed as early as Study Day 7, with the tubular changes observed as early as Study Day 11. Previous reports list renal changes as delayed effects of radiation, and in the above mentioned publication on pigs, tubular necrosis and regeneration were not observed until 6 weeks post-radiation.1,2,4

REFERENCES


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