Histomorphologic features of neonatal and juvenile urogenital development in sprague-dawley rats

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ABSTRACT

This study describes the key histomorphologic postnatal developmental events occurring in the urogenital system of rat pups from birth to postnatal day (PnD) 30. Tissues were collected from 51 pups, using equal numbers from each sex whenever possible, at PnD 1, 2, 4, 6, 8, 10, 14, 17, 21, 24, 26, 28, and 30. The tissues and kidney weight and the organ weight relative to body weight ratios were also calculated. Our study revealed that nephrogenesis in rats ceased by PnD14, while few mitoses were still observed at the corticomedullary junction by PnD21. Individual cell death and mitoses were abundant at birth and followed a caudal to cranial pattern (from outer cortex to medulla), accompanying developing renal structures. At PnD26, the ovary exhibited a sharply demarcated cortico-medullary separation (figure 5). The uterine glands became visible two weeks after birth and leukocyte infiltrates were entirely absent over the investigated period. The vaginal epithelium showed multifocal mucification starting on PnD24 (figure 6). By PnD 26, the superficial layer of the vaginal epithelium was multifocally composed of large cells containing a mucinous material mixed with few apoptotic cells. At birth, the seminiferous tubular epithelium was 1 to 2 layers thick, composed of spermatogonia and Sertoli cells. A seminiferous lumen was rarely seen and the interstitium was abundant and hypocellular. The pachytene spermatocytes were observed around the second week of life, while the first round spermatids became visible on PnD26. The description of these major histologic features of the male and female urogenital systems from birth to PnD30 will serve as a valuable histologic historical database that will be useful in pediatric drug development.

INTRODUCTION

Prenatal and juvenile toxicology studies are required when the pediatric population is the intended target of a new drug. The rat is one of the most commonly used small animal species in developmental and juvenile toxicity studies. When compared to its human counterpart, the glomerular filtration or onset of puberty underlines some of the specific challenges of underdeveloped organs in newborn and juvenile animals. Time-course histomorphological background changes (programmed cell death, increase mitoses) are part of the normal developmental processes during the postnatal period and should be differentiated from treatment-related lesions. The focus of this study was to provide a concise outline of histomorphological features of postnatal urogenital development in Sprague-Dawley rats during the first month of life.

MATERIALS AND METHODS

The 51 pups in this study were the progeny of 6 time-mated Sprague-Dawley rats females CrICD (SD) purchased from Charles River Laboratories Canada Inc. (St-Constant, QC) at Day 0 of pregnancy. The tissue samples were collected during different time points of the post-natal day (PnD) 1 to PnD30. When possible, equal number of females and males were used for each group. The body weight and the absolute testes and kidneys weights were recorded for each time point. The organ weight to body weight ratio was calculated. All tissues were trimmed, processed and paraffin-embedded. Sections were cut at a 4μm thickness and stained with hematoxylin and eosin (H&E).

RESULTS AND DISCUSSION

Our study revealed morphologic dissimilarities between developing organs when compared with adult ones. Throughout the first month of life, the kidney and testes weights proportionally increased with age and body weight, especially after PnD21. The kidney weight to body weight ratio reached a maximum value between PnD10-PnD15 for kidney and PnD26 for testes. This data suggest that, at the end of the first month, the organs were still developing and gaining weight proportionally with the increase of body weight (figure 1) while the kidney increased at a less steep rate than body weight on PnD30 (figure 2).

Generally, at birth, the kidneys showed an increased cellularity due to a mixture of blastemal epithelial cell and undifferentiated, loosely arranged mesenchymal cells, with an edematous interstitium. At birth, the histologic features of kidney immaturity were consistent with the presence of a distinct nephrogenic zone in outer one-fourth of the cortex. There, the actively growing portion of the ureteral buds (ampullae) induced the metanephric mesenchyme differentiation, and lead to different spermatocytes were observed around the second week of life, while the first round spermatids became visible on PnD26. The description of these major histologic features of the male and female urogenital systems from birth to PnD30 will serve as a valuable histologic historical database that will be useful in pediatric drug development.

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