

Case Report

Unilateral noncystic renal dysplasia in a Sprague Dawley rat

Yong-Hoon Lee¹, Duyeol Kim¹, Sun Hee Park¹, Mi Ju Lee¹, Myoung Jun Kim¹, Ho-Song Jang¹, Jin Seok Kang^{2*}, Jongkoo Kang^{1,3*}

¹Department of Pathology, Biototech Co., Ltd., Ochang 363-883, Korea

²Department of Biomedical Laboratory Science, Namseoul University, Cheonan 331-707, Korea

³College of Veterinary Medicine, Chungbuk National University, Cheongju 361-763, Korea

Renal dysplasia is a developmental disorder of the renal parenchyma involving anomalous differentiation. It is characterized by persistent metanephric ducts surrounded by primitive mesenchyme, fetal or immature glomeruli, fetal or immature tubules, interstitial fibrosis, and dysontogenic metaplasia involving tissues such as cartilage. Renal dysplasia has been rarely reported in rats. Here, we observed a small left kidney in a rat used in a short-term repeat toxicity study. The rat showed no clinical signs throughout the study. All parameters, including those reflecting kidney functions, were normal upon hematological examination and urinalysis. Grossly, the kidney was small (5 × 8 mm) and its surface appeared normal. Histological examination revealed that the cortex and medulla were poorly demarcated and contained immature/atrophic glomeruli, immature renal tubules, and mesenchymal cells. The cortex contained immature glomeruli, atrophic glomeruli with cystic dilatation of Bowman's capsular space, and some atypical tubules. Primitive metanephric tubules in the medulla were larger in diameter than normal collecting ducts, lined by a tall columnar epithelium with pale cytoplasm and basal nucleus, and surrounded by loose mesenchymal cells. Occasional tubules contained pale eosinophilic homogenous material in the lumen. Thus, this was diagnosed as a case of renal dysplasia on the basis of histologic features and is the first reported case of renal dysplasia in Sprague Dawley rats.

Key words: renal dysplasia, kidney, Sprague Dawley rat, pathology, case report

Introduction

Renal dysplasia is a developmental disorder of the renal parenchyma involving anomalous differentiation and dis-

ruption in the normal development of the collecting duct system, that is the so-called renal branching morphogenesis in which transcription factors, growth factors, and cell signal peptides are involved [1]. In humans, renal dysplasia is well documented as one of the main causes of childhood end-stage renal failure [2]. It has also been reported in animals including dogs, cats, cattle, horses, pigs and sheep [1, 3-8]. In rodents, renal dysplasia has been reported in the Wistar rat and Syrian hamster [9, 10]. However, there have been no reports of renal dysplasia in the Sprague Dawley rat. To the best of our knowledge, this is the first reported case of renal dysplasia in the Sprague Dawley rat.

Case report

A ten-week-old female Sprague Dawley rat with a small left kidney was discovered accidentally during necropsy of control animals in a short-term repeat toxicity study (four weeks). The rat was kept in a polycarbonate cage and received commercial rodent diet (Harlan, the Netherlands) and purified autoclaved water *ad libitum*. Environmental conditions were controlled to provide a temperature of 18~26°C, a relative humidity of 30~70%, and a 12:12 hr light: dark cycle. All housing procedures and experiments were performed in accordance with Biototech Co., Ltd. Institutional Animal Care and Use Committee Guidelines (Accepted No. 110510).

The animal showed no clinical signs throughout the study, and hematological examination and urinalysis did not reveal evidence of disturbed kidney function. At necropsy, the left kidney was found to be small (5 × 8 mm) with a normal surface (Fig. 1). On the cut surface of the kidney, the cortico-medullary ratio was markedly decreased. The right kidney was normal in size with no

*Corresponding author: Jin Seok Kang, Department of Biomedical Laboratory Science, Namseoul University, Cheonan 331-707, Korea
Tel: +82-41-580-2721, Fax: +82-41-580-2932, E-mail: kang@nsu.ac.kr
Jongkoo Kang, College of Veterinary Medicine, Chungbuk National University, Cheongju 361-763, Korea
Tel: +82-43-261-2607, Fax: +82-43-271-3246, E-mail: jkkang@cnu.ac.kr

gross lesions, and no other organs had obvious macroscopic lesions.

The kidneys were resected and fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned in 3 μm thick slices, and stained with hematoxylin and eosin (H&E). In addition, selected sections were stained with Alcian blue (pH 2.5) and Masson's trichrome stain to differentiate fibrosis from mes-



Fig. 1. Gross findings in the left kidney of a Sprague Dawley rat. The kidney is small in size (5×8 mm). Bar=5 mm.

enchymal tissue.

Histological examination revealed that the cortex and medulla were poorly demarcated and contained immature/atrophic glomeruli, immature renal tubules, and mesenchymal cells (Fig. 2A). The cortex contained immature glomeruli, atrophic glomeruli with cystic dilatation of Bowman's capsular space, and some atypical tubules (Figs. 2B and 2C). Primitive metanephric tubules in the medulla were larger in diameter than normal collecting ducts, lined by tall columnar epithelium with pale cytoplasm and a basal nucleus, and surrounded by loose mesenchymal cells (Fig. 2D). The mesenchymal cells displayed mild staining with Alcian blue but no staining with Masson's trichrome (data not shown). Occasional tubules contained pale eosinophilic homogenous material in the lumen (Fig. 2E). On the other hand the right kidney appeared normal on histological examination.

Discussion

Renal dysplasia is generally defined as an abnormality that results from disorganized development of renal parenchyma associated with altered differentiation of specific cellular elements of renal tissue [1, 11]. This implies that the ureteric bud and the metanephric blastema interacted abnormally during development [12]. Characteristics of renal dysplasia include persistent metanephric ducts surrounded by primitive mesenchyme, fetal or immature glomeruli, fetal or immature tubules, interstitial fibrosis, and dysontogenic metaplasia involving tis-

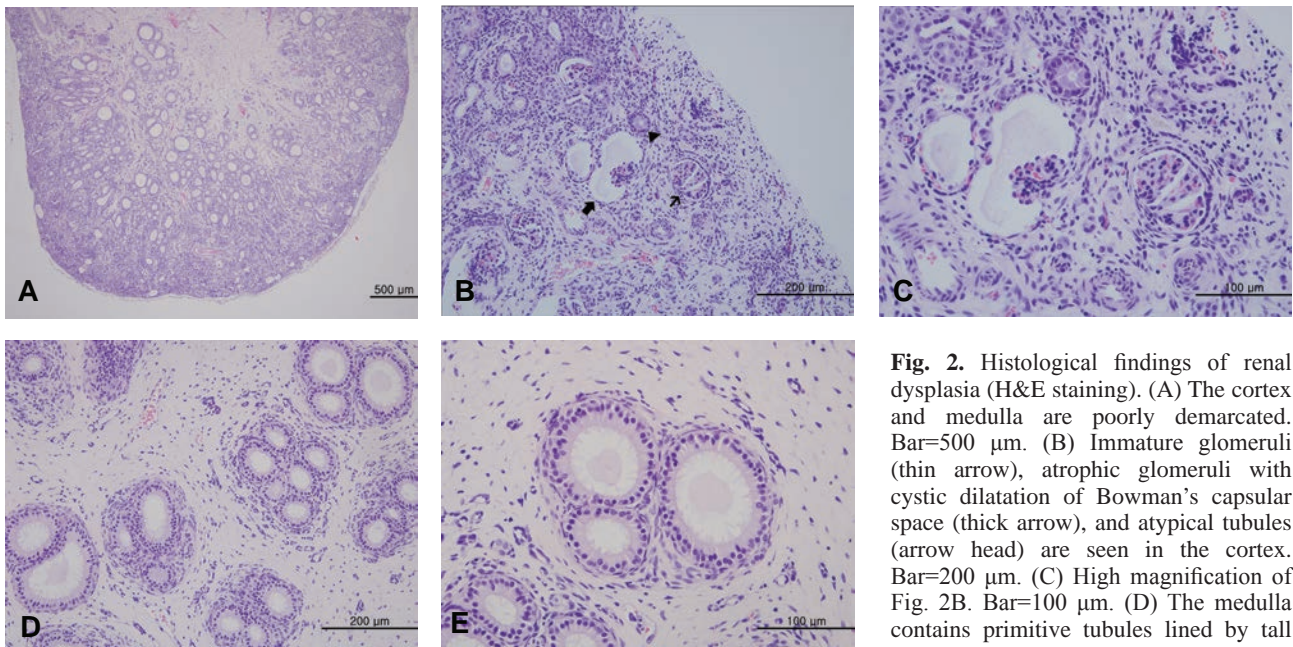


Fig. 2. Histological findings of renal dysplasia (H&E staining). (A) The cortex and medulla are poorly demarcated. Bar=500 μm . (B) Immature glomeruli (thin arrow), atrophic glomeruli with cystic dilatation of Bowman's capsular space (thick arrow), and atypical tubules (arrow head) are seen in the cortex. Bar=200 μm . (C) High magnification of Fig. 2B. Bar=100 μm . (D) The medulla contains primitive tubules lined by tall columnar epithelium with pale cytoplasm and a basal nucleus, and surrounded by loose mesenchymal cells. Bar=200 μm . (E) Occasional primitive tubules contain eosinophilic material in the lumen. Bar=100 μm .

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sues such as cartilage [13]. This case was characterized mainly by immature and fetal glomeruli and primitive metanephric tubules surrounded by loose mesenchymal cells. Thus, the present case was diagnosed as renal dysplasia on the basis of histological findings. The presence of fetal glomeruli as well as atypical tubule epithelium and fetal tubules indicates that the metanephric blastema developed but differentiated incompletely, and the presence of primitive metanephric ducts surrounded by mesenchymal cells and dysontogenic metaplasia signifies that the ureteric bud and the metanephric blastema failed to interact completely [5]. Renal dysplasia should be differentiated from hypoplasia and neoplasia: hypoplasia is characterized by decreased nephron number and kidney size but no abnormal tissue, and neoplasia is invasive and usually includes only one disordered cell type [11].

A previous report of renal dysplasia case in a Wistar rat describes primitive glomerular/tubular structures, tubules resembling collecting ducts and mesenchyme [10]. These findings are in accord with the histological characteristics observed in the present study. Interestingly, among the criteria for renal dysplasia, fibrosis and dysontogenic metaplasia have not been observed in rat cases. In contrast, fibrosis and dysontogenic metaplasia have often been observed in other animals including dog, cat, calf, and hamster [3, 9, 13-16]. Although these histological differences in renal dysplasia are probably attributed to species differences or experimental conditions, more cases are required to elucidate the cause.

In humans, kidney malformations with subsequent neoplasia are associated to chromosomal abnormalities and are often accompanied by other malformations [10]. In domestic animals, cases of familial renal disease in several dog breeds often have dysplastic features [1]. Renal dysplasia reported in Japanese black cattle is due to deletion of the paracellin-1 gene of chromosome 1 [17]. Furthermore, renal dysplasia in puppies is caused by neonatal infection with canine herpes virus [18], in kittens by fetal infection with feline panleukopenia virus [19], and in calves by fetal infection with bovine viral diarrhea virus [20], and renal dysplasia in pig has been attributed to vitamin A deficiency [1]. However, the exact cause in rats has not been determined.

While renal dysplasia in domestic animals such as dog has been well reported in the literature because of its clinical significance, renal dysplasia in rats has rarely been documented. Therefore, this report provides an example of renal developmental background lesions in rats.

Acknowledgements

This study was supported by Biototech Co., Ltd. We are grateful to all the researchers who contributed to this study.

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