POLYCYSTIC KIDNEY DISEASE ASSOCIATED WITH MULTIPLE CYSTS IN OVARIES AND UTERUS IN AN ADULT DONKEY

UN CAS DE POLYKYSTOSE RÉNALE ASSOCIÉE À DE MULTIPLES KYSTES OVARIENS ET UTÉRINS CHEZ UNE ÂNESSE

Par Reza Kheirandish1 and Shahrzad Azizi2

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(1) Department of Pathobiology, Veterinary Faculty, Shahid Bahonar University of Kerman, Kerman, Iran.
(2) Department of Pathobiology, School of Veterinary Medicine, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran;
Corresponding author: azizi.shahrzad@gmail.com P.O. Box: 166.

Polycystic kidney disease (PKD) is a disorder of the nephron characterised by the presence of multiple cysts in kidney. Human beings and various animal species may be affected by this disease. PKD is heritable and classified either as autosomal recessive polycystic kidney disease (ARPKD) or autosomal dominant polycystic kidney disease (ADPKD). The present study describes polycysts in the kidneys, ovaries and uterus in a 3 year-old donkey. Cortex and medulla of both kidneys were affected by several fluid filled cysts ranging from 5 mm to over 3 cm in diameter. The histopathological examination of the kidneys revealed multiple circular, ovoid to polygonal cysts. Renal cysts walls were lined by a single layer of low cuboidal to squamous cells that originated from every segment of nephrons. Connective tissue and lymphoplasmacytic inflammation was observed around the renal cysts. No other inflammatory reaction was detected in the kidneys. Medulla showed fibrosis and hyperplastic changes in the epithelial cells of collecting tubules. Ovaries had multiple follicular cysts up to 10 cm in diameter. The uterus mucosal membrane was slightly pale, thickened and edematous and showed variable sizes of translucent cysts containing clear fluid that bulged into the endometrial surface of uterine body and horns. The size of cysts ranged from approximately 5 mm to 3 cm in diameter and the larger ones were found in the uterus horns. The pathology findings of this case of PKD were similar to those found in human ADPKD.

Key words: polycystic kidney, pathology, polycystic ovary, uterine cyst, donkey, human.

La maladie polykystique des reins est une maladie du néphron caractérisée par la présence de multiples kystes dans le rein. Elle touche non seulement l’homme mais aussi différentes espèces animales. Héréditaire, elle peut être autosomique récessive ou autosomique dominante. Nous décrivons ici les lésions anatomopathologiques de cette affection chez une ânesse âgée de trois ans. Les zones corticale et médullaire des deux reins présentent plusieurs kystes remplis de liquide dont le diamètre varie de 5 mm à plus de 3 cm. A l’examen histopathologique, les kystes, entourés de tissu conjonctif envahi par des lymphoplasmocytes, sont de forme circulaire, ovoïde ou polygonale. Leur paroi est constituée d’une seule couche de cellules cuboïdes et squameuses, caractéristiques de chaque segment de néphron. La zone médullaire montre une fibrose et une hyperplasie des cellules épithéliales des tubules collecteurs. De nombreux kystes folliculaires, allant jusqu’à 10 cm de diamètre, sont également trouvés dans les ovaires. La muqueuse utérine, pâle, épaisse et oedématueuse montre des kystes translucides de taille variable, contenant un liquide clair, et qui déforment la surface de l’endomètre du corps et des cornes de l’utérus. Leur diamètre varie d’environ 5 mm à 3 cm et les plus grands sont trouvés dans les cornes utérines. Selon les critères anatomopathologiques, la maladie polykystique décrite chez cette ânesse rappelle la forme autosomique récessive de cette maladie chez l’homme.

Mots-clés : maladie polykystique rénale, anatomopathologie, kystes ovariens, kystes utérins, ânesse, homme.

SUMMARY

RÉSUMÉ
INTRODUCTION

Renal cystic disease is a disorder in the nephron that may occur as hereditary, acquired or developmental. The affected kidneys enlarge progressively due to cystic expansion of the tubules. It leads to a loss of the normal renal structure and function and ultimately to end stage disease (Palmer & Carpenter, 2004; Wilson 2004).

In humans, polycystic kidney disease (PKD) is heritable and is described in two distinct genetically forms: autosomal recessive polycystic kidney disease (ARPKD or infantile form) and autosomal dominant polycystic kidney disease (ADPKD or adult form). Mutation in the PKHD1 gene (encoding fibrocystin) causes autosomal recessive form of PKD while genetic failure in the PKD1 and PKD2 genes leads to autosomal dominant forms of PKD (Torres & Harris, 2007). Autosomal dominant PKD is the most common form in adults and progresses slowly. It usually leads to death because of renal failure (Wilson 2004). By contrast, the autosomal recessive form occurs rarely in early infancy (one out of 40,000). This form is rapidly progressive and diagnosed by extensive nephromegaly (Zerres et al. 2003). A variety of extra-renal lesions are reported associated with the two forms of PKD.

 Syndromes similar to both the recessive and dominant forms of human PKD have been reported in animals including Shorthair cat (Bonazzi et al. 2007), Persian cat (Biller et al. 2006), cattle (Ushigaki et al. 1999), goat (Krotec et al. 1996; Newman et al. 2000) and sheep (Johnstone et al. 2005). The present study, describes the occurrence of bilateral polycystic kidneys with endometrial and ovarian cysts in a donkey.

CASE HISTORY

A three year-old female donkey was sent for post-mortem examination at the Pathology Department of the Veterinary Faculty, Shahid Beheshti University, Tehran, Iran. The donkey was euthanized. It showed excessive body fat. Multiple cysts were visible on the two kidneys and the two ovaries. In addition, the dissection of the uterus showed numerous cysts which bulged into the endometrial mucosa. No abnormal morphologic changes were observed in the other organs. Tissue samples of the kidneys, ovaries and uterus were collected, fixed in 10% buffered formalin and processed according to routine histopathologic techniques. Paraffin sections at 5 μm thickness were stained with hematoxylin-eosin and studied by an ordinary light microscopy.

At necropsy, right and left kidneys were mildly enlarged. Polycystic kidney disease was diagnosed by the presence of multiple cysts ranged from 5 mm to over 2.5-3 cm in diameter that affected both kidneys. The cysts were identified as spherical to ovoidal structures with smooth surfaces and sharply well-circumscribed borders. They were clearly distinguishable through the thin and translucent renal capsule. Clear to cloudy, yello-
adjacent renal parenchyma leading to the atrophy of glomeruli and tubules in this area. Medulla showed fibrosis and hyperplastic changes in epithelial cells of collecting tubules (figure 3).

Both ovaries had several follicular cysts which were greater than normal follicles. The size of the largest ones reached 10 cm in diameter (figure 4). The corpus luteum on the ovaries were not seen. Mucosal membrane of the uterus was slightly pale, thickened and oedematous. The uterus showed variable sizes of translucent cysts that were distributed in the endometrial surface of uterine body and horns. The range of cysts was about 5 mm to 3 cm in diameter and the larger ones were found in the uterus horns. The endometrial cysts with fluid retention bulged into the lumen of the uterus. The cysts appeared as both unilocular and multilocular (figure 5). Histopathologically, the endometrial mucosa was oedematous. The cysts showed different sizes and shapes. They were made of a single layer of squamous epithelial cells. Eosinophilic fluid filled the endometrial cysts.

**DISCUSSION**

Veterinary literature reports PKD in different animal species (Chandler et al. 2003; Hosseininejad & Hosseini, 2008; Seo et al. 2010). PKD is most commonly described in adult males and females longhaired and Persian cats as an autosomal dominant trait (Lulich et al. 1988; Stebbins 1989; Biller et al. 1996). In human studies, PKD was categorized as infantile and adult forms (Torres & Harris, 2007). The collecting ducts are responsible for renal cysts formation in the infantile form (Lonergan et al. 2000) but in adults, the cysts originate from every segment of the nephron. Different extra-renal abnormalities such as cysts in the pancreas, liver and spleen, colonic diverticulitis, defects in the heart valve and aneurysm in the aorta and cerebral vessels were reported in association with the adult form of PKD (Wilson 2004, Takagi and Umemoto, 2005, Kim et al. 2012).

Usually, ultrasonography of kidneys is used for diagnosis of PKD in humans (Papadopoulou et al. 1999, Savaj et al. 2012) and animals (Hosseininejad & Hosseini, 2008; Seo et al. 2010), renal cysts being identified as anechoic, spherical structures.

The present report describes the occurrence of multiple cysts in both kidneys and ovaries and in the uterus of an adult donkey. Grossly, thin walled cysts of various sizes and containing yellowish, clear fluid were present more in the cortex and less in the medulla of both kidneys. Microscopically, the cyst walls were lined by cuboidal epithelial cells in the small cysts and squamous epithelial cells in the large ones. The epithelial cells arose from different parts of nephron. The gross and histopathologic features of PKD in this case were in conformity with ADPKD reported in human (Lieske & Toback, 1993, Kim et al. 2012) and other species of animals (Biller et al. 1996; O'Leary et al. 1999). In patient affected with ADPKD, the presence of cysts in other organs was observed. Hepatic cysts commonly complicate ADPKD especially in humans and animals.
Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in humans. This syndrome is associated with a high secretion of androgen and has multifactorial etiology (Abbott et al. 2002; Ariffin et al. 2008). Other disorders such as hyperinsulinemia, luteinizing hormone (LH) hypersecretion, obesity in abdominal area, diabetes mellitus type II, atherosclerosis, and endometrial carcinoma may be associated with PCOS (Abbott et al. 2002; Abbott et al. 2005; Giudice 2006). Alvarez-Blasco et al. (2006) showed a 28.3% prevalence rate of PCOS, in overweight women compared with 5.5% in slim women in Spain (Alvarez-Blasco et al. 2006).

In contrast to humans, PCOS is uncommon in animals (Ariffin et al. 2008). In dairy cows, the prevalence of the follicular cysts was 7-13 % by the postmortem examination. PCOS was more frequent 1 to 4 months post parturition. Weakness, high production and being in the pick of the lactation are known as predisposing factors (Gasse et al. 1984; Grohn et al. 1994; Grohn et al. 1995). Other factors such as poor nutrition, high consumption of concentrates, minerals and vitamins insufficiency, keeping animal in closed system and lack of exercise, as well as meteorological influences and seasonal alterations are mentioned as etiological agents (Erb & Martin, 1980). Oestrogenic substances are considered as the main cause (Salvetti et al. 2004).

In the horse, two types of uterine cysts have been described. First lymphatic cysts that are different in sizes from microscopic to several centimeters, and second, glandular cysts ranging from a few millimeters to maximum 1cm in diameter (Kenney 1978; Watson 1994). In the present case, uterine cysts were derived from the lymphatic lacunae. Tannus & Thun (1995) reported lymphatic endometrial cysts ranging from 2 to 48 mm in diameter. They described that lymphatic cysts could be associated with infertility. In the mares, uterine, fluid-filled cysts were found in the endometrium (Kenney & Ganjam, 1975; Ricketts 1975; Kenney 1978), myometrium ( Stanton et al. 2004) or serosal surface (Ginther & Pierson, 1984). Kaspar et al. (1987) reported 13% prevalence of endometrial cysts in 104 grossly examined mares. However, they observed the larger cysts in the uterine body which was different from our study where the large cysts were located in uterine horn. Similarly the largest endometrial cyst had 3 cm diameter. Different techniques such as postmortem examination, histopathology, transrectal palpation and ultrasonography, hysteroscopy, and fiber-optic were used for diagnosis of uterine cysts in the mare (Kenney & Ganjam, 1975; Wilson 1985; Kaspar et al. 1987; Leidl et al. 1987). These techniques are less used in the donkey and postmortem examination is the most common method for diagnosis of uterine cysts. In this study, the diagnosis of the cysts in different organs of the donkey was made at necropsy. A few case reports of PKD in the donkey have been published. To our knowledge, this is the second description of PKD in this species. Similar to our study, van den Brand et al. (2006), reported nephrolithiasis, bilateral polycystic kidney and ovary in a donkey.

Because of few reports of PKD in the donkey, a genetic background for PKD remains unknown. Further studies should be done to confirm the inheritance mode of PKD in various animal species, understanding the pathogenesis and determination of responsible gene (s) of this disease. It is still unclear whether cystic ovaries and the uterus are consistent features of PKD in the donkey.

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