Histologic investigation of the polycystic structures in ovaries of german shepherd dogs with hip dysplasia

KANTER M.[1], DALÇIK H.[2], KÖKSAL V.[3], KARAÖZ E.[3]
Department of Histology and Embryology, Veterinary Faculty, Yüzüncü Yıl University[1], Van
Department of Histology and Embryology, School of Medicine, Hacettepe University[2], Ankara
Department of Histology and Embryology, Gülhane Military Medical Academy[3], Ankara

Objective To evaluate the structural aspects of ovarian follicular cystogenesis in five German Shepherd Dogs with hip dysplasia.

Methods Five German Shepherd Dogs with hip dysplasia were ovariectomized under Ketalar anesthesia. Ovaries were removed and fixed in 10% neutral formalin solution. Tissue samples were then processed for the histological investigation.

Results Different kind of follicles in ovaries of all dogs were observed. Some of these follicles were undergoing atresia or were in the various stages of cystogenesis. However, some of them were odematous or 2 or 3 oocytes containing follicles. These all follicles have been noticed to transform into a cystic structures.

Conclusion Although all German Shepherd Dogs used in this study with hip dysplasia had cystic follicles in their ovaries, more studies are needed to prove that there is a relationship between the hip dysplasia and the formation of the cystic follicles in ovaries by using more samples or different dog species.

Key words German shepherd dog, ovarian follicular cyst, hip dysplasia

Introduction

Researchers independently assessed study quality and data concerning endocrinologic abnormalities, pathogenic mechanisms, and therapy of the polycystic ovary (1). How the various endocrinologic perturbations are interrelated in the polycystic ovary is the subject of intense controversy (2). The most widely accepted theory of the pathogenesis of the polycystic ovary is that it results from a complex cycle of events in which production of androstenedione and its subsequent peripheral conversion to estrone are central (2,3). Recent studies require modification of this estrone hypothesis. The polycystic ovary results when a primary defect increases one of three variables: the ratio of the serum concentrations of luteinizing hormone to follicle stimulating hormone, the ratio of the intraovarian concentration of androgen to estrone or follicular atresia. An increase in one of these variables can then induce successive abnormalities. This model views the polycystic ovary as functional, gonadotropin-dependent ovarian hyperandrogonism (1).

In 1935, Stein and Leventhal described the polycystic ovary (4) in women which is associated with ovarian failure and a plethora of other symptoms (5-13). Since Stein and Leventhal's (4) discovery, investigators have attempted to develop mammalian models to study cystic ovaries (14,15).

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The cause and pathogenesis of canine hip dysplasia (CHD) are poorly understood. Studies to date indicate that CHD is a developmental disorder having both genetic and environmental bases (16-18). Enviromental factors have been shown to modify the clinical and radiografic expression of CHD; however, a causal association has not been established. Dog size, growh rate, and endocrine factors are thought to be important influences. These and other factors have been thoroughly discussed in several reviews on the topic (16-18).

The aim of this study was to investigate the polycystic structures in the ovaries of German Shepherd Dogs with hip dysplasia.

Material and Method

In Gemlik Army Veterinary Clinic 5 German Shepherd Dogs with hip dysplasia were ovariectomized under Ketalar anesthesia. Ovaries were removed and fixed in 10% neutral formalin solution. Tissue samples were then processed for the histological investigation. 6 micrometer thick sections were cut and stained with Hematoxylin Eosin. Mounted slides were examined and pictures were taken under light microscope (Olympus BHT).

Results

During cyst formation, granulosa cells of the affected follicles appeared to undergo structural luteinization. Granulosa cells were observed to undergo a systematic blebbing which began on the surface facing the antrum (Figure1).

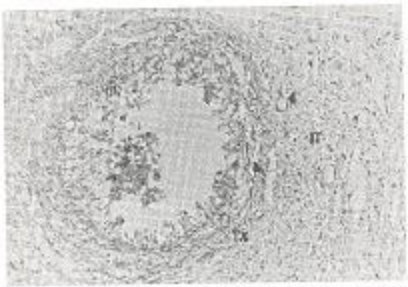

Figure 1. A section of an ovary showing a partial of developing cyst follicle. Note that the granulosa cells are pinched off to the antrum. GC, Granulosa cells; TI, theca interna; TX, theca externa; IT, intersitial tissue; Blood vessels (arrow heads). Hematoxylin-Eosin. X240.

Progressively, the blebs were pinched off and removed with remnants of granulosa cells (Figure 2), leaving a single layer of cells on the basement membrane (Figure 3).

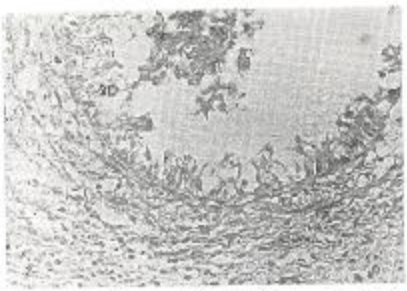

Figure 2. A higher magnification of figure 1 is partially shown particially in the picture. GC, Granulosa cells; TI, theca interna; TX, theca externa. Hematoxylin-Eosin. X480.

Different kind of follicles in ovaries of all dogs were observed. Some of these follicles were undergoing atresia or were in the various stages of cystogenesis. Granulosa cells in some of the cystic follicles were almost depleted (Figure 3). Further depletion of granulosa cells were associated with intense blebbing of their cytoplasm toward basement membran. Formation of the ovarian follicular cyst was completed when the entire cyst was lined by a single layer of transformed granulosa cells (Figure 3).

Figure 3. A section of an ovary showing a partial cyst with reduced layer of cells on the basement membrane; Blood vessels (arrowheads); IT, intersititial tissue. Hematoxylin-Eosin. X240.

These cells rest on a basement membrane. In some of the follicular cysts, cytoplasm of the cells revealed to be highly odematous (Figure 4).

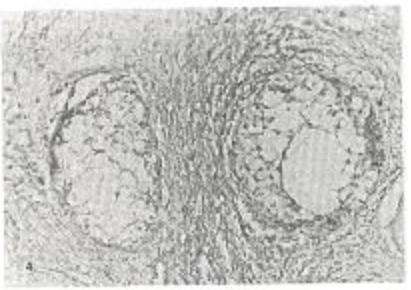

Figure 4. Two Odematous follicles are shown in this figure. Hematoxylin-Eosin. X240.

However in some of the follicles, 2 or 3 oocyctes were also evident (Figure 5).

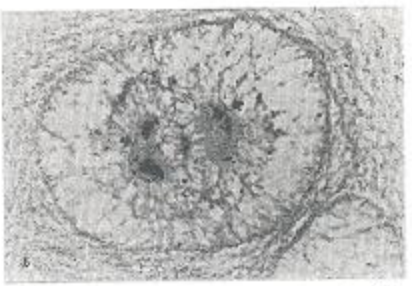

Figure 5. The follicle with 2 or 3 oocytes (arrowheads) is demonstrated in the picture. GC, Granulosa cells. Hematoxylin-Eosin. X240.

These all follicles have been noticed to transform into a cystic structures. There were some blood vessels, theca interna and externa cells that composed of layers of spindle or fusiform cells outside of the basement membrane (Figure 1,2).

Discussion

The studies of Roy et al. (19) and Lee et al. (20) were concerned with light microscopical aspects of ovarian morphology and circulating levels of gonadotropins, androgens, estrogens and prolactin. Furthermore, the polycystic ovary is gonadotropin-dependent.

The polycystic ovary is characterized by increased ovarian androgen production and hyperandrogenemia (21,22). Any disorder that causes an increase in ovarian androgen will cause excessive follicular atresia (1). Polycystic ovary syndrome is the result heteregenous disorders that substantially increase the intraovarian concentration of androgen (1). Progesterone, estrone and estradiol as well as androgen concentration increased in the follicle after pregnant mare serum gonadotropin (PMSG) treatment. During cyst formation circulating levels of estrogen and androgens were found higher than control by Lee et al. (20) and the fluid from cysts contains extremely high levels of these hormons. It is certainly possible that the granulosa cells of developing cyst may be involved in the secretion of estrogen and progesteron (23).

The administration of dehydroepiandrosterone (DHEA) induces the formation of follicular cysts in the ovaries of immature female rats in conjunction with a precocious ovulation, acyclicity and anovulation (24,25). Similarly, ovarian cysts are noted with DHEA administration in the adult cycling rat (26). After an appreciable amount of time subsequent to the withdrawal of DHEA, the animals commence to cycle.

The cells facing the antral cavity commence to bleb in a systematic way until only a single layer of cells remain. The blebs are released into the cavity of the cyst. The cavity of the cyst is usually devoid of blebs and Anderson et al.(23) believe that the population of macrophages found in the cyst cavity are responsible for bleb removal. During cytogenesis in the rat and presumably in other mammalian species, it is this simple layer of transformed, attenuated granulosa cells that designates the formulation of a follicular cyst from an antral follicle and that it is a pathological variation of normal atresia (23). These acquired morphological and physiological features may ensure persistence of the ovarian cyst and thus potentiate a chronic pathological condition (23). The intersititial cells comprises the stromal compartment (27,28).

During cyst formation, granulosa cells of the affected follicles appeared to undergo structural luteinization. Granulosa cells were observed to undergo a systematic blebbing which began on the surface facing the antrum. Progressively, the blebs were pinched off and removed with remnants of granulosa cells, leaving a single layer of cells on the basement membrane.

Different kind of follicles in ovaries of all dogs were observed. Some of these follicles were undergoing atresia or were in the various stages of cystogenesis. Granulosa cells in some of the cystic follicles were almost depleted. Further depletion of granulosa cells were associated with intense blebbing of their cytoplasm toward basement membran. Formation of the ovarian follicular cyst was completed when the entire cyst was lined by a single layer of transformed granulosa cells. These cells rest on a basement membrane. In some of the follicular cysts, cytoplasm of the cells revealed to be highly odematous. However in some of the follicles, 2 or 3 oocyctes were also evident. These all follicles have been noticed to transform into a cystic structures.

It is known that the hip dysplasia is associated with genetics, enviromental bases, dog size, growth rate genetic endocrine factors (16-18). It is also known that the formation of polycystic follicles is involved with the endocrine factors (24-26). But this study could not answer whether there was a relationship between the hip dysplasia of German Shepherd Dogs and the formation of the cystic follicles in their ovaries. More studies are needed to prove that there is a relationship between the hip dysplasia and the formation of the cystic follicles in ovaries by using more samples or different dog species.

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Correspondence to:
Yrd.Doç.Dr. Mehmet KANTER
Yüzüncü Yıl Üniversitesi, Veteriner Fakültesi
Histoloji ve Embriyoloji Anabilim Dalı, Van