



Histological Study of ovaries of female Golden hamster (*Mesocricetus auratus*) with induced thyroid gland disorders

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Abstract: Ovaries are highly important exocrine and endocrine glands, which lead to the production of ovum and then continuity of species. Hypothyroidism and Hyperthyroidism are represents the most important and leading cause of infertility in females as it was cause ovarian dysfunction. Thirty adult female golden hamster, weighting 160-180 gm., were included in the study. Animals were divided to three groups: Carbimazole(12 mg /kg body weight)induced hypothyroidism, eltroxin(100 µg /kg body weight) induced hyperthyroidism and control group. Histological results showed that ovaries of hypothyroid hamsters explained an increase in the thickness of tunica albuginea and atretic follicles with dilation in blood vessels; Whereas ovaries of hyperthyroid hamsters explained degeneration of the primary and secondary ovarian follicles with a vascular congestion. In conclusion hypothyroidism can cause ovarian cysts, follicular atresia, interstitial cells proliferation and delation in the sexual maturation and development; While hyperthyroidism can led to degenerative changes of hamster ovaries, a vascular congestion and a marked decrease in collagen fibers.

Key words : thyroid disorders, eltroxin, Carbimazole, Ovary histology, Hamster .

Introduction

The thyroid glands are responsible for the production of thyroid hormones that are involved in many processes like growth, development, differentiation, and metabolism. thyroid hormones are of two types :thyroxine (T₄), and triiodothyronine (T₃). Thyroxine was converted to T₃ by a glycoprotein called thyroglobulin (TG), and deiodinases (DOI), a proteins that occurs in three isoforms(1).

The role of thyroid gland was very important at the histophysiological level of the female reproductive system. Both thyroid disorders, hyperthyroidism and hypothyroidism was affect the sexual maturation , menstrual function, fertility, and may cause an increase in the rates of gynecological alterations, abortions, and fetal mortality(2).

The endocrine regulation of the body was a complex process that may be disrupted at many stages. Immune system and neuroendocrine system are incorporated in a chain of ovary, thyroid, thymus, and adrenal axes; That was disrupted or regulated through a feedback and forward loops and of hypothalamus, pituitary gland, and an associated endorgans of the neuroendocrine axes (3).

Thyroid gland and ovaries was have two forms of pathological conditions. At the level of hyperfunction, there was poly cystic ovarian syndrome and hyperthyroidism that was affecting ovaries and thyroid gland respectively. Whereas, at the level of hypofunction, there was a premature ovarian failure and hypothyroidism that was affecting the ovaries and thyroid gland respectively, (4) all of these pathological conditions was related to infertility that resulting in abnormal pregnancy outcomes, also[they was responsible of an underlying autoimmune etiology, (5).Many studies have been found out the relationship between thyroid hormones and thyroid receptors and a functional implications on the endometrium (6).

This study was aimed to explain the histological alterations that would take place in the ovaries in hypothyroidism and hyperthyroidism, comparing with euthyroid state.

Materials and Methods

Thirty adult female golden hamster, weighting 160-180 gm., were included in the study. They were kept in normal and healthy conditions and they had access to food and water *ad libitum*.The females were kept away from males for month before starting the study. The vaginal smears were taken from the females and then stained with Hematoxylin, Eosin stain to ensure the regularity of estrous cycle. Waiting for three successive estrous cycles, (4 days for each estrous cycle) were done before beginning the study,(7).Females with regular cycles were included. The experimental female hamsters were divided randomly into the following three groups:

Group 1:- Hypothyroid females, contain 10 female hamsters that received carbimazole drug (12 mg /kg body weight) dissolved in 0.5 ml normal saline orally by the gastric tube for 3 months for the induction of hypothyroidism,(8)

Group 2 :- Hyperthyroid females, contain 10 female hamsters that received eltroxin drug (100 µg /kg body weight) dissolved in 0.5 ml normal saline orally by the gastric tube for 3 months for the induction of hypothyroidism, (9).

Group 3:- Euthyroid females, contain 10 female hamsters that received normal saline orally by the gastric tube for 3 months.

Animals were sacrificed after the three month of experiment. All animals were analyzed for the confirmation of hyperthyroidism and hypothyroidism by using ELISA to estimate T3,T4 concentrations in there plasma. Ovaries were taken out and fixed in 10% formalin solution for the histological sectioning process.

Results

The histological examination of sections stained with H&E of control group ovaries, Pointed out that the ovaries were covered by a layer of simple cuboidal Epithelial cells , that was separated from the underlying tissue by layer of collagen fibers.

The parenchyma of ovary was composed of cortex and medulla, but they were not separated sharply. In cortex, there were a primordial follicles were seen under the tunica albuginea, and different stages of growing follicles; primary secondary and Graffian follicles.

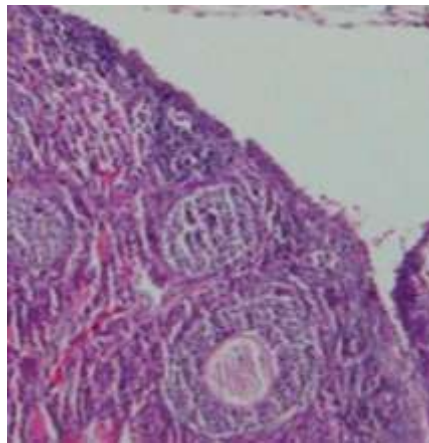


Figure 1: Ovary of healthy hamster explains the ovarian follicles in the ovarian cortex. (H& E, X 200).

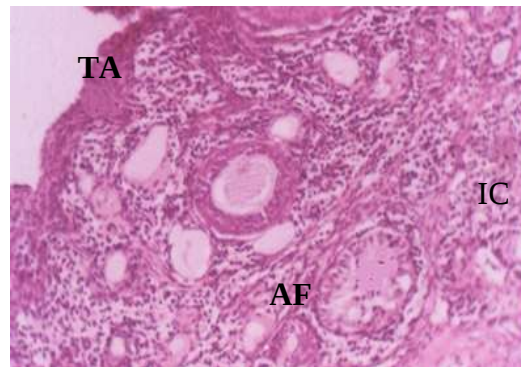


Figure 2: Ovary of hypothyroid hamster explains the increase in the thickness of the tunica albuginea of the ovary (TA), (IC) interstitial cells that invade the spaces among the growing follicles, and (AF) atretic follicle (H& E, X 200).

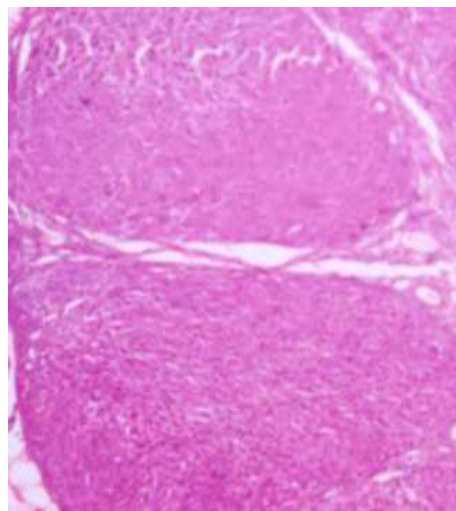


Figure 3: Ovary of hypothyroid hamster explains the reduction in follicles (H& E, X 100).

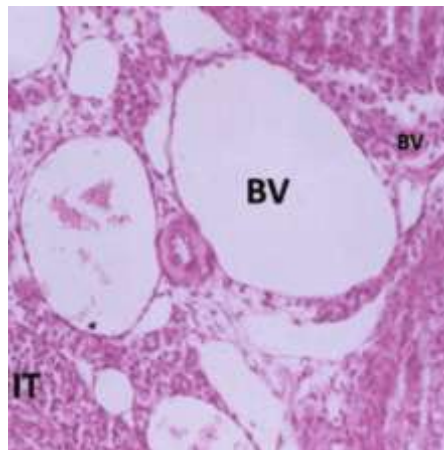


Figure 4: Ovary of hypothyroid hamster explains the dilation in blood vessels (BV) of the interstitial tissue (IT) (H& E, X 200).

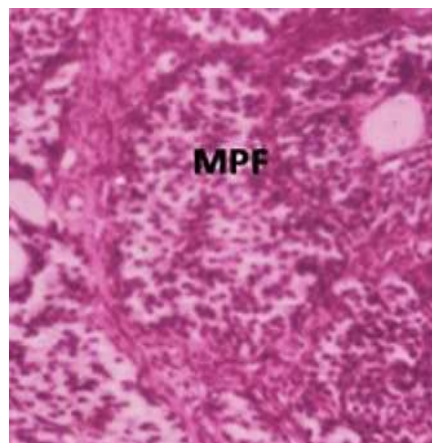


Figure 5: Ovary of hyperthyroid hamster explains the degeneration of the primordial follicles (MPF) (H&E, X200).

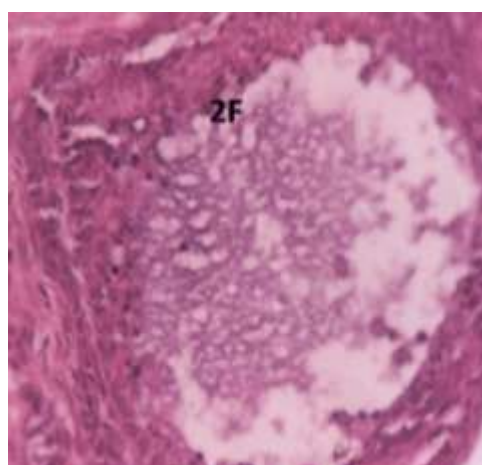


Figure 6: Ovary of hyperthyroid hamster explains the degeneration of the secondary ovarian follicle that appeared as lysis of the primary oocyte and the presence of acidophilic material that fill the antrum cavity (2F) (H& E, X 400).

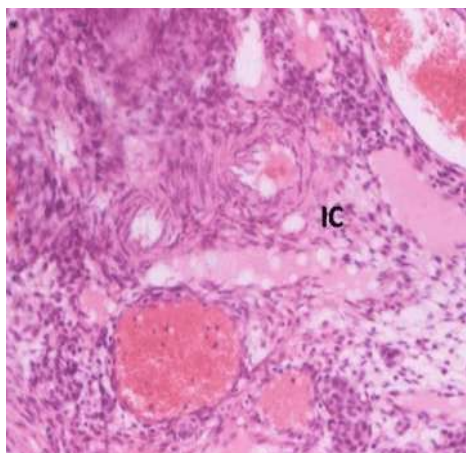


Figure 7: Ovary of hyperthyroid hamster explains the blood vessels in the ovarian stroma . the interstitial cells (IC) were vacuolated (H& E, X 200)

Discussion

Many studies were reported that thyroid hormones play an important role in many aspects of human reproduction, as both cases of hypothyroidism (decreased production T3 and T4) and hyperthyroidism (excessive production of T3 and T4) were seen to have implications on the metabolism of sex steroids and the ovarian and endometrial functions in women causing reproductive disorders like infertility and menstrual irregularities (10).

In our present study, the hypothyroid group that injected with carbimazole were showed increased ovarian activity as seen in the histological sections of the ovary. As surface epithelial cells were crowded in some regions giving the appearance of pseudostratified epithelia, these results were agreed with many studies that treated rats with bromocriptine and carbimazole (11). Also hypothyroid group was showed thickness in tunica albuginea and excessive amounts of collagen fibers in the stroma. These findings were agreed with the study of (12) who found a significant increase in the amounts of collagen fibers, this increase may be results from the decrease in collagen fibers degradation by the decreased lysosomal enzymes in the hypothyroid group.

In the present study the appearance of cysts-like structures was detected. Most ovarian follicles were degenerated in the hypothyroid-treated group. These findings were agreed with the findings of (13,14,15) in that hypothyroidism is a case usually associated with ovarian cysts and hypergonadism which are the most important signs of polycystic ovarian syndrome in women. The case that results from the formation of estriol in hypothyroid females by the replacement of the normal 2- hydroxylation pathway with 16- hydroxylation pathway resulting in estriol formation that is less potent than estradiol in the feedback regulation of the secretion of gonadotrophin and the long duration of hypothyroidism may cause increasing in ovary volume and \ or the formation of cysts (16).

Our results showed a reduction in the ovarian follicles that may be resulted from inadequacy of thyroid hormone supply which cause this disturbance in folliculogenesis (17); Moreover (18) were stated the effects of hypothyroidism on ovary depends on the type of the induction of hypothyroidism, duration of hypothyroidism, animal species, and animals age . Within this (19) were stated that the induction of hypothyroidism in female gerbils can arrest the follicular development and cause atresia of the ovarian follicles.

The results were showed dilation and congestion in blood vessels of hypothyroid and hyperthyroid groups together, the case that resulting from the increase in the vascular supply that is needed for the growing corpus luteum and the increase in its functional activity. (20)

In hyperthyroid group animals that were injected with eltroxin represents a degenerative changes (lysis) in the primary oocytes of the growing ovarian follicles and a degeneration in the granulosa cells, a results that are resembles the observations of (21) who describe the increase in ATPase and alkaline phosphatase activity after

the use of some insecticides; The enzymes that can reflect the degenerative changes happened in the ovarian follicles or it may be results from the lower affinity of follicles for the metabolic degradation.

On the other hand, (22) were revealed that eltroxin administration for 2 months for mice can cause ovarian hyperstimulation, a case that results from granulosa cells action that were stimulated by eltroxin and then producing excessive amounts of estrogen, the main cause of hyperstimulation.

Also the histological sections explain a decrease in the amount of collagen fibers in the stroma of the ovary, the cause behind this result is the administration of eltroxin that inhibits the collagen synthesis; A result that resembles the results of (12) in their study on hyperthyroid rats, then interpreted this result to the increase in collagen degradation by lysosomal enzymes.

Results revealed a vascular congestion of hyperthyroid ovarian vessels, due to the direct effect of eltroxin on the circulatory system (23).

Conclusion

From the present study we conclude that hypothyroidism can cause ovarian cysts, follicular atresia, interstitial cells proliferation and delay in the sexual maturation and development. Also the study was concluded that hyperthyroidism can lead to degenerative changes of hamster ovaries, a vascular congestion and a marked decrease in collagen fibers.

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