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لم ترد بالاصل

Tanta University
Faculty of Medicine
Department of Histology

HISTOLOGICAL STUDY OF THE AGE RALATED CHANGES IN THE ADRENAL GLAND OF MALE ALBINO RAT

Thesis
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ABSTRACT

Key words: Adrenal gland- Age related changes-Histology-Morphometry-Rats.

In this work, 36 male albino rats were studied at different ages including one month (young group), 6-8 months of age (adult group) and at 22-24 months (senile group). Light and electron microscopic examination of adrenal gland in young rats revealed the normal histologic architecture which was more or less similar to that in adult rats. By L/M adrenal cortex of senile rats revealed degenerative changes in some cells particularly zona fasciculata (ZF) cells together with mononuclear cellular infiltration. Congestion of the blood sinusoids was observed especially in the inner two cortical zones as well as increased vacuolation of the cytoplasm of their cells. In adrenal medulla, no changes noticed except congestion of the blood sinusoids. Morphometric & statistical studies revealed a highly significant increase in the mean thickness of ZF and a significant decrease in the mean thickness of zona glomerulosa and reticularis in senile group. By E/M zona fasciculata and zona reticularis cells of senile rats specifically altered in the form of mitochondrial destruction, dilatation of sER as well as accumulation of secondary lysosomes, lipofuscin pigments and dense bodies. Some cells had irregular small nuclei with condensed clumped chromatin. Some ZF cells showed marked lipid droplet repletion. In adrenal medulla, no specific age related changes in the ultrastructure were observed. It was concluded that aging was accompanied with histological changes in the adrenal gland which may reflect on its functions.

فى هذا العمل استخدم ٣٦جرذا ذكرا فى مختلف الأعمار،عمر شهر(المجموعة الصغيرة السن)،ومن٦-٨ أشهر(المجموعة البالغه) وكذلك الجرذان التى تتراوح أعمارها بين ٢٢ – ٢٤ شهرا(المجموعة المسنه).وقد أوضح الفحص بالميكرسكوب الضوئى والألكترونى للمجموعه الصغيره أنها تقريبا مماثله للمجموعه البالغه فى التركيب الهستولوجى للغده الكظريه. كما أوضح الفحص بالميكرسكوب الضوئى وجود تلف فى بعض خلايا القشره وخاصه خلايا المنطقه الحزاميه مع تقدم العمر مع انتشار للخلايا أحادية النواه كما لوحظ احتقان فى الشعيرات الدمويه خاصة فى المنطقتين الداخليتين للقشرة. وقد أظهر البحث وجود فجوات سيتوبلازميه فى خلايا القشره وخاصه المنطقتين الحزاميه والشبكيه. وقد لوحظ أنه لايوجد أى تغير فى نخاع الغدة فيما عدا احتقان فى الشعيرات الدمويه مع تقدم العمر. كما أثبت البحث حدوث زياده ذات دلاله احصائيه فى سمك المنطقه الحزاميه و نقص فى سمك المنطقتين الكبيبيه والشبكيه مع تقدم العمر.وقد أظهرت نتائج الفحص بالميكرسكوب الألكترونى تغيرات خاصة فى المنطقتين الحزاميه والشبكية للمجموعه المسنه فقد لوحظ وجود تدمير فى الميتوكوندريا مع اتساع فى الشبكة الأندوبلازمية الناعمه وتراكم الجسيمات الملتهمه وصبغات الليبوفيوسين وكذلك الجسيمات الداكنه. كما وجدت بعض الأنويه غير منتظمه و المتكاثفة الصبغيات. كما لوحظ امتلاء بعض خلايا المنطقه الحزاميه بالدهون. كما اثبت الفحص بالميكرسكوب الألكترونى لنخاع الغده عدم وجود أى اختلاف فى خلايا النخاع مع تقدم السن. نستنتج من هذا العمل أن هناك تغيرات هستولوجيه تحدث فى الغدة الكظرية مع تقدم السن والتى من المحتمل أن تنعكس على وظائفها.

CONTENTS

REVIEW OF THE LITERATURE

Adrenal glands

I- Anatomy and development:

The adrenal glands are located at the superior poles of the kidneys, embedded in adipose tissue. The right gland is pyramid-shaped and sits directly on top of the right kidney, whereas the left gland is more crescent-shaped and lies along the medial border of the left kidney from the hilus to its superior pole. In the human, they are flattened about 4-6 cm long, 1-2 cm wide and 4-6 mm thick. Together they weigh about 8 gm. but their weight and size vary with age and physiological conditions of the individual **(Gartner and Hiatt, 2001& Junqueira and Carneiro, 2005).**

Adrenal glands are retroperitoneal organs lying beside the upper end of each kidney in front of the lower part of the diaphragm. The right one is partly overlapped by the liver and inferior vena cava while the left adrenal is behind the stomach and pancreas **(Mc Minn et al., 1995).**

On the cut surface of a transected adrenal, a thick yellow cortex is readily distinguishable from a grey medulla in the interior of the gland. The gland is enclosed by a connective-tissue capsule that sends septa into the interior of the gland **(Fawcett and Jensh, 2002).**

The adrenal cortex and medulla can be considered two organs with distinct origins, functions and morphologic characteristics that unite during embryonic development. They arise from different germ layers. The cortex

arises from coelomic intermediate mesoderm while the medulla consists of cells derived from the neural crest which are ectodermal in origin **(Junqueira and Carneiro, 2005).**

Ross and Pawlina, (2006) reported that, the fetal adrenal gland consists of an outer narrow permanent cortex and an inner thick fetal cortex. The gland arises from mesodermal cells located between the root of the mesentry and the developing gonadal zone. At the forth fetal month, the adrenal gland reaches its maximum mass and is slightly smaller than the adjacent kidney. At term, the adrenal glands are equivalent in size and weight to those of the adult. The chromaffin cells originate from the neural crest and invade the fetal zone at the time of its formation.

After birth, the fetal cortex undergoes rapid involution that reduces the gland within the first postnatal month to about quarter of its previous size. With the involution and disappearance of the fetal zone cells, the chromaffin cells aggregate to form the medulla (**Junqueira and Carneiro, 2005**).

Bergman et al., (1996) & Silverberg et al., (2006) had stated that, small accessory adrenal glands (cortical tissue only) may occur in the areolar tissue near the main glands and sometimes in the spermatic cord, epididymes and broad ligament of the uterus.

The adrenal glands have a rich blood supply. Each gland is supplied by three separate arteries that arise from three separate sources: the superior suprarenal arteries which arise from inferior phrenic arteries, the middle suprarenal arteries which arise from aorta and the inferior suprarenal arteries which arise from renal arteries (**Gartner and Hiatt, 2001 & Silverberg et al., 2006).**

Ross and Pawlina, (2006) added that these vessels branch before entering the capsule to produce many small arteries that penetrate it. In the capsule, the arteries branch to give rise to three principle patterns of blood distribution. The vessels form a system that consists of: capsular capillaries that supply the capsule, fenestrated cortical sinusoidal capillaries that supply the cortex and then drain into the fenestrated medullary capillaries and medullary arterioles that transverse the cortex, traveling within the trabeculae and bring arterial blood to the medullary capillaries. The medulla thus has a dual blood supply: arterial blood from the medullary arterioles and venous blood from the cortical sinusoidal capillaries that have already supplied the cortex.

Junqueira and Carneiro, (2005) reported that, the capillary endothelium is extremely attenuated and interrupted by small fenestrate that are closed by thin diaphragms. A continuous basal lamina is present beneath the endothelium. Capillaries of the medulla, together with capillaries that supply the cortex, form the medullary veins which join to constitute the suprarenal vein.

Ross and Pawlina, (2006) added that the suprarenal vein drains into the inferior vena cava on the right side and into the left renal vein on the left side. They also added that the lymphatic vessels are present in the capsule, connective tissue around the large blood vessels in the gland and in the parenchyma of the adrenal medulla. In addition they stated that the lymph vessels play an important role in distributing high molecular weight secretory products of chromaffin cells, such as chromogranin A, into the circulation.

The main nerve supply to the adrenal gland is from myelinated preganglionic sympathetic fibers from the splanchnic nerves via the celiac plexus; the fibers synapse directly with the medullary cells **(Sinnatamby, 2001).**

II- Histological organization of the adrenal cortex:

The adrenal gland is surrounded by a thick capsule of dense irregular connective tissue. The capsule contains a rich plexus of blood vessels and numerous nerve fibers. Some blood vessels and nerves enter the substance of the gland in the trabeculae that extend inward from the capsule and then leave the trabeculae to enter the cortex. The parenchyma of the cortex consists of continuous cords of secretory cells that extend from the capsule to the medulla, separated by blood sinusoids. The cortex is subdivided into three layers according to the arrangement of the cells within the cords **(Krause, 1996).**

Fawcett and Jensh, (2002) & Ross and Pawlina, (2006) stated that the characteristic zonation of the adrenal cortex that is divided into zona glomerulosa, zona fasciculata and zona reticularis. The transition from zone to zone is gradual, but their boundaries are more apparent if the blood vessels are injected with a contrast medium. The zonation of the cortex is reflected in its production of different hormones in the three zones. When isolated from their natural location, cells of all three layers produce the same product. This has led to the suggestion that products of the peripheral zone carried in the blood downstream to the next zone may influence the nature of the product formed in that zone.

Fawcett, (1994) & Junqueira and Carneiro, (2005) reported that cells of the adrenal cortex don't store their secretory products in granules rather; they synthesize and secrete steroid hormones only upon demand. Steroids, being low molecular weight lipid soluble molecules, can freely diffuse through the plasma membrane and do not require specialized process for their release. Cells of the adrenal cortex have the typical ultrastructure of steroid secreting cells which are endocrine cells found in various organs of the body (testes, ovaries, adrenals) and are specialized for synthesizing and secreting steroids with hormonal activity. They are polyhedral or rounded acidophilic cells with a central nucleus and a cytoplasm that is usually rich in lipid droplets, smooth endoplasmic reticulum, and spherical or elongated mitochondria with tubular cristae.

The synthesis of cholesterol from acetate takes place in smooth endoplasmic reticulum, and the conversion of cholesterol to pregnenolone takes place in the mitochondria. The enzymes associated with the synthesis of progesterone and deoxycorticosterone from pregnenolone are found in smooth endoplasmic reticulum; those enzymes that convert deoxycorticosterone → corticosterone → 18-hydroxycorticosterone → aldosterone are located in mitochondria – a clear example of collaboration between two cell organelles. Thus a precursor molecule may move from sER to a mitochondrion and back again several times before the definitive molecular structure of a given corticosteroid is obtained **(Junqueira et al., 1998 & Ross and Pawlina, 2006).**

1- Zona glomerulosa:

It is the narrow outer zone that constitute up to 15% of the cortical volume. It lies immediately beneath the connective tissue capsule in which the columnar or pyramidal cells are arranged in closely packed, rounded or arched clusters that are continuous with the cellular cords in zona fasciculata. The cells are relatively small and a rich network of fenestrated capillaries surrounds each cell cluster. In human, some areas of the cortex may lack a recognizable zona glomerulosa. However in such instances, it is replaced by cells of zona fasciculata that extend out to the capsule **(Johnson, 1992; Junqueira and Carneiro, 2005 & Ross and Pawlina, 2006).**

The cells of this zone have spherical nuclei appear closely packed and stain densely. The chromatin of their nuclei is mainly heterochromatin and each nucleus contains one or two prominent nucleoli. The cells have an acidophilic cytoplasm containing occasional angular basophilic areas **(Gartner and Hiatt, 2001 & Fawcett and Jensh, 2002).**

Gartner and Hiatt, (2001) reported that ultrastructurally, the cells of zona glomerulosa are joined by occasional desmosomes and small gap junctions and some cells have short microvilli. **Standring et al., (2005),** added that the cytoplasm displays abundant smooth endoplasmic reticulum, which is typical of steroid secreting cells.

In contrast, profiles of rER are limited and most ribosomes are free and many of them are arranged as rosettes of polyribosomes. The Golgi complex has stacks of cisternae with small vesicles and the cells have also relatively few small, scattered lipid droplets. The cells also contain large mitochondria