SURGERY OF
ADRENAL GLAND TUMOURS

Essay

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To my Wife

and Karim

بسم الله الرحمن الرحيم

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INTRODUCTION

The surgical treatment of diseases of the adrenal glands has evolved during the past half century during which the endocrinology of the adrenal cortex and medulla were elucidated. In a sense, surgery of the adrenal glands is the treatment of functional and neoplastic disorders of two different organs, the cortex and medulla. The secretory products of the cortex are essential to life and excess secretion of the medulla may be life threatening ***(Thompson, 1982).***

Currently, adrenal operations are done primarily for the treatment of a variety of endocrinopathies caused by tumours or hyperplasias of functionally different cells within the cortex and medulla.

Advances in adrenal surgery occurred as the adrenal cortical hormones and catecholamines were identified and synthesized. The ability to detect their presence in blood and urine by biochemical and immunoassay testing has made the diagnosis of adrenal disorders a practical reality. Furthermore, the operative treatment of functional tumours has been greatly aided by localization techniques such as computed tomography (C.T.), isotope scanning, NMR and selective plasma hormone sampling. In addition, the use of pharmacologic agents to counter the deleterious effects of hormone excess, before operation, has made formerly hazardous procedures safe and almost routine today.

The most common functional adrenal tumours treated today are pheochromocytomas, aldosteronomas and adrenal cortical tumours producing excess cortisol. Less frequently encountered are tumours causing virilization or feminization. In addition, adrenocrotical carcinomas in children and adults and neuroblastomas in children are indications for surgical removal of adrenal glands ***(Thompson and Allo, 1985).***

The aim of this work is the pathological, clinical, diagnostic and operative study of tumours of the adrenal cortex and medulla that are commonly overlooked with review of the most recent advances in the laboratory investigations and the precise localization of adrenal tumours by the different radiographic techniques.

SURGICAL ANATOMY OF THE ADRENAL GLAND

The adrenal glands are two small bodies of a deep yellowish colour, flattened anteroposteriorly and situated one on each side of the median plane, behind the peritoneum along the anteromedial border of the superior pole of each kidney.

They are surrounded by areolar tissue containing a considerable amount of perirenal fat. They are enclosed, together with the kidneys, in the renal fascia but are separated from the kidneys by a layer of loose fibroareolar tissue ***(Warwick and Williams, 1973).*** This fascial relationship permits easy separation of the kidney from the adrenal gland in case of nephrectomy ***(Mc Vay, 1984).*** The normal gland has a plebby, glistening surface with a characteristic golden colour that serves to distinguish it from the surrounding perirenal fat or adjacent pancreatic tissue ***(Cerny, 1977).***

The right adrenal gland is pyramidal in shape and lies at the level of the first lumbar vertebra ***(O'Neal, 1968).*** The left gland is semilunar or crescentic in shape and drapes the medial border of the left kidney above the hilum ***(Last, 1986).*** It is usually larger and extends to a more higher level than the right. Each gland, in the adult, weighs from 3 to 5 gm. and measures about 30 to 50 mm.in height, 30 mm. in breadth and 10 mm. in thickness.

The adrenal gland of the human foetus is 20 times larger than the adult gland relative to body weight. This is due to a large foetal cortex ***(Decker, 1986).***

In a foetus of 2 months, the adrenals are larger than the kidneys. By the end of the 6^{th} month, the kidneys become about twice as larger as the adrenals. At birth, the adrenal gland is about one-third the size of the kidney, while in the adult it is only about one-thirtienth ***(Di George, 1983).*** This change in proportions is not only due to renal growth but also due to involution of the foetal cortex after birth ***(Warwick and Williams, 1973).***

Relationships of the Adrenal Glands

Between the two adrenals are the crura of the diaphragm, the aorta, the coeliac artery, the coeliac ganglia and plexus and the inferior vena cava *(Decker, 1986), Figure 1.* Each gland has an anterior and a posterior surface.

The thin medial border of the right gland is related to the right coeliac ganglion and to the right inferior phrenic artery as the vessel courses superolaterally on the right crus of the diaphragm.

The convex medial border of the left gland is related inferiorly to the left coeliac ganglion and to the left inferior phrenic and left gastric arteries as they ascend on the left crus of the diaphragm ***(Warwick and Williams, 1973).***

The hilum is situated a little inferior to the apex and near the anterior border of the right gland where the right suprarenal vein emerges to join the inferior vena cava, while it is near the lower end of the anterior surface of the left gland where the left suprarenal vein emerges to join the left renal vein.

The gland is displaced by respiratory movements of the diaphragm with the kidney. Short fibrous ligaments fix the right gland to the right crus of diaphragm and to the inferior vena cava and it is further held by the sympathetic nerves. When the right kidney is excessively mobile, the adrenal gland does not descend with the kidney to any great extent ***(O'Neal, 1968).***

Vasculature of the adrenal gland

The adrenal glands have an abundant and variable arterial supply, although generally, the **adrenal arteries** come from 3 main sources: the inferior phrenic artery superiorly, the aorta medially and the renal artery inferiorly ***(Harrison, 1981). Figure 1.*** In addition, branches from the ovarian and internal spermatic artery on the left side and branches from the intercostal arteries on either side are often present ***(Symington, 1969).***

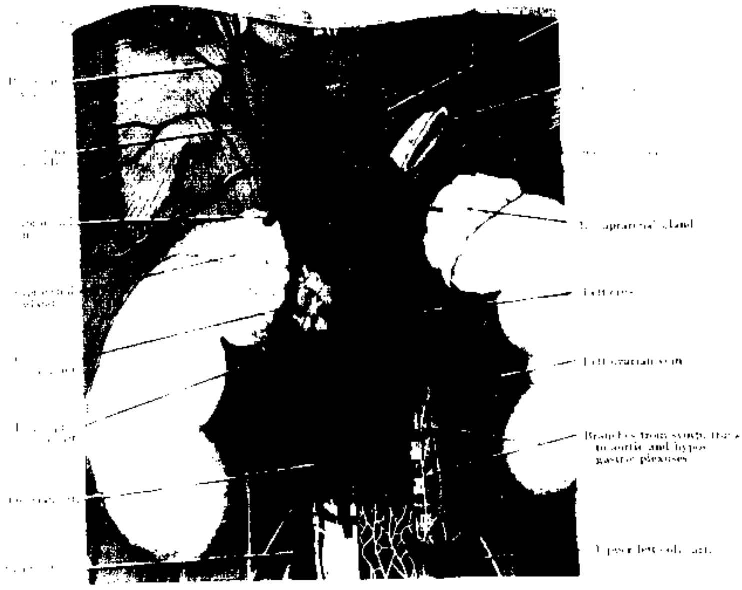

Fig. (1): Relations and Blood Supply of the Adrenal Glands *(After, Jamieson, 1956).*

These arteries form an arcade about the superior, medial and inferior aspects of the gland, from which about 50 to 60 small arterioles penetrate the gland forming an extensive subcapsular plexus ***(Cerny, 1977).*** From this plexus, some branches supply the cortical papillary system and others penetrate the cortex to supply the medulla. The capillary system of the cortex is sinusoidal and the venous sinuses of the medulla are surrounded by musculoelastic tissue, an arrangement that permits rapid release of cortical and medullary products into the central vein and systemic circulation ***(Dobbie and Symington, 1966).*** The blood flow of the normal adrenal in humans is about 10 ml./min. ***(Coupland, 1975).*** With large adrenal tumours this blood flow is magnified many times. It has been assumed that constriction of the adrenal medullary blood supply takes place in trauma to provide a better blood supply to the cortex, and it was found that the blood supply to both medulla and cortex increases under stress; ACTH produces an immediate marked increase in the adrenal blood flow ***(Kramer and Sapirstein, 1967).***

The adrenal veins are more constant; The right vein is short and drains into the inferior vena cava just distal to the hepatic vein, while the left vein is somewhat longer and drains either into the left renal or into the inferior phrenic vein. Occasionally, there may be small accessory veins which drain into the inferior vena cava on the left and renal vein on the right ***(Hume and Harrison, 1974).***

Lymphatic Drainage

The adrenal gland lymphatics form 2 plexuses, one directly under the capsule and the other in the medulla. From the right adrenal, lymphatic drainage is to the para aortic nodes and nodes near the right crus of diaphragm. On the left side, drainage is to nodes at the origin of the left renal artery and para aortic nodes. Lymphatics may accompany any vessel reaching the gland and, for this reason, lymphatic drainage may reach the posterior mediastinum directly along the inferior phrenic artery ***(Decker, 1986).***

Innervation

The adrenal gland has a rich nerve supply, which is predominantly of sympathetic origin and innervates only the medulla, while cortical innervation has not been demonstrated.

Medullary innervation is derived from sympathetic preganglionic fibres arising from the tenth thoracic (T_{10}) to the first lumbar (L_1) ventral rami that pass to the sympathetic ganglia and from which they emerge as the splanchnic nerves. These in turn go to the coeliac, aorticorenal, renal and adrenal ganglia. The post ganglionic fibres penetrate the adrenal and form synaptic endings with the chromaffin cells. Other fibers supply the smooth muscles of the blood vessels *(Cerny, 1977)*.

Histology of the Adrenal Gland

To the nacked eye, a section across the adrenal resembles a sandwich; 2 layers of cortex *(The bread)* enclose a much thinner layer of medulla *(The meat)* between them. In places, there is no medulla and the two layers of cortex then meet each other. The gland is enclosed in a capsule of fibrous connective tissue.

The suprarenal cortex consists of 3 layers or zones:

a. Zona Glomerulosa

Which is a narrow zone immediately under the capsule and consists of oval or rounded groups of columnar cells *(glomeruli)* separated by fenestrated capillaries. The cells have small deeply stained oval nuclei and a basophilic cytoplasm. With the Electron Microscope they have rich smooth endoplasmic reticulum and lysosomes. They secrete mineralocorticoids *(Aldosterone)*.

b. Zona Fasciculata

Which is the intermediate and widest zone, consists of parallel rows of large pale cells lying at right angles to the surface and separated by blood sinusoids. The cells are polyhedral with large vesicular nuclei and their cytoplasm is faintly basophilic and vaculolated being distended with steroid secretion. With the Electron Microscope they show characteristic mitochondria.

They secrete mainly glucocorticoids *(cortisol and others)* and also a little amount of androgens.

c. Zona Reticularis

Which is the narrow inner zone closely applied to the medulla consisting of a network of small polyhedral cells with darkly stained nuclei. These cells secrete mainly sex hormones and very little glucocorticoids ***(Kramer and Sapirstein, 1967).***

The suprarenal medulla is surprisingly small in volume. It constitutes about 10% of the total gland weight. It consists of large polyhedral cells with eccentric nuclei and eosinophilic granules of pre-adrenaline lying in the cytoplasm. The granules are positive to the chromaffin reaction and so called chromaffin cells; they are stained golden brown by chromium salts. Large venous spaces are numerous in the medulla. Under conditions of stress, the post-ganglionic nerve fibres stimulate the chromaffin cells to secrete adrenaline and nor-adrenaline directly into the circulation ***(Last, 1986).***

So, the rich innervation and blood supply of the medulla account for the almost instantaneous release and systemic effects of adrenal catecholamines *(Cerny, 1977)*.

Embryology of the Adrenal Gland

The adrenal cortex and medulla originate separately. The cortex develops from mesodermal elements and the medulla from ectodermal cells of the neural crest ***(O'Neal, 1968)***

The adrenal cortex develops by proliferation of cells derived from the mesoderm of the coelomic mesothelium. Mesothelial buds appear at the level of the upper third of the mesonephron and project into the celom at each side of the root of the dorsal mesentry. Eventually, they coalesce to form a compact mass of cells, the adrenal cortex, lateral to the aorta.

After vascularisation and encapsulation by surrounding mesenchyme, nests of proliferating mesothelial cells under the capsule form the primitive glomerular zone. From these, cords grow centripetally to constitute the foetal cortex which is bulky and responsible for the relatively large size of the suprarenal gland in the new born *(Smith et al., 1984)*. Involution and degeneration of the foetal cortex starts during the last ten weeks of intra-uterine life and is complete by the end of the first year. At term, the permanent cortex forms only about one third to one fourth of the volume of the whole cortex *(Snell, 1981)*. The zona glomeruloza can be identified shortly after birth, the zona fasciculata appears by the third week and the zona reticularis by three to six months of age *(O'Neal, 1968)*.

The cortical buds that do not join the main cellular mass disappear or may be left behind in various locations to form accessory adrenal cortical tissues. These are most commonly found close to the adrenal, within the kidney, in the ovarian pedicle, in the ovary itself, in the broad ligament, in the spermatic cord and in the testis.

The anomalous locations of the adrenal cortex are clinically important for the following reasons:

i. Hyperplasia in the accessory adrenal tissue may produce continued adrenal activity after adrenalectomy for Cushing's syndrome or for metastatic cancer.

ii. Adrenal insufficiency occasionally develops when misplaced normal adrenal glands are inadvertently ablated during nephrectomy.

iii. Neoplastic transformation of hetertopic or accessory adrenal tissue may take place *(Schechter, 1968)*.

The adrenal medulla develops by migration of sympathetic primordial cells (Sympathogonia) from the neural crest where they cluster ventrolateral to the spinal cord to form the sympathetic ganglion primordia and ventrolateral to the aorta to form the preaortic ganglion primordia *(O'Neal, 1968)*. Some of these cells differentiate into chromaffin endocrine cells and penetrate the capsule of the proliferating adrenal cortical primordium from the medial side, thus forming the adrenal medulla *(O'Neal, 1968)*.

The medulla is fully developed by the end of the second year, but remains illdefined until puberty *(Smith et al., 1984)*. Some of the chromaffin endocrine