Surgical Anatomy

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2.1 Hints of Embryology

The adrenal glands were first described in 1552 by the Italian anatomist Bartolomeo Eustachi in his *Opuscula Anatomica* as "glandulae renis incumbentes" (glands lying on the kidney) [1], but their function remained controversial for the next 300 years [2].

The adrenal have a dual origin (Fig. 2.1a, b), i.e. the cortex arises from mesoderm whereas the medulla has a neuroectodermal origin [2]. The cortex develops during the second month of gestation as a proliferation of coelomic mesothelium into the underlying mesenchyme between the root of the dorsal mesogastrium (the root of the mesentery) and the urogenital ridge (the mesonephros and the developing gonad). Here, these cellular proliferations differentiate into large acidophilic organs that form the *fetal* or *primitive cortex* of the adrenal gland [3]. The proliferating tissue extends from the level of the sixth to the 12th thoracic segments and becomes larger than the kidney at midgestation [4]. Shortly afterward, a second wave of cells from the mesothelium penetrates the mesenchyme and surrounds the original acidophilic cell mass; these cells, smaller than those of the first wave, later form the definitive cortex of the gland. The fetal cortex undergoes rapid degeneration during the first 2 weeks after birth, accounts for only one quarter of the cortical at age of 2 months, and has vanished by 1 year. When the proliferation of the coelomic epithelium ceases, the cortex becomes enveloped by a mesodermal capsule, probably derived from the mesonephros.

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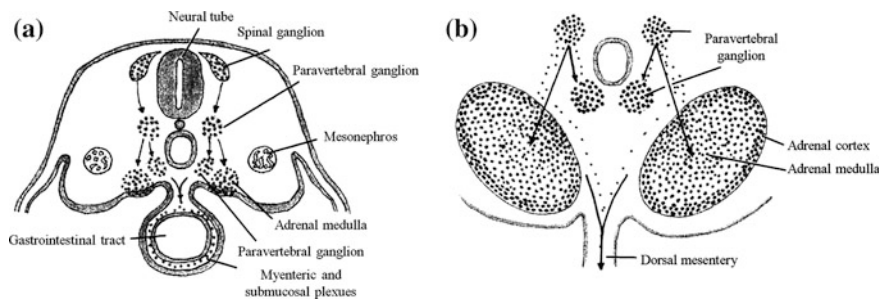e-mail: Carmela.decrea@rm.unicatt.it

Fig. 2.1 **a**, **b** The adrenal have a dual origin, i.e. the cortex arises from mesoderm whereas the medulla has a neuroectodermal origin. The cortex develops during the second month of gestation as a proliferation of coelomic mesothelium into the underlying mesenchyme between the root of the dorsal mesogastrium (the root of the mesentery) and the urogenital ridge (the mesonephros and the developing gonad). Shortly after the genesis of the fetal cortex, the medulla is soon disorganized dorsomedially by an invasion of cells originating in the neural crest to form the medulla of the suprarenal gland

The nests of cortical cells under the capsule are the rudiment of the zona glomerulosa [2]. The fascicular and reticular zones of the adult cortex proliferate from the glomerular zone after birth and are fully differentiated by about the 12th year [4]. Shortly after the genesis of the fetal cortex, the medulla is soon disorganized dorsomedially by an invasion of cells originating in the neural crest to form the medulla of the adrenal gland. During the fourth week of embryonic life, the neural plate develops and then enfolds to form the *neural tube*. A portion of the neuroectoderm adjacent to the tube separates and remains between the neural tube and the definitive ectoderm as the *neural crest*. Its cellular elements migrate throughout the embryo to form a wide variety of organs in adult life: the peripheral sympathetic nervous system, the paraganglionic system, and the adrenal medulla [2]. The embryogenesis of the adrenal medullary cells starts in the second month of gestation. The cells derived from the neural crest (sympathogonia) migrate ventrally from the apex of the neural tube to the dorsal aorta (where they aggregate and differentiate into pheochromoblasts to form chromaffin cells) [5]. Some primitive adrenal medullary cells remain closely associated with the developing sympathetic nervous system and give rise to the extra-adrenal chromaffin cells and chromaffin bodies. Most extra-adrenal chromaffin cells are, therefore, found in the abdominal preaortic sympathetic plexus or in the paravertebral sympathetic chain (places predictable on the basis of the embryonic development) [2]. Extra-adrenal chromaffin cells mature earlier (from 9 to 11 weeks of gestation) in fetal and neonatal life than the sympathetic nervous system or the chromaffin cells of the adrenal medulla; in the fetus increasing catecholamine secretion occurs in response to hypoxia and hypoglycemia [6]. Postnatally, most of the extra-adrenal chromaffin cells begin to degenerate, whereas those of the adrenal medulla complete maturation. The chromaffin reaction is positive by the fifth month of fetal life, but epinephrine is present as early as the third month. The acquisition of an arterial

supply occurs at a very early stage in development, and venous sinuses appear concurrently. Capillaries, which arise from the adjacent mesonephric arteries, penetrate the cortex in a radial manner. The main source is from the aorta and from the vessels to the septum transverse (lateral the central part of the diaphragm) and from the mesonephric arteries. These sources of arterial supply remain in the adult as branches from the aorta, inferior phrenic and renal arteries, which require control during adrenalectomy [2].

Morphologically, the gland, at birth, is about one third the size of the kidney, whereas in the adult, it is only one thirtieth. This change in proportions is due not only to renal growth but also to involution of the fetal cortex after birth, so that by the end of the second postnatal month its weight is only one half that at birth. In the latter half of the second year, the gland begins to increase in size and gradually attains its birth weight at or just before puberty, after which it only increases slightly in weight in adult life [2].

2.2 Surface Anatomy

The adrenal are suprarenal endocrine organs [2, 7], located in the lateral retroperitoneal area and surrounded by perirenal fascia [7], adjacent on either side to the diaphragm's crus and in close contact with the superior pole of the kidney [2]. They lie on each side of the vertebral columns (T11–12) on the superior-medial surface of the corresponding kidney [2]; even if the right kidney is almost always lower than left, because of the presence of the liver, the right adrenal is usually *higher* than the left [8]. The adrenal glands are held in their position by the means of fibrous bands and vascular attachments with the ipsilateral kidney so that an inferior retraction of the kidney involves a consensual adrenal's retraction [2, 9].

Each adrenal gland comprises two embryological and physiologically distinct parts: the cortex, essential to the maintenance of life and producing steroid hormones; and the medulla, synthesizing catecholamine [7]. The cortex is the visible part of the adrenal gland and is distinguished from perirenal fat by its dark yellow or golden color, finely granular surface, and firm consistency [2, 7]. Normally each adrenal gland weights approximately 4–6 g regardless of age, body weight, and gender but may weigh as much as 22 g at autopsy, apparently due to the stress of terminal illness [2, 7, 9, 10], and its average dimensions in adults are approximately 50 mm vertically, 30 mm transversely, and 6–10 mm in the anterior–posterior plane [2, 7]. The prevalence of single or multiple adrenal nodules in the normal adult population is highly variable from 1 to 53.7 %, depending on the different series [11, 12].

Each gland has an anterior and posterior surface and a medial border [2]. The right adrenal gland is triangular or pyramidal in shape [2, 7, 13], with the apex superiorly and the base surrounding the kidney upper pole. It lies anterior to the diaphragm and the right kidney and posterior to the inferior vena cava and the right lobe of the liver. Superiorly, the gland is in contact with the bare area of the liver

to which it is fixed by loose areolar tissue [8]. The right adrenal hilum is on the anterior surface, a little inferior to the apex, and usually a single right adrenal vein emerges from the hilum and empties directly into the posterior part of the inferior vena cava [13]. The left adrenal gland is semilunar in shape [2, 7, 13] and extends inferiorly on medial margin of the kidney. It is in contact anteriorly with the stomach and pancreas and posteriorly with the diaphragm. Unlike the right adrenal gland, the left one is largely covered anteriorly by peritoneum of the lesser sac; moreover, in some cases, in which the reflection of gastrophrenic ligament is medially extended, it is also covered by the posterior peritoneum of the paracolic gutter. A variable small area of the left adrenal gland may lie in immediate contact with the stomach, near the cardioesophageal junction, with no intervening peritoneum [13]. The left adrenal it is more closely related to the kidney than the right, because its main vein drains into the left renal vein, while on the right the main vein fixes the gland high on the inferior vena cava [8].

The adrenal glands have a proper capsule which extends as connective tissue septa containing vessels for the inferior part of the gland. In addition they share with the kidneys a second capsule—the perirenal fascia (Gerota's fascia). A considerable amount of fat lies within the perirenal space between the perirenal fascia of Gerota and the true capsules of the adrenals and the kidneys. Superiorly, the perirenal fascia fuses with the inferior surface of the diaphragm; inferiorly, the perirenal fascia is open and the perirenal fat is fused with that of the iliac fossa. The anterior lamina of the perirenal fascia fades out in the fascia over the aorta, inferior vena cava, and other midline structures; the perirenal space does not extend across to the other side [14]. The inclusion of the adrenal within Gerota's fascia implies the adrenal's dissection within the perirenal fat without compromising the peritoneum or the midline structures [2, 7]. The fascia posterior to the perirenal space is the Zuckerkandl's fascia. Posterior to this lies the posterior pararenal space which does not contain any abdominal organs. The anterior fascia and posterior fascia fuse laterally to form the lateroconal fascia which fuses with the fascia transversalis.

2.3 Blood Supply

The arteries of the adrenals glands are numerous, and run to the glands as multiple fine straight vessels [8]. We can distinguish three distinct sources: the inferior phrenic artery, the aorta, and the renal artery [2, 7–9]. Anson et al. [15] and Busch [16] have described the variations of the adrenal arterial supply. The main point of interest is that the individual arteries are always very small [8]. As the inferior phrenic arteries pass just above and medial to the adrenal glands, each artery usually gives off a series of branches into the gland before it supplies the diaphragm. These arteries constitute the superior adrenal arteries, which enter the upper part of the gland over a considerable extent [2]. The adrenal arterial supply is supported by at least one artery to each gland from the aorta, just above the origin of the renal arteries, or the middle adrenal artery. One or more arteries reach the gland from the adjacent renal artery, and these are the inferior adrenal arteries [2, 9]. In addition to these three

regular sources of blood supply, other vessels running close to the adrenal region may provide further branches to the adrenal gland. Most constant of these are branches from intercostal arteries, the left ovarian or left internal spermatic arteries [2]. The cortex and medulla are vascularized by arterial and venous capillaries. Consequently, blood containing steroid hormones passes through the medulla, which could promote the transformation of norepinephrine into epinephrine [7]. Despite the rich vascularity, the blood flow of the normal adrenal is about 10 ml/min, but the supply to both the medulla and cortex under stress could be promptly increased by means of corticotropin [17].

In contrast to the arteries, the adrenal veins are much more constant [8]. The main venous drainage of the adrenal gland is usually into a single large adrenal (main) vein, leaving the gland through the hilum [2]. The left main vein is much longer than the right [2, 8]. It drains into the left renal vein just at the left margin of the aorta, usually in conjunction with the left inferior phrenic vein. It leaves the anterior surface of the gland in its lower one-third [8]. On the right, the main vein also takes its origin from the anterior surface of the gland, but it does so in the upper one third, frequently from the apex. It is very short and large, and enters the posterior-lateral border of the inferior vena cava. It very frequently drains into the vena cava above the entrance of the lowest hepatic veins, a point of critical surgical importance [2, 8]. On the left side, communication with branches of the portal system through veins about the tail of the pancreas has been observed [18]. The main vein has two to four longitudinal smooth muscle bundles, that presumably constrict the outflow from the gland and may increase the exposure of medullary cells to cortisol [2]. Variations of the adrenal main veins are not common. The variations consist usually of a double main vein, and do not present a great problem during dissection [19, 20].

The adrenal glands are the origin of numerous collecting lymphatic vessels [21] that follow large blood vessels in three pathways. On the right side, a first pathway ends in the right lateral aortic nodes, in front of the right crus of the diaphragm and proximal to the celiac trunk. A second pathway also ends in the right lateral aortic nodes, proximal to the junction between the left renal vein and the vena cava. A third pathway ends in the thoracic duct or in the posterior mediastinal nodes after the lymphatic vessels cross the crura of the diaphragm, which explains the frequent and precocious distant metastases of the adrenocortical carcinoma [7]. On the left side, the first two pathways end in the left lateral aortic nodes proximal to the celiac trunk and left adrenal vein. The third pathway is through the diaphragm, as on the right side. This lymphatic drainage is an image of physiologic and embryologic duality. Lymphatic vessels drain the cortex, not the medulla; indeed corticoids can be found in the thoracic duct [7].

2.4   Innervation

During adrenalectomy, nerves and vessels are ligated simultaneously [2, 22]. The medulla is a neuroendocrine transducer that converts nervous signals in endocrine signals. The adrenal glands are characterized by conspicuous innervations consisting of myelinated cholinergic preganglionic sympathetic fibers, which pass through the hilum and synapse on cells in the medulla [8]. These fibers terminate in synapse with the medulla's cells, which are, therefore, equivalent to postganglionic sympathetic neurons [2]. The cell bodies of the neurons innervating the adrenal medulla originate in the intermediolateral cell column between T3 and L3 [2]. The greater portion of the innervation reaches the adrenals through the ipsilateral greater thoracic splanchnic nerve (T5–9). Efferent parasympathetic axons from the celiac branch of the posterior vagal trunk (through the adjacent celiac ganglion and celiac plexus) also exist [2]. The adrenal cortex receives only a vasomotor nerve supply. Sympathetic axons innervate the subcapsular arteriolar plexus. In addition, zona glomerulosa cells and subcapsular plexus are innervated by axons containing vasoactive intestinal polypeptide and neuropeptide Y. These axons arise and radiate outward from the adrenomedullary cells; their function is unknown, but they may be involved in the paracrine control of steroidogenesis [23, 24].

2.5   Anatomical Variances

The adrenal sometimes may be located away from its usual position, or it may be so united to surrounding structures even when occupying its normal position that difficulties are experienced in its removal. True renal ectopia is rare [8]. Weller [25] reviewed 12 reports of adrenal-renal heterotopia, and added one of his own. In 11 of the 13 cases the condition was bilateral. Donnellan [8] reported, in 1961, a series of 225 autopsies, whereby unilateral inclusion of the left adrenal at the upper pole of the kidney was found in one specimen. Absence of one adrenal due to aplasia or extreme hypoplasia is an even more infrequent finding. In such cases, there is usually a considerable hyperplasia of the remaining gland. Fusion of the adrenals with surrounding structures is much more frequent. From a surgical point of view the fusion of the right adrenal with the liver represents a real challenge for dissection [8].

Instead, the frequency of occurrence of aberrant adrenal tissue has now been fairly well established by careful regional dissection of the various areas where it is known to occur [8]. In a study of adult testicles, Nelson [26] reported ten cases of aberrancy occurring in or near the epididymis. In only one was the nodule of greater than microscopic size [26]. Marchetti [27] found only two microscopic rest of adrenal tissue in the ovaries of 1,200 postmortem cases. The occurrence of macroscopic gonadal aberrancy of adrenal tissue must therefore be relatively evaluated [27]. In Donnellan's study [8], 50 complete retroperitoneal dissections were carried out to verify these findings in a general way. The dissection included the area of the adrenals

and the celiac plexus, the tissues about the gonadal vessels and ureters, and a careful examination of the testicles or ovaries. The findings were 42 % in strands of celiac plexus, 14 % in periadrenal fat, 6 % in spermatic cord and 26 % multiple accessories [8]. Accessory adrenal cortical nodules were found in 29–50 cases, an incidence of 58 %. These accessory adrenals are almost invariably of a similar color to the cortex of the main glands, and are much easier to find when the main adrenals are hyperplastic and rich in lipoid. They are small round or oval structures varying in size from 2 to 8 mm or more, and usually appear as brownish nodules, irregular flecked, with lighter yellow areas. They do not usually contain medulla. Donnellan was able to identify medullary elements in only four of the 53 accessory glands which were found [8]. The importance of accessory adrenals at present is in their capacity for tumor development. This is not frequent, considering the frequency of aberrant adrenal tissue. On the other hand, extra-adrenal medullary tumors, known as para-gangliomas, although rare, are a well-known entity.

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