Aberrant Adrenal Tissue

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IN 1740, Morgagni[22] made passing mention of having noticed yellowish nodules with the characteristics of adrenal tissue in the near vicinity of the gland. Systematic documentation of accessory or heterotopic adrenal structures began 150 years later, when Marchand[16] found deposits juxtaposed to the broad ligament or kidney of some fetuses and infant cadavers. Subsequently, the nodules were observed at various anatomic locations in adults and the young of several species.

Developmental anomalies of the adrenals have commanded increasing attention in recent years because of potential clinical implications. These problems include:

a) *Hyperplasia* of *accessory* adrenal tissue after adrenalectomy for Cushing's syndrome or for metastatic cancer;

b) *Adrenal insufficiency* when heterotopes, that is *misplaced normal* adrenal glands, have been inadvertently ablated during nephrectomy or resection of other organs;

c) *Neoplastic transformation* of *either* heterotopic or accessory adrenal tissue, with or without endocrinopathic manifestations.

This report describes an adrenal cortical mass discovered fortuitously during inguinal herniorrhaphy, and is followed by a brief discussion of adrenal gland anomalies.

Case Report

A 19-year-old Caucasian man, who had been experiencing mild aching sensations in the left groin for several months, underwent uncomplicated repair of an indirect inguinal hernia.

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A 1 mm. × 2 mm. deep yellow mass was embedded at the apex of the sac which had the microscopic appearance and consistency of fat.

Microscopic examination was performed by Dr. David Arbiter. The section revealed a serosal surface with a thick, fibrous sheath surrounded by a fibroadipose zone. Within, a well circumscribed, finely encapsulated island of epithelial tissue was identified. The epithelial cells generally had a cord-like arrangement with a minimal, fine, fibrous stroma, and thin-walled sinusoidal channels lined by endothelium in the interstices. The cells in the outermost portion were slightly vacuolated and grouped in small islands such as in the zona glomerulosa of the adrenal gland. The more central zones revealed a fascicular arrangement with several venous channels in the central regions. No medullary zone was identifiable.

These histologic features are shown in the accompanying figures.

The patient's postoperative course was uneventful without evidence of adrenal insufficiency.

Discussion

Embryologic Development of the Adrenal Gland. The adrenal has a double origin. It really consists of two distinct glands secondarily combined as one within a common capsule. The cortex is derived from coelomic mesodermal epithelium and the medulla from chromaffin ectodermal cells of the neural groove.

Cortical material is first recognizable in the human embryo at the beginning of the fourth week or when it becomes 6 mm. in size. Cells on each side of the mesentery near its root start to proliferate. These ingrowing buds of peritoneal mesothelium separate entirely at the 8 mm. to 12 mm. stage and acquire an independent blood supply. The primordial suprarenals then form a projecting ridge from the dorsal

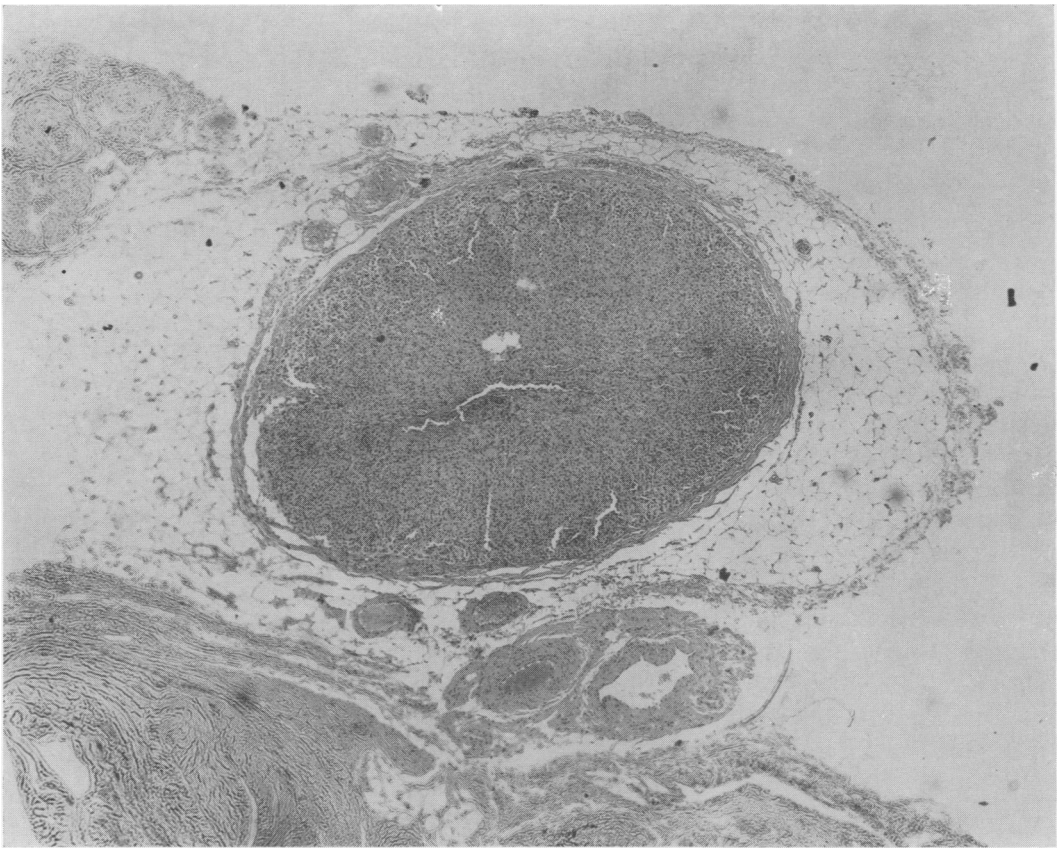

FIG. 1. Encapsulated nodule in adipose tissue external to the hernial sac (35×).

wall of the coelom, between the mesonephros and mesentery.

When the adrenal cortex is already prominent in embryos of 7 weeks or 19 mm. in size, chromaffin cells of the medulla descend toward it from the coeliac plexus of the sympathetic system. They gradually invade the medial side of the cortical primordium along its central vein and thus gain a central position. The conclusion of this penetration as well as the differentiation of the cortex into its three zones do not take place until the end of the 9 month period.

As the medullary elements migrate into the cortical anlage, multiple primordia or secondarily separated fragments of the parent gland may split off, forming accessories. Usually, such accessory glands are composed of cortical substance only. They may remain close to their original position; but others become included in or are dragged along with the genital gland structures which change position during development. In this way accessory adrenals may appear in the pelvis or the scrotum.

In fishes the cortex and medulla occur normally as separate organs. In higher animals there is an increasingly closer association between the two parts until the climax is reached in mammals where the cortex encloses the medulla.

Classification of Adrenal Anomalies. If during development the primordial adrenal does not separate from the coelomic epithelium, it may become partly or

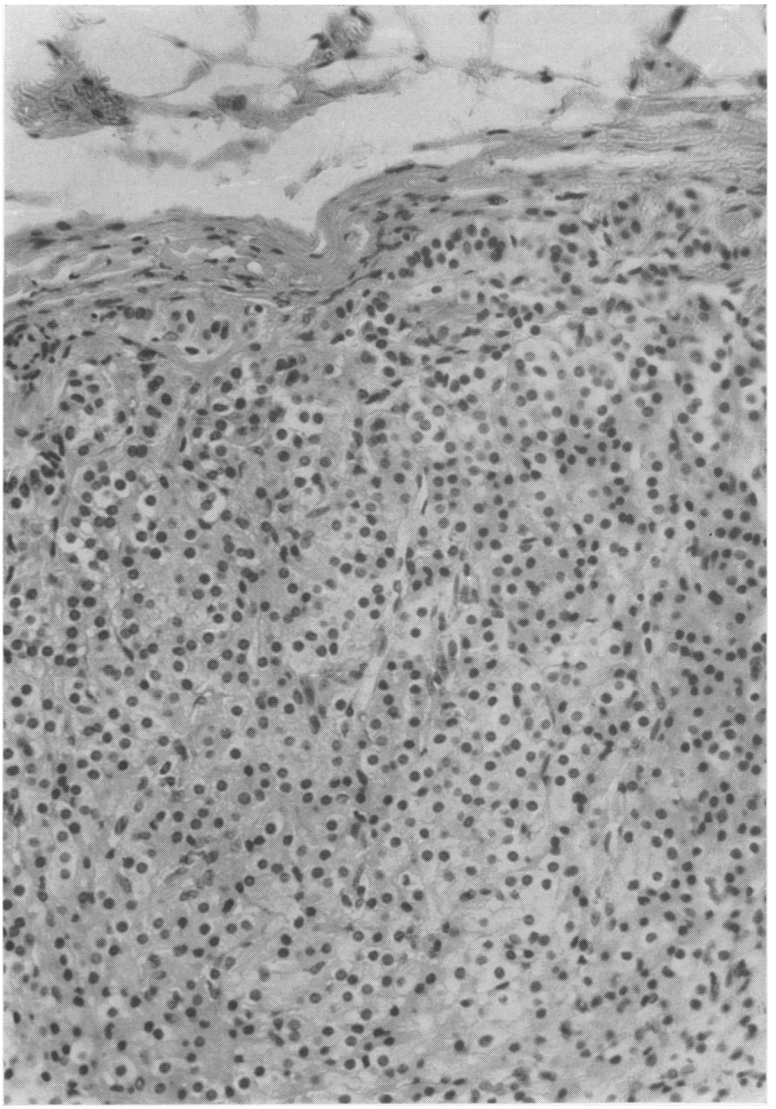

FIG. 2. Adrenal rest, finely encapsulated with well-defined zonae glomerulosa and fasciculata (200×).

wholly incorporated into contiguous organs, such as the kidney or liver. This constitutes true *heterotopia*, which is further subdivided into *complete* or *partial* according to whether none or a portion of the adrenal remains in its normal position.

While fragmentation of the parent gland toward the end of intra-uterine life may also result in displacement or ectopia of adrenal tissue, the latter is distinguished from true heterotopia by being referred to as *accessory* or *quasi-heterotopia*.

Evidently, accessories may exist with no genuine adrenals in their normal position, but this seldom occurs. More often, the accessories either involute entirely in early life or persist through adulthood.

Adrenal cortical rests are said to occur in 50 per cent of newborns and to usually atrophy and disappear within a few years. Accessory tissue found by Wiesel[36] in young persons appeared to be in a stage of regression. Conversely, accessories seem to occur more frequently and to remain longer

in the genital tract of certain lower animals. Lacassagne and Nyka [15] found consistently, in a series of adult male rabbits, a nodule of adrenal cortical tissue in the adipose matter around the posteroinferior portion of the head of the epididymis at the level of the junction of the rete testis and efferent ducts.

Foci of Aberrant Adrenal Tissue. Ordinarily, heterotopic adrenal tissue either clings intimately to or nidates in the immediate neighborhood of the kidney.[4, 23, 27, 34] In the course of 5,000 consecutive autopsies, O'Crowley and Martland [24] found eight instances of either complete or partial adrenal-renal heterotopia. Culp [6] collected 21 cases of true adrenal-renal heterotopia and gave an account of an additional one encountered at postmortem. Rapaport [28] and Mitchell and Angrist [21] provided further examples of this predilection of the anomalous tissue for the kidney.

As might be expected, accessory adrenal masses are distributed erratically. They have been found most often, clinically and in pathologic specimens, in association with pelvic structures, such as the broad ligament, spermatic and ovarian vessels, spermatic cord, ovary, canal of Nuck, and uterus.[3, 9, 18, 25, 31, 33]

Other points of attachment in the abdomen have included the pancreas, transverse colon, appendiceal mesentery, retroperitoneum, coeliac plexus, and capsule of the liver.[11, 18, 23, 34]

Accessory adrenocortical tissue is sometimes scattered in structures around the testis. It has been encountered in the epididymis and tunica albuginea [19, 23, 37] but not deep within the testicular parenchyma. McLennan [17] examined the hernial sacs removed at operation from 700 children, 600 of whom were boys, and found nodules of adrenal tissue implanted in six of them. Stout [32] has uncovered one such mass in a hydrocele, and three in hernia sacs.

Exceptionally, adrenal accessory tissue has been observed at bizarre sites which defy convincing explanation on an embryologic basis. Thus Meyer [19] noted an encapsulated adrenal nodule on the spinal portion of the eleventh cranial nerve and Wiener and Dallgaard [35] an intracranial one.

Because of the distinctive derivations of the cortical and medullary anlage, different adrenal accessories will possess varying proportions of each type of cell. Thus, accessories at a distance from the adrenal gland have uniformly revealed cortical tissue only, while those closer to the gland proper are more likely to be composed also of medullary tissue.[11]

Clinical Implications

The capacity of adrenal accessories to undergo compensatory hypertrophy and function after removal of the normal glands was demonstrated in rats in 1898 by Wiesel.[36] Clinical confirmation of such a mechanism was obtained 8 years later by Karakascheff,[13] who recorded its occurrence in a woman whose adrenals had been destroyed by tuberculosis. Since then, a number of other cases have been published.[9, 29, 30]

It is probable that, because compensatory hyperplasia takes place slowly and progressively, some of the relapses after adrenalectomy for Cushing's syndrome or advanced mammary and prostatic cancer may be due to heightened secretion from that endocrine source.[5, 9, 14] Its presence may be determined by appropriate hormone assays at suitable intervals.[9]

The accidental removal of heterotopic adrenal tissue is most likely to occur during nephrectomy. This catastrophe has occurred on several occasions and the absolute need to identify the anatomical relationship of the adrenal gland to the kidney before the latter is excised is emphasized. David and Kardos [7] gave an account of death from adrenal insufficiency precipitated by resection of liver containing an

adrenal heterotope. Pengelly[26] excised a pheochromocytoma arising from adrenal medullary tissue trapped within the renal capsule.

In 1908, Bovin[2] reported a case of functional tumor arising in an adrenal cortical rest in the broad ligament. There are now many more such neoplasms on record. The majority have been adenomas, some of which have undergone malignant transformation. Others have been carcinomas *ab initio*.[1, 8] These tumors, whether benign or malignant, may on occasion be accompanied by profound endocrine changes reflected in virilization and kindred sequelae of hypercorticalism.[10, 12] Pure *medullary* functional neoplasms of accessory adrenal tissue are extremely rare. It is possible that some of the reported tumors of Zuckerkandl's "organ"[20] are actually in the latter category, being of identical chromaffin origin. It was formerly thought that aberrant adrenal masess were a manifestation of the so-called thymico-lymphatic complex,[34] but this view has since been discounted.

Summary

A case is described of accessory adrenal tissue residing in a hernia sac. This site is rare in adults.

The cortical and medullary constituents of the adrenal gland arise from a dual origin. During fetal development, all or portions of the gland may be transported to adjacent or distant structures. They remain involute ordinarily during early life, but may often persist as functioning tissue throughout adulthood.

Aberrant adrenal nodules are of clinical significance. They may undergo compensatory hypertrophy after adrenalectomy, thereby defeating the purpose for which the operation was intended. Heterotopic implants may be excised inadvertently during unrelated surgical procedures, resulting in adrenal insufficiency. The aberrant masses may themselves become neoplastic, both benign and malignant tumors being at times marked by overt endocrine changes.

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