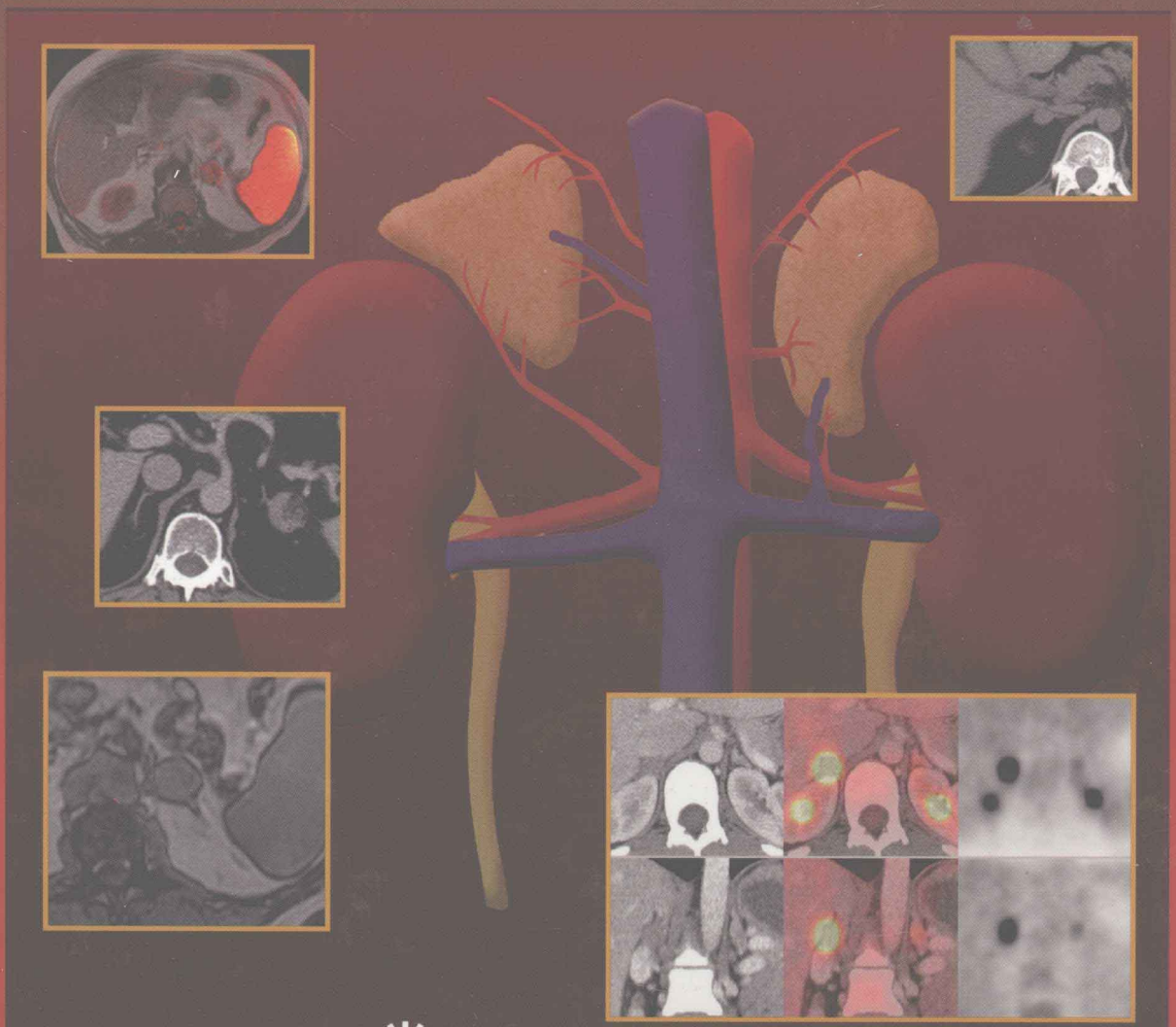
Adrenal Imaging

Edited by

Michael A. Blake, MB, MRCPI, FFR(RCSI), FRCR

Giles W. L. Boland, MD



Humana Press

Adrenal Imaging

Edited by

Michael A. Blake, MD, MBA, FSIR, FACR, FACRO

Cahir M. L. McDonald, MD

Adrenal Imaging

Edited by

Michael A. Blake, MB, BCh
Massachusetts General Hospital, Department of Radiology, Boston, MA, USA

and

Giles W.L. Boland, MD
Massachusetts General Hospital, Department of Radiology, Boston, MA, USA

Humana Press

Editors
Michael A. Blake, MB, BCh
Massachusetts General Hospital
Dept. Radiology
55 Fruit St.
Boston, MA 02114
White Bldg.
USA
mblake2@partners.org

Giles W.L. Boland, MD
Massachusetts General Hospital
Dept. Radiology
55 Fruit St.
Boston, MA 02114
White Bldg.
USA
gboland@partners.org

Series Editor
U. Joseph Schoepf, MD
Department of Radiology
Medical University of South Carolina
Charleston, SC

ISBN: 978-1-934115-86-2 e-ISBN: 978-1-59745-560-2

DOI 10.1007/978-1-59745-560-2

Library of Congress Control Number: 2008940633

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

springer.com

Adrenal Imaging

CONTEMPORARY MEDICAL IMAGING

U. Joseph Schoepf, MD, SERIES EDITOR

Adrenal Imaging, edited by *Michael A. Blake, MB, BCh, and Giles W.L. Boland, MD, 2009*

CT of the Airways, edited by *Phillip M. Boiselle, MD, and David A. Lynch, MB, 2008*

Preface

The small size of the adrenal gland belies its critical importance in medicine. Imaging of the adrenal gland has made tremendous strides in the last decade as new technologies continue to evolve. Consequently, we feel that it is an opportune time to distill, for the first time, the current state of knowledge available concerning imaging of the adrenal gland, into a single volume. In order for this text to offer widespread appeal and for completeness, we also considered it important to solicit current adrenal insights from medical disciplines other than imaging experts. These contributions are designed to be both independent (i.e. can be read on their own) and also be complementary to the remainder of the chapters. To allow this independence, specific information has been re-emphasized across different chapters according to the individual authors' different perspectives. We thus hope that the individual chapters and the complete text will serve as relevant and up-to-date references of adrenal gland imaging for both radiologists and non-radiologists (particularly oncologists, surgeons and endocrinologists), and will be helpful to physicians in practice and in training, and indeed to all interested in the adrenal glands.

We have tried to highlight the pertinent clinical and pathological information that underpins the accurate interpretation and use of adrenal imaging. Established adrenal imaging findings, algorithms and techniques in CT, MR, nuclear medicine, PET and PET/CT, as well as intervention and trauma, are reviewed. We chose to put the adrenal pathology chapter first as it provides a basis for the rest of the book serving as a comprehensive overview of the diseases that can effect the adrenal gland. We chose to place summary sections at the end of each of the other chapters, illuminating their key teaching points to enhance their retention.

We were also very fortunate to have been joined on this project by such a prestigious group of international contributors for whose support we are very grateful. Drs Ronald DeLellis and Sham Mangray give the overview of adrenal embryology and pathology in the first chapter. The pivotal adrenal role in endocrinology is highlighted by both Drs Subbulaxmi Trikudanathan and Robert Dluhy who cover adrenal cortical dysfunction, and also by Dr William Young who writes on adrenal medullary dysfunction. The important adrenal role in oncology from endocrinology, radiation oncology and radiology viewpoints is

supplied by the collaboration of Drs Claire Higham, Peter Trainer, John Coen and Giles Boland. Adrenal surgeons Drs Antonia Stephen, Alex Haynes and Rich Hodin contribute a chapter from the adrenal surgeon's point of view. The imaging of adrenal hyperfunction and pheochromocytoma is then described by Drs Sahdev Anju and Rodney Reznek and Drs Eric Remer and Frank Millar respectively. The team of Drs Mel Korobkin, Mahmoud Al-Hawary and Isaac Francis demonstrate how to use CT to differentiate adrenal adenomas and metastases. Dr Phil Kenney gives an overview of adrenal MRI while Drs Jim Scott and Ted Palmer give their insight into adrenal nuclear medicine. Dr Johannes Roedl discusses with us the still emerging role of PET and PET/CT of the adrenals. Dr Brian Lucey shares his experience with adrenal intervention and trauma. To conclude the book, we look into the future with Dr Nagaraj Holalkere, who highlights new developments in adrenal imaging.

We are very grateful to our world-renowned adrenal experts whose contributions have made this a practical, well-illustrated, and authoritative text. We are most thankful to Springer and Humana for giving us this opportunity and for all their support and, in particular, to Yana Mermel and Paul Dolgert.

Boston, USA

Michael A. Blake
Giles W.L. Boland

Contributors

Mahmoud M. Al-Hawary, MD, Department of Radiology, University of Michigan Hospitals, Ann Arbor, Michigan

Michael A. Blake, MB, BCh, BAO, MRCPI, BSc, FRCR, FFR (RCSI), Division of Abdominal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital, Boston, MA

Giles W.L. Boland, MD, Division of Abdominal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital, Boston, MA

John J. Coen, MD, Department of Radiation Oncology, Massachusetts General Hospital Boston, MA

Ronald A. DeLellis, MD, Department of Pathology, Rhode Island Hospital and The Miriam Hospital, The Warren Alpert Medical School of Brown University, Providence, R.I.

Robert G. Dluhy, MD, Endocrine-Hypertension Division, Brigham and Women's Hospital, Boston, MA

Isaac R. Francis, MD, Department of Radiology, University of Michigan Hospitals, Ann Arbor, Michigan

Alex B. Haynes, MD, Division of General Surgery, Massachusetts General Hospital, Boston, MA

Claire E. Higham, DPhil, Department of Endocrinology, Christie Hospital, Manchester, UK

Richard A. Hodin, MD, Division of General Surgery, Massachusetts General Hospital, Boston, MA

Nagaraj Setty Holalkere, MD, DNB, Department of Radiology, Boston Medical Centre, Boston, MA

Philip J. Kenney, MD, Department of Diagnostic Radiology, University of Alabama at Birmingham, Birmingham, AL

Melvyn Korobkin, MD, Department of Radiology, University of Michigan Hospitals, Ann Arbor, Michigan

Brian C. Lucey, MB, BCh, BAO, MRCPI, FFR (RCSI), Department of Radiology, VA Healthcare System, West Roxbury, MA

Shamlal Mangray, MB, BS, Department of Pathology, Rhode Island Hospital and The Miriam Hospital, The Warren Alpert Medical School of Brown University, Providence, R.I.

Frank H. Miller, MD, Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL

Edwin L. Palmer III, MD, Division of Nuclear Medicine, Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts

Erick M. Remer, MD, Section of Abdominal Imaging, Division of Diagnostic Radiology, Cleveland Clinic, Cleveland, OH

Rodney H. Reznek FRANZCR (Hon), FRCP, FRCR, Cancer Imaging, Institute of Cancer, St Bartholomew's Hospital, West Smithfield, London, UK

Johannes B. Roedl, MD, Department of Radiology, Massachusetts General Hospital, Boston, MA

Anju Sahdev, MB, BS, MRCP, FRCR, Department of Diagnostic Imaging, St Bartholomew's Hospital, West Smithfield, London, UK

James A. Scott, MD, Division of Nuclear Medicine, Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts

Antonia E. Stephen, MD, Division of Surgical Oncology, Massachusetts General Hospital Cancer Center, Boston, MA

Peter J. Trainer, MD, FRCP, Department of Endocrinology, Christie Hospital, Manchester, UK

Subbulaxmi Trikudanathan, MD, Department of Medicine, St Elizabeth's Medical Center, Boston, Massachusetts

William F. Young Jr, MD, Division of Endocrinology, Diabetes, Metabolism, Nutrition and Internal Medicine, Mayo Clinic Rochester, Rochester, MN

Contents

Adrenal Embryology and Pathology

1

Shamlal Mangray and Ronald A. DeLellis

Contents

S. Mangray (✉)
Attending Pathologist, Rhode Island Hospital and The Miriam Hospital, The Warren Alpert Medical School of Brown University, Providence, R.I. 02903
E-mail: SMangray@Lifespan.org

Introduction

The adrenal glands are composite endocrine organs consisting of the steroid hormone producing cortex and the catecholamine synthesizing medulla. Each of these compartments can give rise to a variety of proliferative lesions that can be visualized by computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET). The increased use of these modalities has demonstrated the presence of varying sized mass lesions in up to 5% of individuals subjected to CT studies for reasons unrelated to adrenal dysfunction [1]. Most of these incidentally discovered lesions (incidentalomas) are asymptomatic and the vast majority are of cortical origin.

The specific goals of this chapter are to provide an overview of the anatomy and development of the adrenal glands together with a review of the pathological features of a variety of adrenal abnormalities presenting as mass lesions with or without endocrine hyperfunction. In addition, this chapter will review adrenal abnormalities associated with hypofunctional states.

Embryology and Developmental Disorders of the Adrenal Glands

The adrenal glands have a dual embryological origin with the cortex being derived from the celomic mesoderm of the urogenital ridge and the medulla arising

M.A. Blake, G. Boland (eds.), *Adrenal Imaging*, DOI 10.1007/978-1-59745-560-2_1,

from the neural crest [2]. In the 5th week of gestation (9-mm embryo stage), mesothelial cells from the posterior abdominal wall, between the root of the bowel mesentery and developing mesonephros/gonad (urogenital ridge), proliferate and form the primitive cortex of the adrenal gland [3]. In the 6th week, a second wave of mesothelial cells surrounds the primitive cortex. By 8 weeks, the cortical cells separate from the mesothelium and become surrounded by a fibrous capsule. In the fetus, the cortex is divisible into a broad inner zone composed of large eosinophilic cells (provisional zone or fetal cortex) and an outer zone that is destined to become the adult (definitive) cortex. The major secretory product of the fetal cortex is dehydroepiandrosterone sulfate, reflecting its importance in the development of the genital system during gestation, whereas the cells of the adult cortex produce cortisol, aldosterone and sex steroids.

The combined weight of the glands at birth is approximately 10 g, with 75% of the cortical volume represented by fetal cortex. At this time the adrenal glands are 10–20 times larger than adult glands relative to body weight and approximately one third the size of the neonatal kidney. Shortly thereafter, a series of involutional changes occurs associated with an approximate 50% reduction in the gland weight [3, 4]. Much of the fetal cortex involutes while the permanent cortex proliferates toward the center of the gland. As a result, the fetal cortex accounts for 20% of cortical volume by the 12th postgestational week.

The intra- and extra-adrenal paraganglia and the sympathetic nervous system are intimately associated during embryonic development and arise from the neural crest. The cortical anlage is invaded on its medial aspect by primitive sympathetic cells and nerve fibers that originate from the contiguous prevertebral and paravertebral sympathetic tissue in the 14-mm embryo (about 7 weeks of gestation). Some primitive sympathetic cells, however, may penetrate the anlage without associated nerve fibers [5, 6]. The primitive sympathetic cells are first apparent as nodular aggregates in the cortex, where they may form rosettes or pseudorosettes. Chromaffin cells (mature medullary cells) are identifiable among the primitive sympathetic cells between the 27- and 33-mm stages and gradually increase in number. The nodules of primitive sympathetic cells peak in number and size between 17 and 20 weeks and then decline. Groups of primitive cells may, however, persist until birth and may also be apparent in early infancy (see section on neuroblastoma). In the fetus, the extraadrenal chromaffin cells account for most of the chromaffin tissue and are most prominent in the organ of Zuckerkandl in the region proximal to the aortic bifurcation, where they are identifiable grossly [7]. There is a progressive involution of the extra-adrenal chromaffin cells while the medullary chromaffin cells reach maximum volume at birth.

The eventual shape of the adrenal glands is affected by the development of the kidneys and gonads. The gonadal component of the urogenital ridge is located medial to the mesonephros. The gonads descend caudally, the mesonephros becomes largely involuted and the kidneys are derived predominantly from the metanephros of the pelvis migrating cephalad to lie eventually inferolateral to the adrenal glands [2, 3]. The ultimate pyramidal or crescent shape of the adrenal glands is dependent on the normal development and migration of the kidneys as is demonstrated by the flattened appearance of the adrenal glands in cases of renal agenesis.

The most common congenital anomaly of the adrenal is *heterotopia* [8]. Although the term "heterotopia" is commonly used for this condition, a more accurate description is *accessory* adrenal tissue since in most cases orthotopic adrenal gland is also present. Most accessory adrenals consist exclusively of cortical tissue, but a few examples, particularly those in the region of the celiac ganglion, may also contain medulla [7]. Accessory adrenal cortex is most frequently found in the retroperitoneal space along the course of the urogenital ridges. In addition, accessory adrenal tissue may also be discovered incidentally just beneath the renal capsule in the upper pole, at the hilar regions of the ovaries and testes, and along the course of the spermatic cord. The studies of MacLennan [9] have shown that adrenal cortical tissue is present in approximately 1% of inguinal hernia sacs from children undergoing inguinal herniorrhaphy. Rare sites of accessory adrenal tissue include pancreas, spleen, liver, mesentery, lung and brain. Accessory adrenals may undergo hyperplasia in response to increased levels of ACTH and may serve as the site of origin of cortical neoplasms [7, 10]. True heterotopic adrenals may be fused with the liver or kidney and are typically surrounded by a common connective tissue capsule [11, 12].

Adrenal *union (fusion)* and adhesion are rare anomalies that are distinguished respectively by the presence (adrenal union) or absence (adhesion) of a connective tissue capsule. Fusion is occasionally associated with midline congenital defects, including spinal dysraphism, indeterminate visceral situs, and the Cornelia de Lange syndrome [7]. Fusion of the adrenals can occur in patients with bilateral renal agenesis.

Aplasia of the adrenals has been reported in association with anencephaly; however, in most instances, the adrenals are markedly hypoplastic rather than completely absent. In approximately 10% of patients with unilateral renal agenesis, the ipsilateral adrenal is also absent. Several types of adrenal hypoplasia have been reported. Affected infants typically show signs and symptoms of adrenal insufficiency. In so-called primary hypoplasia, the adult cortex is markedly hypoplastic, but the fetal zone is retained and often demonstrates cytomegalic features [12]. This disorder has an X-linked pattern of inheritance and is associated with mutations or deletions of the DAX-1 gene (Xp21) [13, 14]. The miniature adult type of hypoplasia may appear sporadically or as an inherited abnormality with an autosomal recessive pattern of inheritance. The adrenals have a normal architecture despite their small size.

Gross and Microscopic Anatomy of the Adrenal Glands

In the normal adult, each gland weighs between 4 and 5 g, although greater weights have been recorded in hospitalized patients dying after prolonged illnesses presumably due to prolonged stimulation by endogenous ACTH [7]. Adrenals from patients treated with prolonged corticosteroid administration, on the other hand, are atrophic. Each normal adrenal measures approximately 5 × 3 × 1 cm. The right gland has a roughly pyramidal shape, while the left gland has a crescent shape (Fig. 1.1). The glands have a tripartite structure that consists of head (medial), body (middle), and tail (lateral) portions [7]. The central vein emerges from the ventral aspect of the gland at the junction of the head and body (Fig. 1.1B). Within the gland itself, the muscle bundles of the central vein are eccentric and are oriented toward the medulla.

In the fresh state, the outer cortex is bright yellow, while the inner cortical zone is brown to tan. The cortex measures approximately 1 mm in thickness in adults and comprises approximately 90% of the total glandular weight. It consists of the glomerulosa, fasciculata, and reticularis zones [6]. The glomerulosa comprises up to 15% of the cortical volume and is composed of relatively small lipid-poor cells (Fig. 1.2A), which synthesize mineralocorticoids. Since this layer is often incomplete, the fasciculata may abut the capsule of the gland directly. The fasciculata is composed of columns of lipid-rich cells, which synthesize both glucocorticoids and sex steroids. This zone occupies 70%–80% of the cortical volume. Stimulation of the adrenal by adrenocorticotropic hormone (ACTH) leads to depletion of lipid stores from the fasciculata [12]. The remainder of the cortex is composed of the reticularis, which is capable of synthesis of both glucocorticoids and sex steroids. These cells are characterized by eosinophilic cytoplasm, scanty lipid vacuoles, and prominent deposits of lipochrome pigment, which are responsible for the brown color of the reticularis. Adrenal cortical cells demonstrate positive immunohistochemical staining with antibodies to the intermediate filament proteins vimentin and cytokeratin, and the steroid cell markers inhibin and calretinin. In addition, cortical cells are positive with the monoclonal antibody, A103 (*melan-A*).

On microscopic examination cortical extrusions are found frequently in association with the adrenal glands of adults. They are characterized by the presence of nodular groups of cortical cells that extend into the peri-adrenal fat. Typically, they are attached to the adjacent cortex by a small pedicle and are surrounded by a fibrous capsule; however, they may be completely separated from the gland in some instances.

In the adult, the adrenal medulla occupies 8%–10% of the gland volume and has an average weight of 0.44 g [7]. The major portion of the medulla lies within the head of the gland (*medial*), while the body of the gland contains medullary cells within its crest and usually within one alar region [7]. The average corticomedullary ratio is 5:1 in the head of the gland and 14.7:1 in the body. The tail (*lateral*) of the adrenal does not normally contain medullary tissue. An understanding of the normal distribution of the medulla is essential for the recognition of the early phase of adrenal medullary hyperplasia.

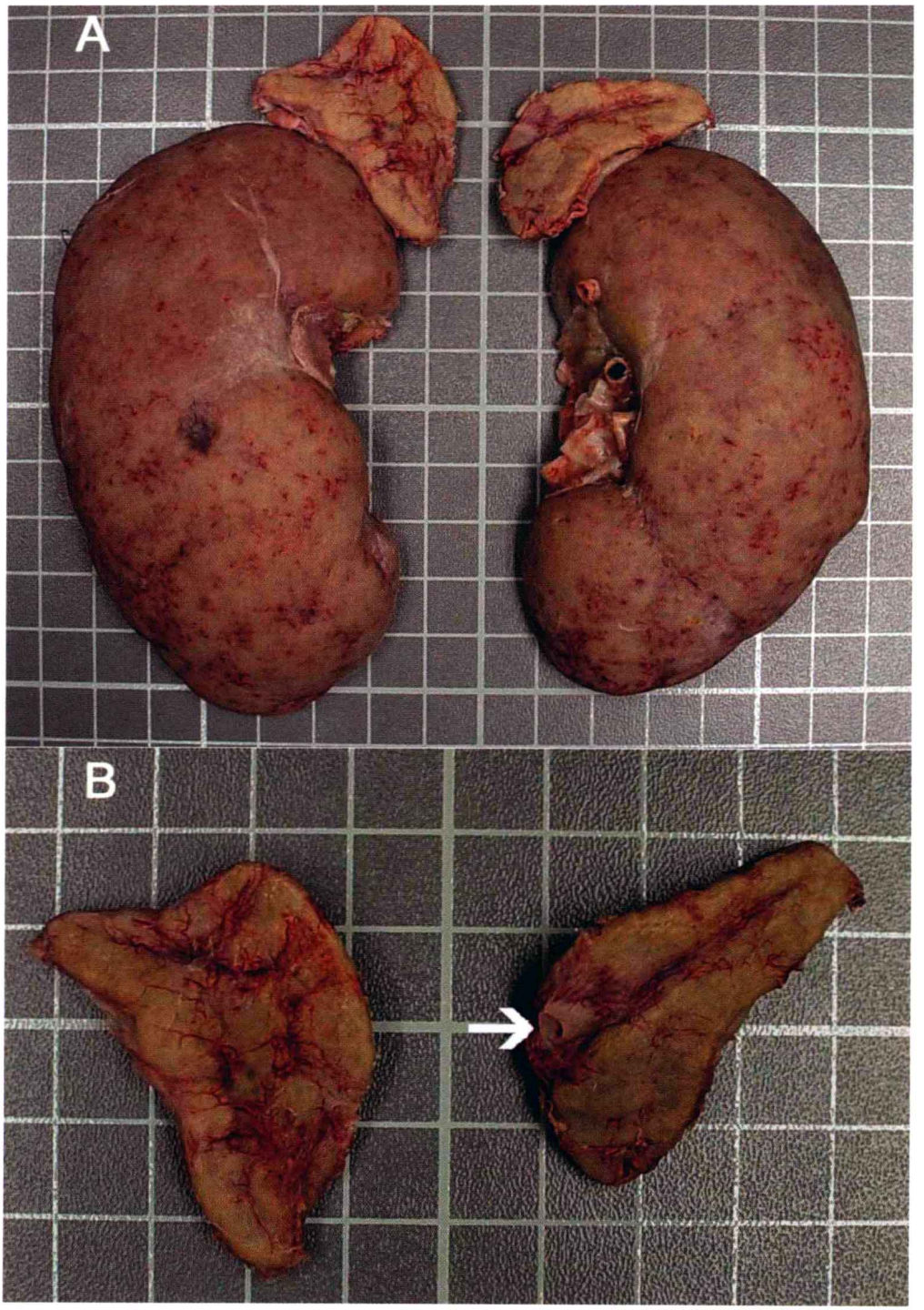


Fig. 1.1 Normal relationship of adrenals to kidneys (autopsy specimen). The adrenal glands are located superiorly and medially to the kidneys (A). Close up view of the adrenal glands with the head located medially and tail located laterally (B). The adrenal central vein is easily seen in the left gland (*arrow*)

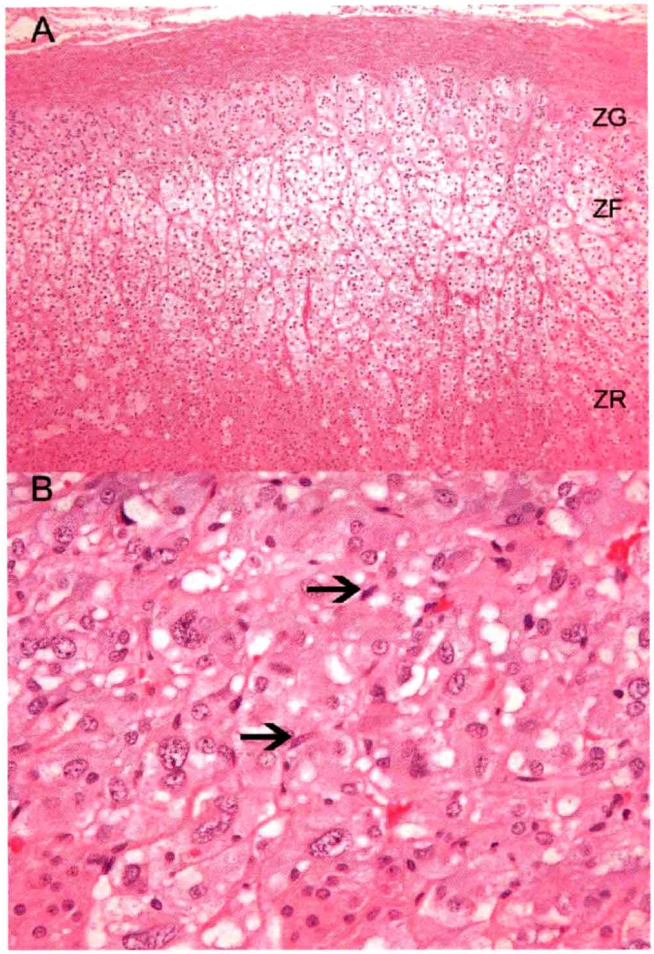


Fig. 1.2 Microscopic section demonstrating the layers of the adrenal cortex. The *zona glomerulosa* (ZG) is present just beneath the capsule, the clear cell containing *zona fasciculata* (ZF) occupies an intermediate position and the *zona reticularis* (ZR) is present in the lowest portion of the figure (A). The medulla (B) is composed of large cells with basophilic cytoplasm and large nuclei that demonstrate variation in size and shape. Sustentacular cells have spindle shaped nuclei (*arrows*). A few cells from the *zona reticularis* are present in the lowest portion of the field

Medullary cells are typically arranged in small nests and cords that are separated by a rich capillary network (Fig. 1.2B). A few ganglion cells are present within the medulla either as single cells or small cell clusters. Sustentacular *or supporting* cells are present at the peripheries of the medullary cords and nests and are also evident around the ganglion cells. In current pathology practice, immunohistochemical stains can be used to demonstrate the component cells of the adrenal medulla. The most commonly utilized antibodies are the neuroendocrine markers chromogranin and synaptophysin that stain the cytoplasm of the medullary cells while the S-100 protein antibody stains the sustentacular cells.

The medulla contains both norepinephrine and epinephrine in addition to their biosynthetic intermediaries. The major catecholamine product of the medulla is epinephrine, which affects the activities of a wide variety of cells and tissues following its interactions with specific receptors. The extra-adrenal sympathetic paraganglia are identical morphologically and histochemically to the adrenal medulla.

Hyperplastic Disorders

Cortical Hyperplasia

Hyperplasia of the adrenal cortex, which represents an increased cortical mass resulting from stimulation of the cortex by ACTH derived from the pituitary or from a variety of extrapituitary sources, can be associated with a wide variety of clinical syndromes. Cortical hyperplasia can also selectively involve the zona glomerulosa in patients with idiopathic hyperaldosteronism.