Adrenal Glands

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29.1 General Information

The adrenal glands (glandula suprarenalis, glandula adrenalis) are paired organs. Their function is to produce vital hormones in humans and other mammals as well as reptiles and birds. They partake in the structural organisation that releases hormone secretion.

Adrenal gland diseases interfere with a normally functioning system by forming autonomic areas of independent hormone production. Resulting in cellular proliferation, which leads to the formation of tumours.

29.2 Anatomy

Normal adrenal glands are located anteromedial and cranial to the superior renal pole in the perirenal fascia. The right adrenal gland is posterior to the inferior vena cava and presents a V-shape, whereas the left adrenal gland is posterolateral to the aorta and presents a Y-shape (Fig. 29.1). The limbs of the adrenal glands are ca. 2–3 cm long and their thickness measures 6–8 mm. In craniocaudal view, size varies between 4–5 cm. The weight of a normal adrenal gland is 5–15 g. They are surrounded by an adipose capsule and renal fascia. Knowledge of specified measurements and outer contours is important for diagnosis and assessment of the adrenal glands. Each adrenal gland has two distinct areas, the cortex and the medulla.

The adrenal cortex comprises three zones:

- **Outer zone (zona glomerulosa) produces aldosterone**
- **Middle zone (zona fasciculata) produces glucocorticoids**
- **Inner zone (zona reticularis) produces androgens**

The medulla is comprised of two zones that originally derive from the suprarenal ridge and differentiate along two lines: chromaffin cells, which produce epinephrine, and autonomic ganglion cells.

29.3 Imaging Techniques

Ultrasonography

The adrenal glands are relatively large in infancy and are therefore easy to identify via sonography on both sides. Sonographic images of the adrenal glands in adulthood may be difficult on account of, for example, intestinal gas. Therefore, masses often become detectable only after reaching a size of > 2 cm.

Computed Tomography

CT is the imaging technique of choice. It not only produces high-resolution images of the adrenals but may also facilitate puncture in unclear cases. Thin-section tomography (0.5–1.25 mm) is used when assessing the adrenals alone; its narrow collimation also serves as a basis for multiplanar reconstructions. An examination can be performed with thicker sections for larger adrenal tumors. In the suspicion of pheochromocytoma, the entire retroperitoneum (at least up to the aortic bifurcation) is commonly examined as well.

Special preparation for CT examination is only necessary when an "active" pheochromocytoma is known or suspected. In such cases, a blockade of alpha- and beta-adrenergic receptors should be given prior to contrast agent administration in order to prevent hypertensive crisis. Recent studies reveal that injection of a nonionic contrast agent greatly or even entirely reduces the chance of hypertensive crisis.

Magnetic Resonance Tomography

MR imaging is used to characterise adrenal gland lesions and to localise extra-adrenal pheochromocytoma. It is frequently used for planning the surgical treatment of patients with reported allergic reaction to contrast material or other contrast-related reactions.

For MRI a body array coil with high-resolution technique is used with a slice thickness of < 5 mm. T1W and T2W pulse sequences are used which, as a general rule today are performed as gradient echo sequences and/or turbo spin echo sequences.

In-phase and out-of-phase sequences are used with highly sensitive chemical shift MR imaging for the characterisation of adrenal masses. Water and fat ideally shift at 180°. Sequences

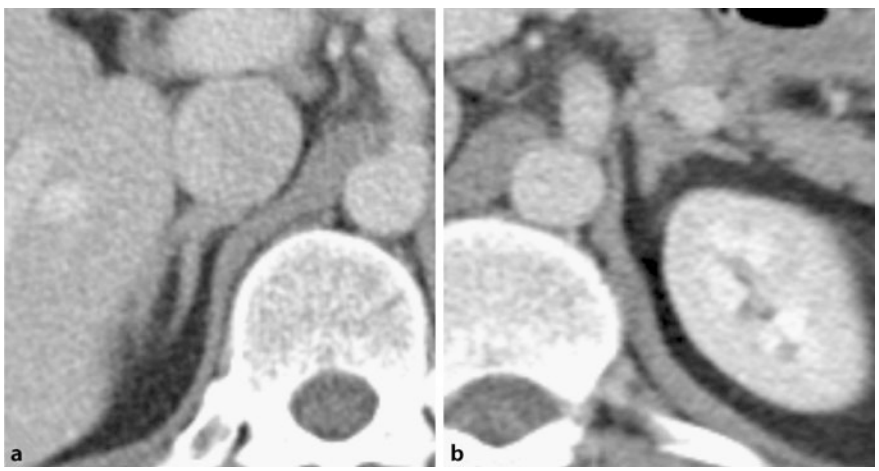

Fig. 29.1 Adrenal gland, normal findings. Normal presentation of both adrenal glands in CT (portal venous phase). Typical V-configuration of the right (**a**) and Y-configuration of the left (**b**) adrenal glands

with spectral fat saturation and dynamic T1-weighted contrast-enhanced sequences are used for further classification.

Nuclear Medicine Techniques

Among nuclear medicine techniques, MIBG scintigraphy and sometimes PET and PET/CT are useful for the diagnosis of pheochromocytoma and suspicion of malignant tumours.

MIBG scintigraphy uses ^{i}radiolabelled metaidobenzylguanidine, which is a norepinephrine analogue. PET and PET/CT imaging predominately uses the tracer ^{18}F-FDG; other tracers like, e.g., ^{18}F-DOPA are seldom used. Due to expenditure in time for patients and staff as well as high costs, this diagnostic technique is only used for selected cases.

29.4 Adrenal Diseases

29.4.1 Benign Lesions and Adrenal Diseases

Adrenal Cysts

Epidemiology, Pathogenesis and Clinic

Cysts of the adrenal gland are rare. They are generally of lymphangiomatous origin and their dimensions tend to be small and asymptomatic. Seven percent of adrenal cysts may be parasitic.

Imaging

Cysts exhibit usual characteristics with dorsal sound amplification in ultrasonography and a noticeably hypodense appearance in CT. Density values in CT reveal watery fluid and possible wall calcifications. In MR tomography, simple cysts have a significantly hypointense signal in T1-weighted images and a hyperintense signal in T2-weighted images. Hence, the differentiation and diagnosis of a simple adrenal cyst may be easy as long as typical patterns are present (Fig. 29.2).

Treatment

Cysts that exhibit a thickened wall with enhanced visual uptake or internal septation, are known as complicated cysts and the suspicion of premalignancy or malignancy cannot be ruled out. Therefore, complicated adrenal cysts should be removed.

Myelolipoma

Definition and Pathology

Myelolipoma is a benign adrenal tumour that does not produce hormones. It is mostly asymptomatic and commonly detected incidentally in cross-sectional imaging. Pathologic features typically show myelolipoma as unilateral, well-localised masses of mature fat interspersed with haematopoietic elements.

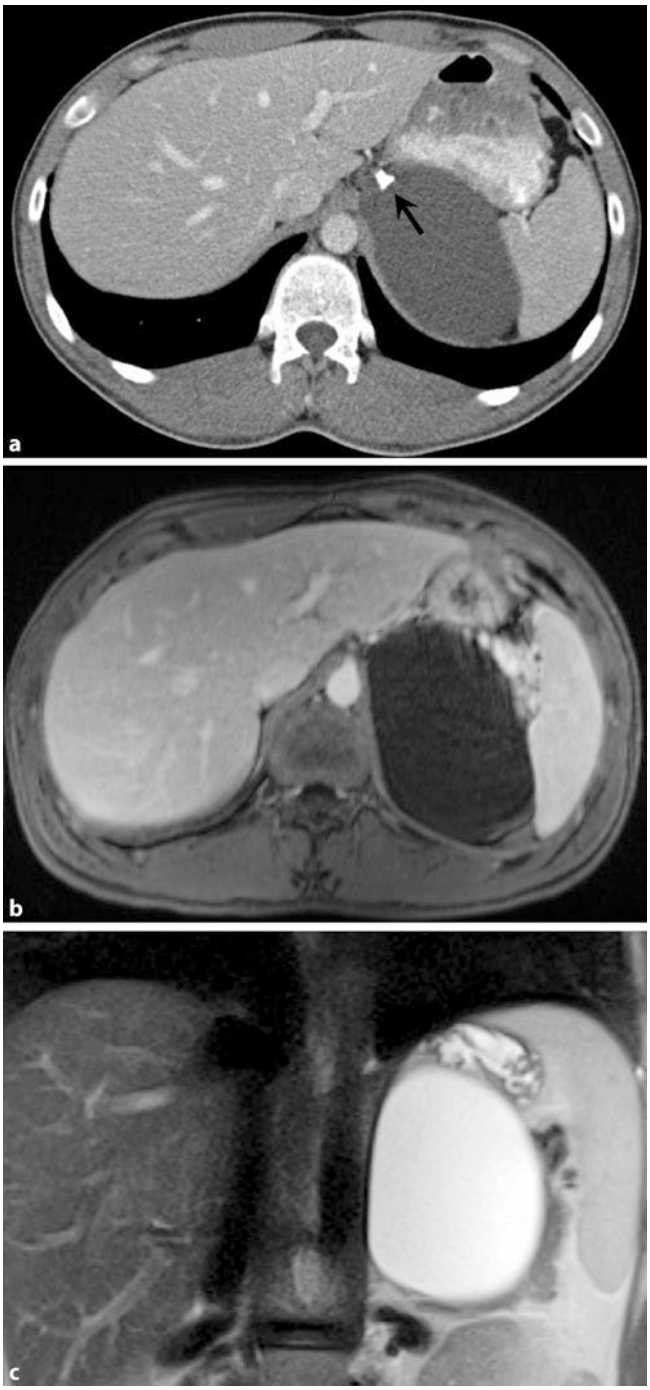

Fig. 29.2 Adrenal cysts. Image of a mass in the area of the left adrenal gland. **a** In CT the lesion appears hypodense, and **b** hypointense in fat-supplemented T1W images following administration of contrast agent. **c** In T2W images it appears noticeably hyperintense in the form of a cyst. Following administration of contrast agent, neither CT nor MR imaging reveals uptake in the thin wall. In CT, detection of localised wall calcification (arrow, **a**)

Imaging

On account of their fatty composition, myelolipomas appear in **CT** as hypodense and vary according to specific tumour composition (−30 to −90 HU).

In T1W **MR** images, fat content is hyperintense. Depending on haematopoietic content, a haemorrhagic cyst may be difficult to discern. In such cases, the fatty component is hyperintense on T1W images and hyperintense on T2W images depending on blood content (haemosiderosis). The successful diagnosis of fatty lesions generally occurs via fat suppression or chemical shift sequences which, compared to normal sequences, demonstrate a significant decrease in signal intensity.

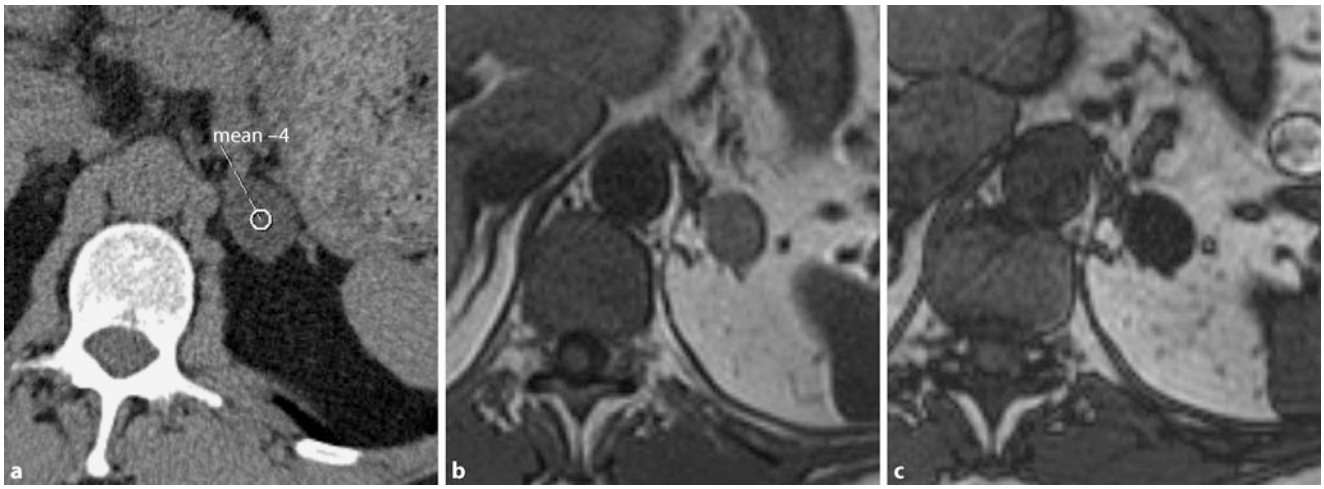

Fig. 29.3 Incidentaloma (here: adenoma). Mass detected by coincidence near the left adrenal gland displaying incidentaloma attributes. **a** Lesion reveals low-density values in unenhanced CT. **b, c** Suspicion of adenoma confirmed during T1W in- and out-of-phase gradient echo sequence. The high signal intensity shows the simultaneous occurrence of fat and water within a single voxel (chemical shift)

Retroperitoneal lipoma, liposarcoma or teratoma must be diagnostically differentiated from one another. In addition, differentiation from angiomyolipoma of the kidneys can be problematic.

Treatment

Because myelolipomas are benign masses with a tendency to degenerate, therapy is generally unnecessary.

Incidentaloma

Definition, Epidemiology, Pathology

As the term indicates, incidentaloma is an asymptomatic adrenal tumour found by coincidence via imaging techniques. Most cases involve small (< 2 cm) hormonally inactive adenomas found in 2–8% of all autopsies. The chances of incidentaloma are elevated in patients with diabetes (ca. 16%) and hypertension (ca. 12%). Frequent pathological evidence directs us to approach these adenomas as clinically irrelevant, as they are generally inactive or produce undetectable hormonal precursors. This can be difficult in cases involving oncology patients, as clinical outcomes rely solely on the course of time.

Imaging

Computer tomography and sonography most frequently detect abdominal incidentalomas by coincidence. Lesions often exhibit a noticeable fat content and therefore appear hypodense in unenhanced CT. MRI may be recommended for further differentiation (Fig. 29.3).

Treatment

Therapy is generally unnecessary for coincidentally discovered, hormonally inactive adrenal adenomas (so-called incidentalomas).

29.4.2 Endocrine Diseases

Conn's Syndrome

Conn's syndrome is characterised by excessive secretion of aldosterone and hypokalemic hypertension. Unilateral adrenal adenoma is present in 70% of all cases; 30% of cases may be caused by bilateral idiopathic adrenal hyperplasia.

Diagnosis, Imaging

The morphological appearance of adenoma in CT is frequently < 2 cm and slightly hypodense. The detection of cortical hyperplasia is difficult with imaging techniques but does work best with CT. The most decisive diagnostic method is to measure the hormone levels in selective blood samples from the renal veins.

Addison's Disease

Counter to Conn's syndrome, hypoadrenalism occurs when the adrenal cortex fails to produce sufficient hormones, as seen in Addison's disease or within the framework of congenital adrenal hyperplasia. Addison's disease arises from an insufficiency caused by a damaged adrenal cortex (primary adrenal insufficiency) or an insufficiency of the pituitary gland (secondary and tertiary adrenal insufficiency). Primary adrenal insufficiency is mostly caused by infection of autoimmune nature, haemorrhages, tumours, amyloidosis, etc. A mass in the pituitary gland is commonly the cause of pituitary insufficiency.

Clinic, Diagnosis, and Treatment

Characteristic chronic symptoms include but are not limited to fatigue, exhaustion, and anorexia; the clinical course is seldom acute (Addisonian crisis). John. F. Kennedy, for example, suffered from Addison's disease and underwent corresponding cortisone treatments.

Medical imaging plays only a small role in the diagnosis of adrenocortical insufficiency. Enlarged or seemingly hypodense adrenals are recognisable in CT only in the event of an insuffi-

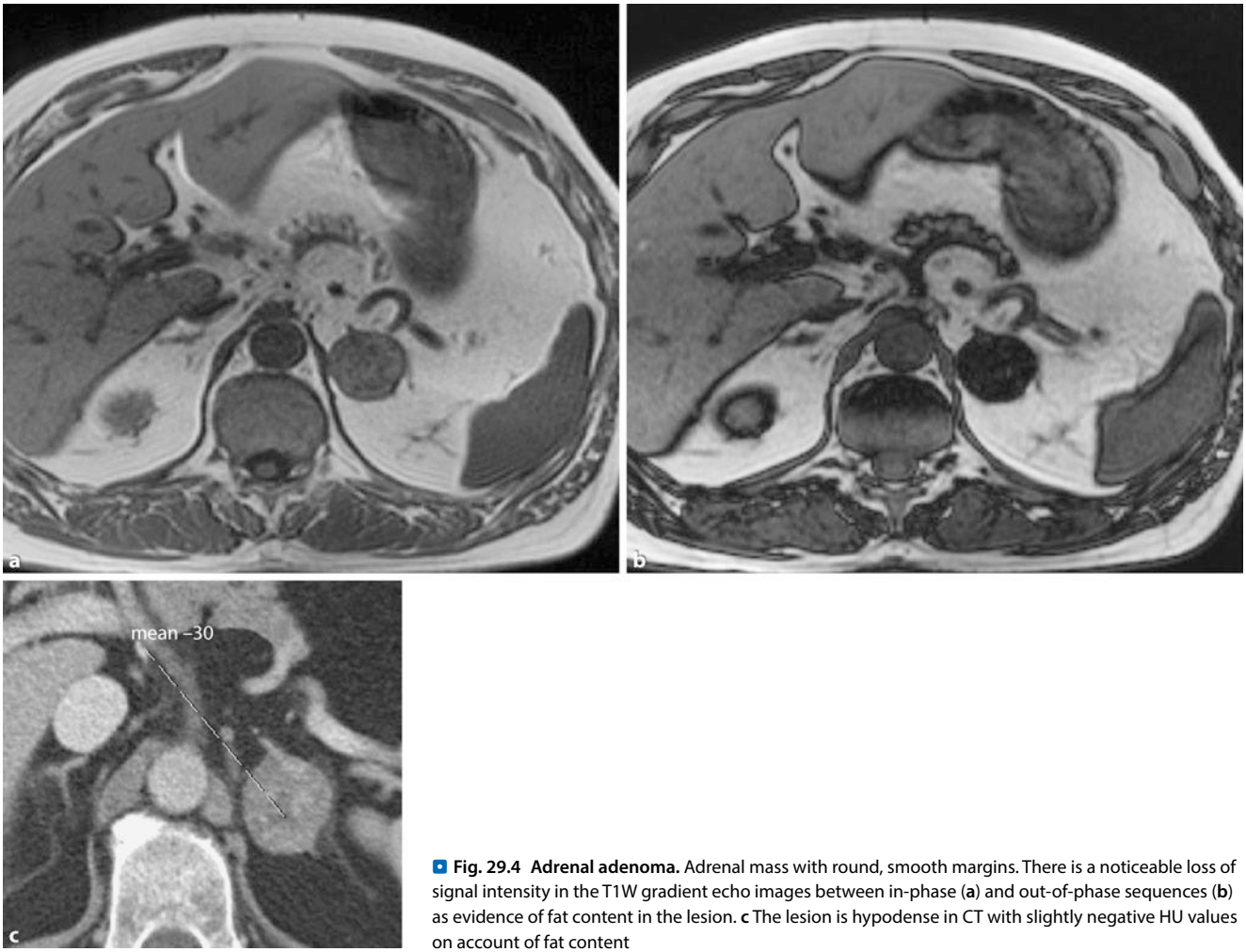

Fig. 29.4 Adrenal adenoma. Adrenal mass with round, smooth margins. There is a noticeable loss of signal intensity in the T1W gradient echo images between in-phase (**a**) and out-of-phase sequences (**b**) as evidence of fat content in the lesion. **c** The lesion is hypodense in CT with slightly negative HU values on account of fat content

ciency caused by adrenal haemorrhages, e.g., postnatal bleeding, shock or septicaemia.

Possible causes for adrenal haemorrhage are:
- Neonatal stress
- Underlying adrenal tumour
- Haemorrhagic diathesis or coagulation disorder

Cushing's Syndrome

Aetiology, Pathology, Clinic

Cushing's syndrome results from excessive production of ACTH. About 70% of cases reveal pituitary adenomas with adrenocortical hyperplasia. Excessive cortisone production in the adrenals themselves occurs in about 10 to 15% of cases. Symptoms caused by excessive production of ACTH include elevated blood sugar levels and truncal obesity as well as alterations of the skin, bone and muscles (Table 29.1).

Imaging

Cushing's syndrome producing adenomas are generally 2–5 cm in diameter and present a round or oval shape in CT. In unenhanced CT images they appear as slightly hypodense masses while showing a minimal contrast uptake in iodine-enhanced images.

Because of their lipid content, fat-saturated or out-of-phase MR images exhibit noticeable loss of signal intensity. The reduction in signal intensity, e.g., between in-phase and out-of-phase images, can be seen as evidence of adenoma fat content. Thus, the implementation of the MRI sequence leads us to decipher fatty and generally benign masses from less fatty and often malignant masses (Fig. 29.4).

Differential diagnoses in suspicion of adrenal adenomas
- Metastases and lymphoma
- Adrenal carcinoma
- Pheochromocytomas

Treatment and Prognosis

Treatment is indicated for all patients with Cushing's syndrome. The goal is to normalise cortisol production, e.g., via surgical resection of the causative tumour in the adrenal gland or more often the pituitary gland. In difficult cases or relapse, a drug-induced steroid synthesis inhibitor may follow.

Pheochromocytoma

Definition and Prognosis

Pheochromocytoma, also known as hyperadrenal medulla activity, is a neuroendocrine tumour derived from chromaffin cells in

Table 29.1 Hormonally active adrenal lesions

Name	Origin	Hormone	Clinic	Imaging
Conn's syndrome	Adrenal cortex (zona glomerulosa)	Aldosterone	Hypertension Hypokalemia	CT/MRI mostly undetectable
Cushing's syndrome, ACTH dependent	Pituitary gland, paraneoplastic	Cortisol	Truncal obesity Muscle weakness Hypertension Diabetes	CT/MRI mostly undetectable
Cushing's syndrome, ACTH independent	Adrenal cortex (zona fasciculata)	Cortisol		CT: mostly hypodense (< 10 HE) MRI: SI ↓ in-/opposed phase
Pheochromocytoma	Adrenal medulla	Catecholamines	Hypertension Profuse perspiration Anxiety	CT/MRI: contrast uptake MRI: T2 hyperintense

the adrenal medulla. Tumours of this kind that arise outside of the adrenal gland in an otherwise healthy sympathetic trunk are called paragangliomas. Ninety percent of pheochromocytomas are found in the adrenal medulla, whereas 10% are found outside of the adrenal gland in the sympathetic trunk. Most extra-adrenal pheochromocytomas are infradiaphragmatic; only 3% are supradiaphragmatically localised.

The 10% Rule in Pheochromocytomas
- 10% of pheochromocytomas are bilateral
- 10% are extra-adrenal
- 10% of cases are malignant

Clinic and Diagnosis

Clinical presentation is characterised by permanent or episodic strain on the system with catecholamines. The hypersecretion of epinephrine and norepinephrine leads to hypertension, which is often demonstrated in the severe increase of blood pressure. Anxiety and fever also arise due to an elevated basal metabolic rate. Patients tend to be young. A 24-hour urine collection will show clear signals of elevated secretions of catecholamines for diagnosis.

Pheochromocytoma occurs in association with several syndromes:
- MEN syndrome (multiple endocrine neoplasia)
- Neurofibromatosis
- Von Hippel-Lindau disease

Imaging

The primary purpose of imaging is for localisation and operation preparation. As already mentioned, diagnosis is established following clinical and laboratory research (24-hour urine collection).

CT images show adrenal tumours with a general diameter of > 2 cm. Extra-adrenal and retroperitoneal tumours may also be present. Smaller tumours generally appear homogenous, whereas larger tumours, although well defined, round or ovular, tend to exhibit central necrosis or haemorrhage. Following the injection of a contrast agent, pheochromocytomas show intense enhancement. This clearly differentiates them from adenomas for example.

Pheochromocytomas appear noticeably hyperintense on T2-weighted **MR** images, whereas large tumours appear inhomogeneous, necrotic, cystic, and haemorrhagic with corresponding signal intensities on T1- and T2-weighted images. Chemical shift MR shows that pheochromocytomas maintain their signal intensity in out-of-phase images as opposed to in-phase images. As in CT, T1W MR images (e.g., T1W GE images) exhibit strong contrast enhancement (Fig. 29.5).

Ten percent of pheochromocytoma cases demonstrate metastatic malignancies. In searching for metastases and the localisation of extra-adrenal pheochromocytomas (paragangliomas), both MRI and **MIBG scintigraphy** play an important role. CT and MRI sensitivity for detection of adrenal pheochromocytomas is 80–95%. Specificity of MR imaging is likewise very high. Sensitivity for detection of extra-adrenal paragangliomas is about 85% and thus correlates with a MIBG scintigraphy sensitivity of 90%. MIBG scintigraphy is superior with a specificity of about 99%.

The last several years have also seen an increase in PET/CT using the tracer ^{18}F-FDG for the diagnosis of pheochromocytoma. Compared to MIBG scintigraphy, ^{18}F-FDG PET appears to show lower specificity but noticeably higher sensitivity, though studies involving greater patient groups are still pending.

Treatment and Prognosis

Early diagnosis of pheochromocytoma is important in order to cure the disease as soon as possible via surgical resection of the tumour and to normalise the catecholamines. Cardiovascular complications can be avoided by doing so.

Additional drug-induced therapy of alpha/beta blockers usually proceeds for malignant pheochromocytomas. Metastasised pheochromocytomas require treatment using radionuclides (^{131}J-MIBG) and/or cytostatics.

29.4.3 Malignant Adrenal Tumours

Adrenal Carcinoma

Definition, Localisation, Pathogenesis

Adrenal carcinoma is predominately unilateral; they are bilateral in up to 10% of cases. First detection often shows hormonally active tumours with a diameter of 2–5 cm and hormonally inactive tumours with a diameter of up to 10 cm.

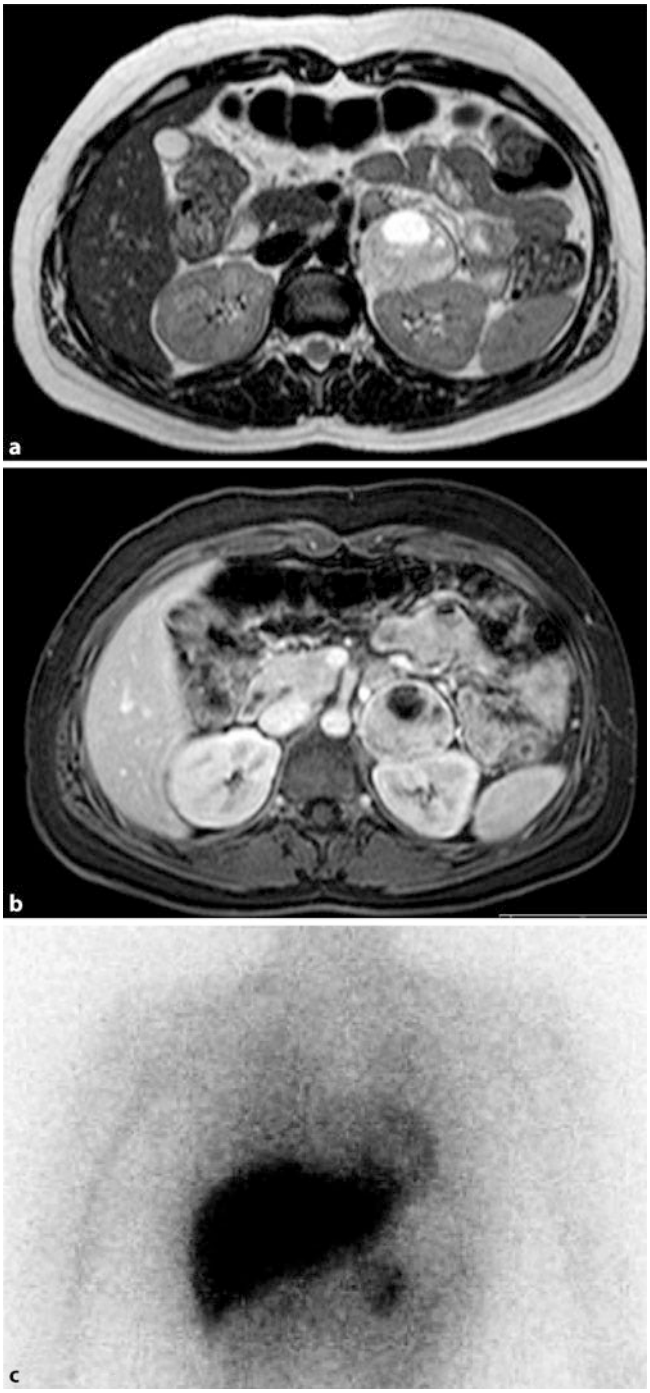

Fig. 29.5 Pheochromocytoma in a patient with MEN-2 syndrome.
a Tumour in the area of the left adrenal gland reveals smooth, round margins in T2W images; appearance is hyperintense with localised and early necrosis.
b Fat-suppressed T1W images show strong, inhomogeneous contrast uptake.
c Pronounced tracer uptake in MIBG scintigraphy

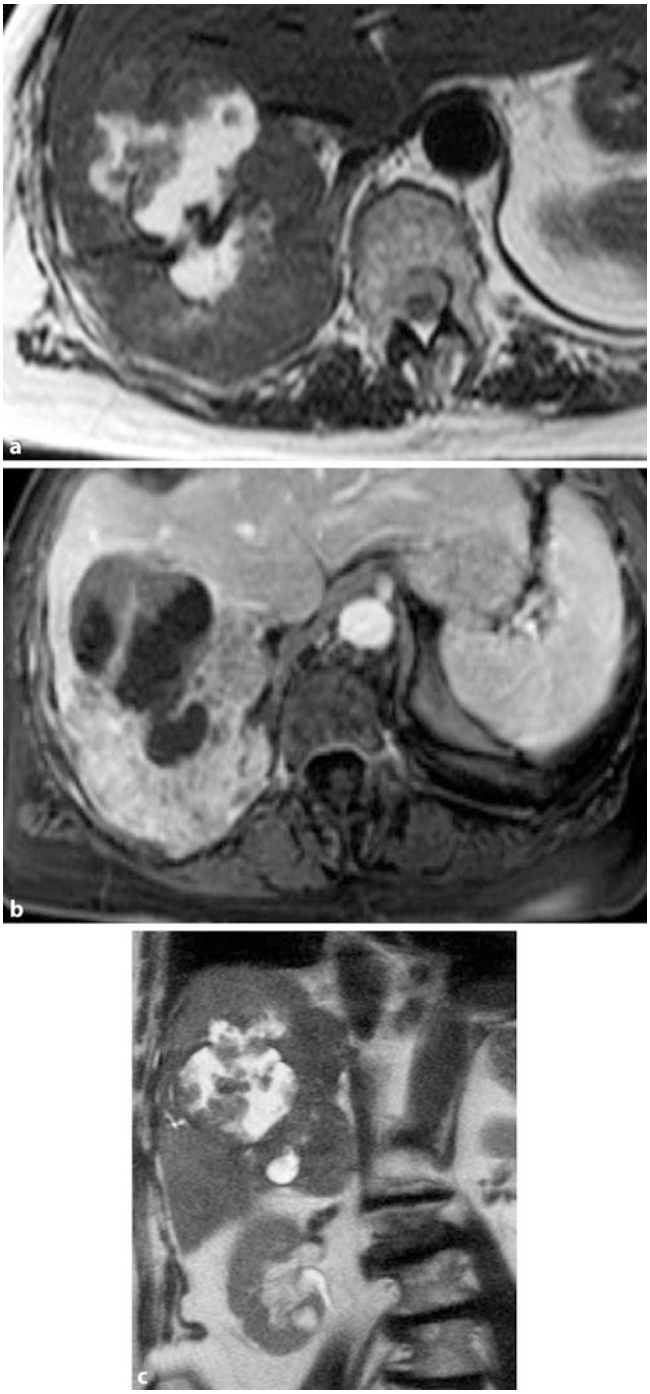

Fig. 29.6 Adrenal carcinoma. Expanded, infiltrating tumour with outward growth in the right adrenal gland. Inhomogeneous signal behaviour in T2W images (**a**, **c**) and in fat-suppressed T1W contrast-enhanced images.
b Continuing infiltration to the liver and right diaphragmatic crus

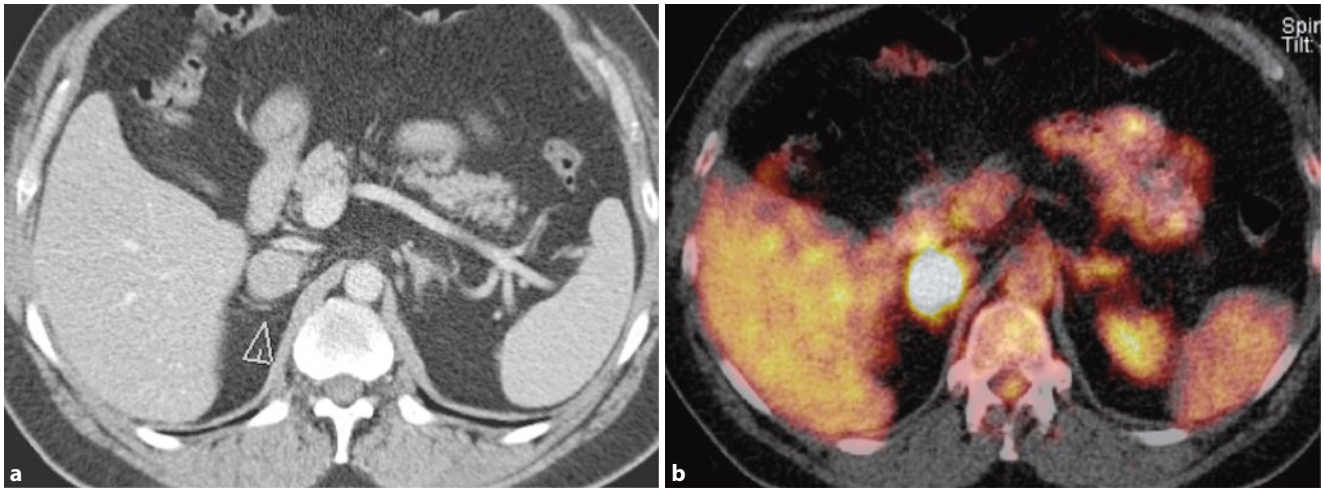

Fig. 29.7 Adrenal metastases. a Appearance of a round mass in the right adrenal gland in staging examination (PET/CT) of a patient with bronchial carcinoma. **b** Demonstration of augmented tracer uptake

Imaging

CT reveals growing, invasive tumours with central areas of necrosis and contrast-enhanced inhomogeneity (Fig. 29.6). Calcification and haemorrhages are common. Adrenal carcinomas tend to metastasise to regional and pulmonary lymph nodes.

Tumours reveal inhomogeneous signal intensity in MRI. Their invasive character, e.g., the invasion of the inferior vena cava or renal parenchyma, becomes easily distinguishable through the use of MR tomography.

In contrast to ultrasonography and angiography, FDG-PET(/CT) plays a significant role in diagnosis of the extent of spread.

Treatment and Prognosis

Adrenal carcinoma is difficult to classify. Diagnosis generally does not occur until having reached locally advanced or particularly metastasised stages. Treatment of localised cases is surgical resection via adrenalectomy and locoregional lymphadenectomy. For treatment of advanced stages, tumour radiation therapy and systematic chemotherapy (e.g., mitotane) are preferred.

Adrenal Metastases

Definition and Pathogenesis

Adrenal metastases most commonly occur in malignancies of the lung, female breast, kidneys, lymphatic system, and gastrointestinal tract. Metastases are bilateral in about 40–50% of all cases, but they can also be unilateral.

Imaging

Whether adrenal metastases appear in images as homogeneous (< 2 cm) or inhomogeneous (> 3 cm) depends on size, as it is common for larger metastases to contain necrotic areas and haemorrhages. Calcification is rare, especially in mucus-producing tumours.

In **CT** metastases show invasive growth and can appear either hypo- or hypervascular. Ring-like contrast enhancement commonly shows signs of progressive washout. Metastases also appear as masses with inhomogeneous echogenicity in **sonographic** images.

In **MRI** metastases appear hypointense on T1W images and hyperintense on T2W images. In large clusters with regressive changes, one also recognises also a corresponding, homogeneous, colourful image with necrotic and haemorrhagic areas.

Use of **FDG-PET** and **PET/CT** is becoming increasingly common for diagnosing the extent of spread, especially in bronchial carcinomas and in malignant melanoma (Fig. 29.7). Metastases show noticeably increased tracer uptake. As this also occurs occasionally in adrenal adenomas, it could lead to a false positive result.

Neuroblastoma

Most neuroblastomas develop between the second and third year of life. It is the most common abdominal tumour in children and is more common in children than Wilms' tumour or leukaemia. Thirty-five percent of neuroblastoma cases originate in the region of the adrenal glands. Histopathologically, the tumours can be completely dedifferentiated and clinically lead to adrenal medullary hyperfunction. Typical but vague clinical findings of neuroblastomas include fatigue, appetite loss, or a slight fever. A swollen abdomen or even palpable stomach tumour may occasionally be present.

Imaging

MRI is superior to CT and other imaging techniques in defining the location of neuroblastoma and the extent of its spread. Because of their size, the tumours are histologically inhomogeneous and therefore reveal different signal intensities in T1W or T2W images. Contrast-enhanced images are often inhomogeneous. MR images reveal the exact dimensions of the tumour on several levels and its possible spread to the spinal canal or even vertebral metastases. It can be difficult to distinguish a haemorrhagic neuroblastoma from postpartum adrenal haemorrhage in infancy.

Treatment and Prognosis

The prognosis of neuroblastomas is exceedingly variable as it ranges from spontaneous regression to a highly malignant spread

with extended metastases and rapid tumour growth. Treatment mostly involves multi-modal therapies including surgical resection, chemotherapy, radiation, and immunotherapeutic approaches.