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Adrenal imaging

Diagnostyka obrazowa guzów nadnerczy

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Abstract

The differentiation of adrenal nodules is wide and varies from primary benign neoplasia, through hormone secreting lesions, to primary and secondary malignant masses. With the rapid development of cross-sectional imaging, incidental detection of adrenal nodules has become an everyday practice, leaving clinicians with the necessity of further investigation. In this article, we present the current possibilities of adrenal gland imaging and we propose a diagnostic schema for differential diagnosis of incidentaloma. Non-contrast enhanced computer tomography (CT) is a modality of choice used for the differential diagnosis of adrenal lesions. It allows the detection of 95% of adrenal masses, and the characterisation of most of them. Magnetic resonance imaging (MRI) is a good modality for cases in which CT examination cannot determine the character of an adrenal tumour. Nuclear medicine study with the use of Iodine-131 meta iodobenzylguanidine (MIBG) is helpful in the diagnosis of pheochromocytoma. Positron Emission Tomography–Computed Tomography (PET–CT) is considered a useful method in patients with a known malignancy history. Ultrasound has a low sensitivity for the detection of small lesions and is not capable of reliable characterisation of visualised masses. However, this technique plays an important role in the follow-up of non-hypersecreting adrenal lesions. **(Pol J Endocrinol 2012; 63 (1): 71–81)**

Key words: *adrenal gland, adrenal adenoma, incidentaloma, adrenal imaging*

Streszczenie

Diagnostyka różnicowa guzów nadnerczy jest dość szeroka, od łagodnych, pierwotnych zmian, przez zmiany hormonalnie czynne, aż po zmiany złośliwe, pierwotne i wtórne. Wraz z szybkim rozwojem technik obrazowania, codziennością stało się przypadkowe wykrycie guzków nadnerczy. Stawia to klinicystę w potrzebie różnicowania tych zmian. W tym artykule przedstawiamy przegląd współczesnych możliwości obrazowania gruczołów nadnerczowych oraz proponujemy schemat diagnostyczny w przypadku przypadkowo wykrytego guzka nadnercza (tzw. incidentaloma). W zarysie, tomografia komputerowa bez podania środka kontrastowego jest metodą obrazowania z wyboru w diagnostyce różnicowej zmian w nadnerczach. Pozwala ona na wykrycie 95% zmian i scharakteryzowanie większości z nich. Rezonans magnetyczny jest dobrą techniką u pacjentów, u których nie udało się określić charakteru zmiany za pomocą tomografii komputerowej. Techniki medycyny nuklearnej z zastosowaniem specyficznych znaczników są przydatne w diagnostyce guza chromochłonnego. Z kolei stosowanie pozytonowej tomografii emisyjnej jest wskazane u pacjentów z rozpoznaną chorobą nowotworową. Ultrasonografia nie pozwala na wykrycie małych zmian oraz nie daje możliwości scharakteryzowania stwierdzonej zmiany, ale jest dobrą i niedrogą techniką sprawdzającą się w badaniach kontrolnych. **(Endokrynol Pol 2012; 63 (1): 71–81)**

Słowa kluczowe: *nadnercze, gruczolak nadnarcza, incidentaloma, obrazowanie nadnerczy*

Anatomy

Adrenal glands are inverted V- or Y-shaped organs located in the retroperitoneal space and composed of an outer cortex and an inner medulla. The limbs are 4 to 5 cm in length and up to 7 mm in thickness, but the site of limb connection is always thicker than the rest of the adrenal.

The right adrenal gland lies above the upper pole of the right kidney, posterior to the inferior vena cava, medial to the right lobe of the liver and lateral to the right diaphragmatic crus. The left adrenal gland lies medial and anterior to the upper pole of the left kidney, posterior to the splenic vessels (Figures 1, 2). Because adrenals develop independently from kidneys, in case of renal ectopy or agenesis, their location remains unchanged.

It is important to remember that computed tomography and magnetic resonance imaging are the only modalities which allow imaging of normal adrenals in adults.

Diagnostic methods

Computed tomography

If an adrenal mass is suspected, helical CT is a primary modality for its detection and characterisation. Thin slices, i.e. of 3 mm or less, are recommended, allowing reliable attenuation measurement even with small

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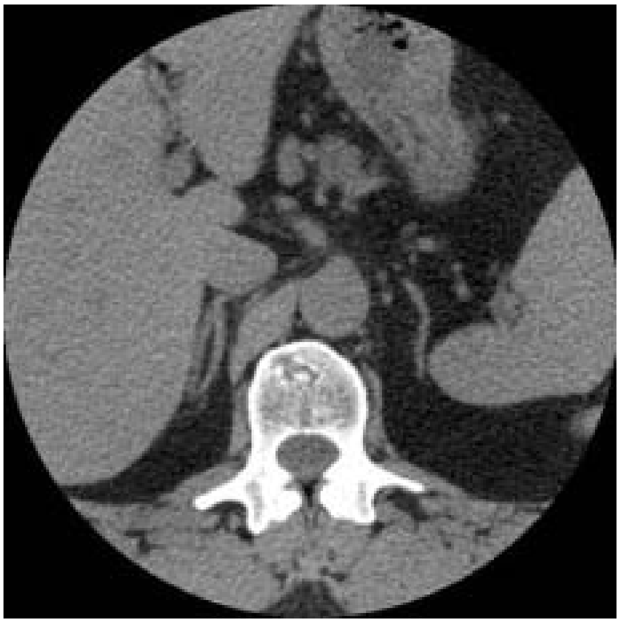

Figure 1. *Non-contrast enhanced CT, axial plane. Normal adrenal glands*

Rycina 1. *Tomografia komputerowa bez dożylnego podania środka cieniującego, płaszczyzna poprzeczna. Prawidłowe gruczoły nadnerczowe*

lesions. A non-enhanced scan should be performed followed by a contrast material-enhanced acquisition if necessary, as described later in this chapter [1].

CT allows a precise assessment of such features of adrenal tumours as their size, shape, homogeneity, and calcifications. The larger the tumour, the greater the risk of malignancy. Most masses larger than 5 cm in diameter are non-adenomas. Up to 25% of adrenal tumours > 6 cm are adrenocortical carcinomas [2]. On the other hand, small masses may correspond with adenomas, as well as with small carcinomas or pheochromocytomas. The homogeneity depends on tumour size and its growth rate: small, slowly growing masses tend to be homogenous, whereas large, rapidly growing tumours often appear inhomogeneous with areas of central necrosis. Change in lesion size is also a useful indicator of malignancy. Adenomas may also change in size in subsequent examinations, although the maximum diameter should not increase by more than 5 to 6 mm during a one year follow-up [1].

Round and oval shaped masses with smooth margins are often benign; however, small pheochromocytomas and metastases usually have the same appearance. Irregular shape usually indicates malignancy.

Calcifications are more often present in adrenal carcinomas, but may also be visible in other lesions such as neuroblastoma or tuberculosis.

When invasion of surrounding anatomic structures is present, the diagnosis of adrenocortical carcinoma is most likely.

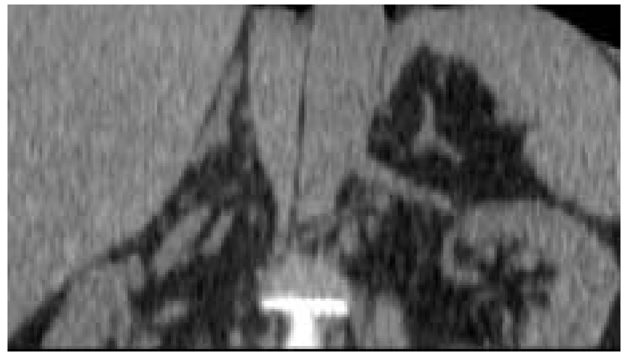

Figure 2. *Non-contrast enhanced CT, coronal plane. Normal adrenal glands*

Rycina 2. *Tomografia komputerowa bez dożylnego podania środka cieniującego, płaszczyzna czołowa. Prawidłowe gruczoły nadnerczowe*

Figure 3. *Non-contrast enhanced CT, axial plane. Low attenuation right adrenal mass (star) consistent with a lipid-rich adenoma*

Rycina 3. *Tomografia komputerowa bez dożylnego podania środka cieniującego, płaszczyzna poprzeczna. Guzek prawego nadnercza o niskiej gęstości (gwiazdka) odpowiadający gruczolakowi o dużej zawartości tłuszczu*

Attenuation at non-enhanced CT

Most adenomas contain intracellular lipids and thus have low attenuation at non-enhanced CT scans (Figure 3). Therefore, attenuation measurement is currently the most important parameter used to differentiate benign adenomas from malignant adrenal masses. When measuring attenuation with the use of region of interest (ROI), it should be as large as possible but without inclusion of the lesion's margins or retroperitoneal fat. Boland et al., in a meta-analysis of ten studies, determined an optimal threshold value

Figure 4. *Non-contrast enhanced CT, axial plane image shows a right adrenal mass (star) of a very low attenuation (below –50 HU) similar to retroperitoneal fat, which is consistent with a myelolipoma*

Rycina 4. *Tomografia komputerowa bez dożylnego podania środka cieniującego, płaszczyzna poprzeczna. Obraz przedstawia guz prawego nadnercza o bardzo niskiej gęstości, zbliżonej do gęstości tłuszczu przestrzeni zaotrzewnowej (poniżej –50 j.H.), odpowiadający myelolipoma*

of +10 Hounsfield Units (HU), which allows obtaining a 71% sensitivity and 98% specificity for the diagnosis of adrenal adenomas [3].

On the other hand, myelolipoma, a tumour composed mainly of fatty tissue, contains areas with a density lower than –50 HU, far below the density typical for adenomas. Distinguishing between these two lesions is straightforward with unenhanced CT (Figure 4) [4].

To conclude, a finding of an adrenal mass of a density lower than +10 HU on a non-contrast enhanced CT scan allows a confident diagnosis of adenoma, and does not require further investigation. Using this threshold value, a false positive diagnosis will happen rarely (2%), and may be related to the presence of infrequent adrenal cystic lesions.

Among the tumours which present with an attenuation higher than +10 HU, adenomas are still the most frequent lesions. Higher attenuation is related to lower lipid content. Lipid-poor adenomas represent 10–40% of adenomas [5]. Apart from lipid-poor adenomas, the most frequent adrenal masses with an attenuation higher than +10 HU are: metastases, pheochromocytomas and adrenocortical carcinomas (Figures 5, 6). In these tumours, non-enhanced CT is insufficient and they require further investigation [6].

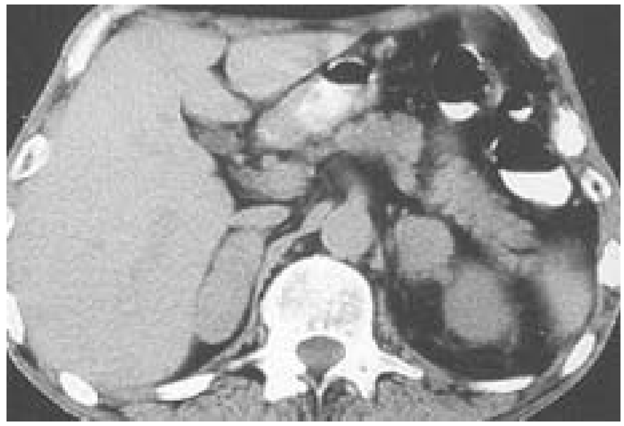

Figure 5. *Unenhanced CT scan. Bilateral adrenal metastases from lung cancer demonstrating density above +30 HU*

Rycina 5. *Tomografia komputerowa bez dożylnego podania środka cieniującego. Obustronne przerzuty z raka płuca przedstawiające gęstość powyżej +30 j.H.*

Figure 6. *Unenhanced CT scan. The right adrenal mass demonstrating density above +30 HU and central calcifications — adrenocortical carcinoma*

Rycina 6. *Tomografia komputerowa bez dożylnego podania środka cieniującego. Guz prawego nadnercza o gęstości powyżej +30 j.H. zawierający zwapnienia — rak kory nadnerczy*

Contrast media washout

Another CT technique successfully used for the differentiation of adrenal masses is assessment of washout of intravenously administered contrast material (CM). Adenomas, as well as other tumours, enhance rapidly after CM injection, but due to perfusion differences the washout of CM from adenomas is relatively rapid compared to other adrenal lesions, which demonstrate significantly slower washout.

In a case of adenoma attenuation, values gradually return to the level of non-enhanced examination 5–45 minutes after CM injection. Other lesions, such as adrenocortical carcinomas, metastases and pheochromocytomas enhance rapidly, but then maintain relatively higher attenuation values. This phenomenon is probably related to increased perfusion and vessel permeability in these tumours, causing marked contrast media diffusion to the extracellular space and, in consequence, prolonged accumulation. The assessment of contrast media washout is most frequently performed 10–15 minutes after injection, which usually allows differentiation of lipid-rich and lipid-poor adenomas from other adrenal tumours (Figure 7) [7].

Three parameters are used in the differential diagnosis of adrenal tumours using washout assessment:

— Attenuation value at delayed contrast enhanced CT images (usually 10–15 minutes after contrast injection);
— Absolute percentage washout (APW) (attenuation values of non-enhanced, 1 minute and 10–15 minutes delayed images are required);
— Relative percentage washout (RPW) (attenuation values of 1 minute and 10–15 minutes delayed images are required, non-enhanced examination is not necessary).

Attenuation value at delayed CT depends on the amount of intravenous contrast media and time from the beginning of injection. A Hounsfield unit of less than +35 at 10–15 minutes delayed CT is highly indicative of adrenal adenoma.

Absolute percentage washout (APW) is calculated using the following formula:

Figure 7. *CT contrast media washout assessment, axial plane, pre-contrast (a); portal venous phase (b); and 15-minutes delayed phase (c). CT images show a well-defined right adrenal mass (star). The attenuation measurements demonstrate marked contrast media washout (> 50%) consistent with an adenoma*

Rycina 7. *Tomografia komputerowa, ocena wypłukiwania środka cieniującego. Faza badania przed podaniem środka cieniującego (a), faza wrotna (b), faza opóźniona 15 min (c). Obrazy przedstawiają dobrze odgraniczony guz prawego nadnercza (gwiazdka). Pomiary współczynnika osłabienia promieniowania przedstawiają istotne wypłukiwanie się środka cieniującego (> 50%) charakterystyczne dla gruczolaka*

[(1 min. delayed enhanced HU value – 10 min. delayed enhanced HU value) / (1 min. delayed enhanced HU value – non-enhanced HU value)] × 100%

Absolute percentage washout values are greater for adenomas than for other adrenal tumours. Multicentre analysis has revealed an optimal threshold value of 50% for a 10-minute delayed CT. Values greater than 50% are typical for adenomas. This method allows differential diagnosis of adenomas and non-adenomas with high sensitivity and specificity, 98% and 92% respectively [7].

Relative percentage washout (RPW) is calculated using the following formula:

[(1 min. delayed enhanced HU value – delayed enhanced HU value) / (delayed enhanced HU value)] × 100%

According to several authors, RPW is as effective as APW. For a 10-minute delayed CT, values greater than 40% are typical for adenomas. The higher this parameter is, the greater the accuracy of the method. This method is used most frequently when adrenal mass is incidentally found during contrast-enhanced CT examination performed for other indications (without non-enhanced phase).

Potential interpretation difficulties may appear in a case of adrenal hyperplasia, especially when a single dominant nodule is present. A nodule is usually less than 3 cm in diameter and on CT scans it may present the same attenuation values as adrenal adenoma. A comparative assessment to the opposite adrenal is useful in these cases. In a case of hyperplasia, the contralateral adrenal gland is also markedly prominent, whereas in a case of non-hyperfunctioning adenoma, the contralateral adrenal has usually a normal appearance. When an adenoma is hyperfunctioning, the contralateral gland is often atrophic.

Additionally, contrast-enhanced CT study without assessment of washout may be useful in several situations. In a case of suspected adrenal haemorrhage, attenuation values of adrenal mass on unenhanced CT scans exceed +10 HU. After contrast administration, these lesions, unlike other hyper-attenuating adrenal masses, do not show significant contrast enhancement. Patients with adrenal cysts usually demonstrate a homogenous water-density mass (with attenuation in the range of adrenal adenoma), which, on contrast enhanced CT scans, does not show any enhancement. Contrast-enhanced CT study may also be useful in patients with adrenal metastases and adrenal carcinoma for the evaluation of possible metastatic liver lesions.

CT — conclusion

Patients referred for CT for a suspected adrenal tumour should initially undergo a non-contrast enhanced study. If normal adrenals are demonstrated, an adrenal tumour may be excluded and no further examinations are needed. A finding of an adrenal tumour with an attenuation value lower than +10 HU allows the confident diagnosis of adrenal adenoma, and no further investigation is required.

However, finding an adrenal mass with an attenuation greater than +10 HU requires further procedures, such as contrast enhanced CT with early (1-minute delayed) and 10-minute delayed phases, with subsequent attenuation value measurement and evaluation of CM washout (APW). When a lesion is incidentally found on contrast-enhanced CT, an additional 10-minute delayed phase may be performed and a relative percentage washout (RPW) of the contrast material may be assessed.

CM washout may also be assessed with magnetic resonance imaging (MRI), although this method is used rarely. Another MRI technique, chemical shift imaging, is frequently used in a case of undetermined (on unenhanced CT) adrenal masses and demonstrates high accuracy for their characterisation.

In conclusion, the main advantages of CT are high sensitivity in the detection of adrenal lesions and high sensitivity and specificity in differentiating between benign and malignant masses. CT is a primary modality for the detection and characterisation of adrenal masses and is useful in the verification of ultrasound (US) findings.

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is used frequently for characterising adrenal lesions in cases in which CT examinations are equivocal. A standard MRI study of adrenal glands consists of non-contrast enhanced sequences. Only in certain cases may contrast-enhanced examination be helpful (e.g. adrenal haemorrhage, cyst, carcinoma, metastases).

MRI allows the detection of adrenal masses with a similar sensitivity as CT. Several MRI parameters, such as signal intensity on T2-weighted images or enhancement rates were used in the past, but today the most important role in the description of adrenal masses is played by chemical shift imaging. This technique, similar to non-enhanced CT attenuation values measurement, relies on the detection of lipids within an adrenal mass (indicative of an adenoma), although it is more sensitive for the identification of intracellular lipids [8]. It is based on the T1 gradient echo technique, which allows acquiring of so called in-phase and out-of-phase images.

Only adenomas and myelolipomas may demonstrate relative loss of signal intensity on out-of-phase images (Figure 8); however, many myelolipomas do not contain enough water in the fatty tissue to cause

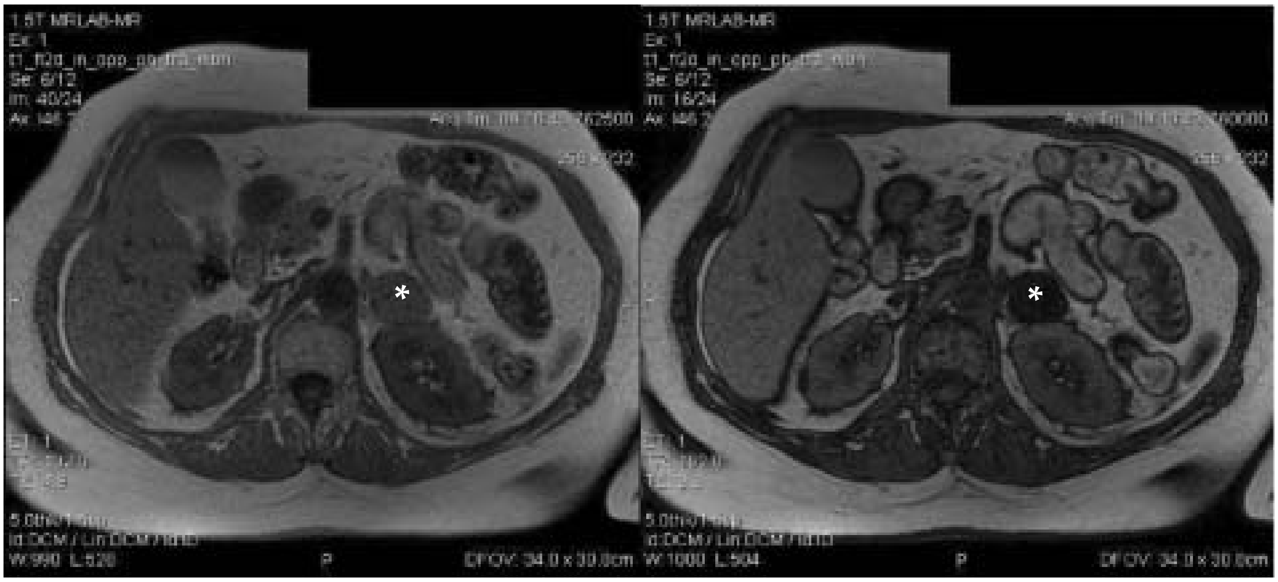

Figure 8. *MR T1 gradient echo in-phase and out-of-phase images, axial plane. Well-defined left adrenal mass, which shows marked relative signal intensity loss on out-of-phase images, indicative of fatty content — appearance consistent with adrenal adenoma*

Rycina 8. *Rezonans magnetyczny, obrazy T1-zależne echa gradientowego w fazie oraz w przeciwfazie, płaszczyzna poprzeczna. Dobrze odgraniczony guz lewego nadnercza, przedstawiający istotny spadek intensywności sygnału w obrazach w przeciwfazie, oznaczający tłuszczową zawartość zmiany — obraz charakterystyczny dla gruczolaka*

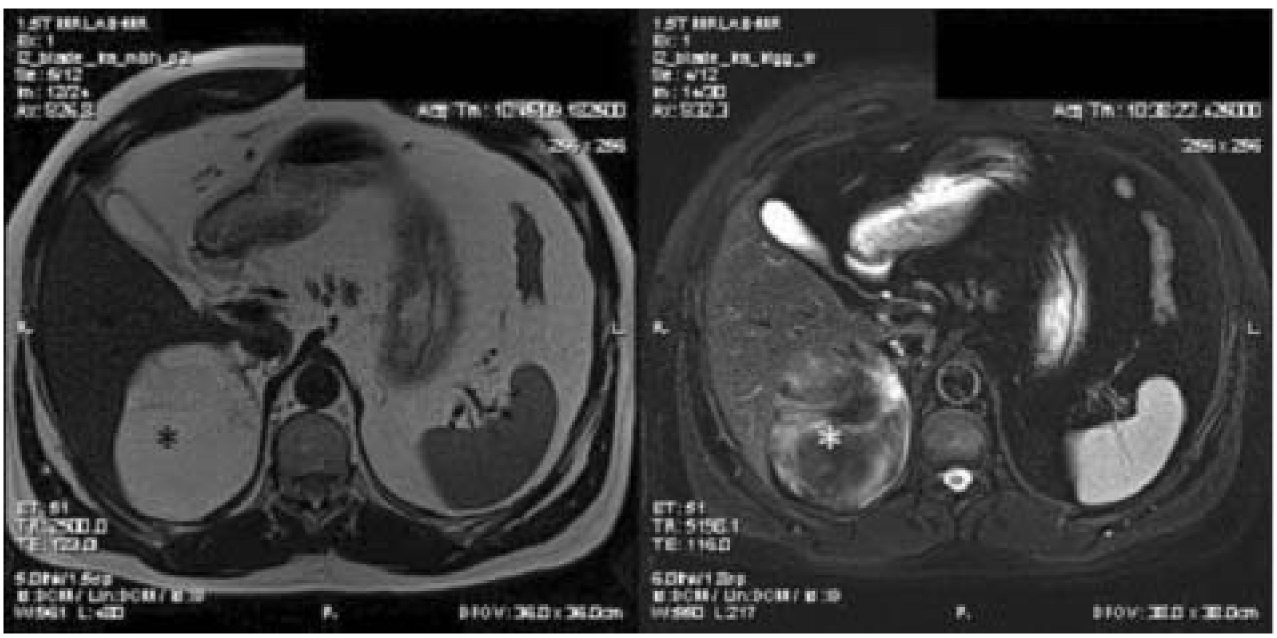

Figure 9. *MR T2 weighted images without and with fat saturation show a well-defined large right adrenal mass (star), which consists mainly of fatty tissue (signal intensity loss on fat saturated image). This appearance is typical for myelolipoma*

Rycina 9. *Rezonans magnetyczny, obrazy T2-zależne bez i z saturacją tkanki tłuszczowej, przedstawiają dobrze odgraniczoną masę (gwiazdka), która zawiera głównie tkankę tłuszczową (spadek intensywności sygnału w obrazach z saturacją tkanki tłuszczowej) — obraz typowy dla myelolipoma*

a visible signal drop. Nevertheless, MRI diagnosis of myelolipoma is straightforward and is based on the use of fat saturated images acquired with sequences applying spectral fat saturation or inversion recovery technique (Figure 9). Chemical shift imaging allows the differentiation of adenomas from other tumours in 90% of cases. However, similarly to CT, it does not allow differentiation between other masses such as metastases, adrenocortical carcinomas or pheochromocytomas [9].

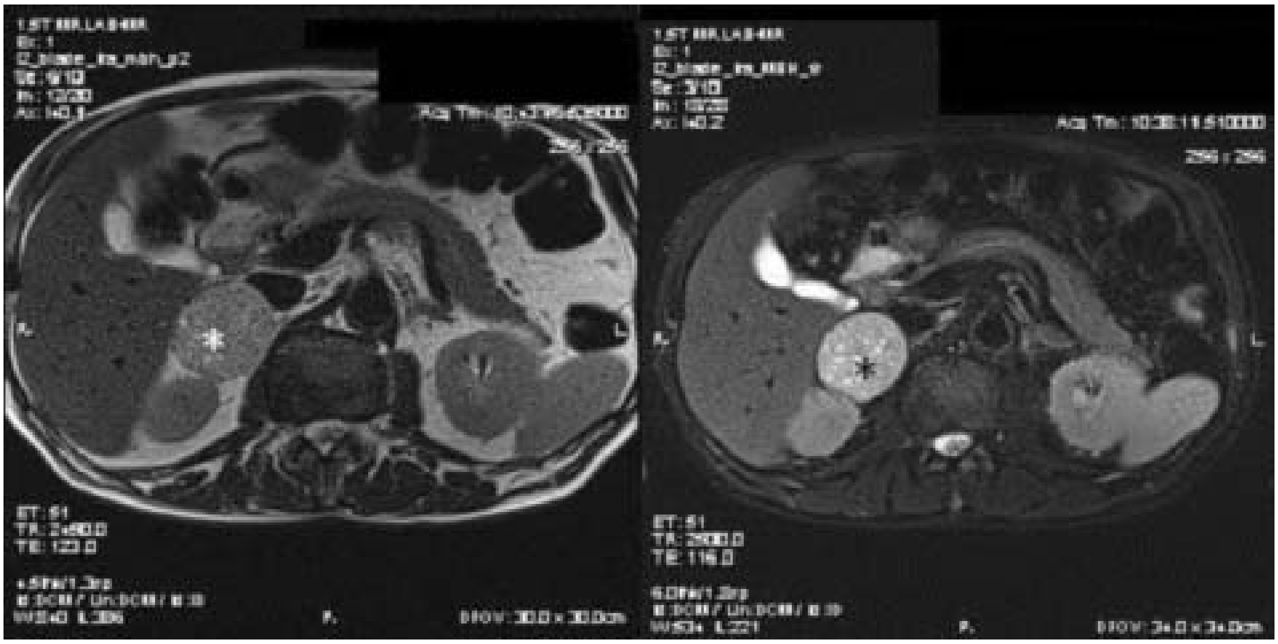

Figure 10. *MR T2 weighted images without and with fat saturation show a well-defined, large, heterogeneous right adrenal mass (star), which does not demonstrate signal intensity loss on fat saturated image. The final diagnosis (based on surgery specimen) was pheochromocytoma*

Rycina 10. *Rezonans magnetyczny, obrazy T2-zależne bez i z saturacją tkanki tłuszczowej, przedstawiają dobrze odgraniczoną, heterogenną masę (gwiazdka), której sygnał nie ulega obniżeniu w obrazach z saturacją tkanki tłuszczowej. Na podstawie badania histopatologicznego rozpoznano guz chromochłonny*

Qualitative as well as quantitative analysis of signal intensity is used for the evaluation of adrenal lesions on in-phase and out-of-phase images. In most cases, qualitative analysis is sufficient for the differentiation of tumours that contain fat from those that do not. On out-of-phase images, there is loss of signal intensity in adenomas, while in nonadenomas signal intensity does not change significantly [10].

In the rare cases in which loss of signal intensity is unclear, quantitative analysis should be performed. Several studies have shown that among methods used for quantitative analysis, signal intensity index is the most accurate. It is calculated using the following formula:

[(SI in-phase – SI out-of-phase) / SI in-phase] $\times$ *100%*

An SI index greater than 16 is strongly indicative of an adenoma.

Even though differentiation of adrenal tumours on chemical-shift MRI, as well as on non-enhanced CT images, is based on lipid contents of adenomas, it has been shown that MRI is more sensitive for intracellular lipid detection than CT. Heider et al. performed a retrospective analysis of adrenal lesions with attenuation of more than +10 HU at non-enhanced CT, which subsequently underwent MRI examination [11].

Among adrenal tumours with attenuation values between +10 and +30 HU at non-enhanced CT, MRI was effective in 89%, enabling detection of small amounts of fat in these low-lipid adenomas. However, in cases of adenomas containing minimal or no fat, with attenuation values of more than +30 HU, MRI was ineffective [11].

Similarly to CT, evaluation of contrast material washout may also be employed during MRI, although this method is used rarely.

Another advantage of MRI is the possibility of the identification of some pheochromocytomas, showing characteristic high signal intensity on T2-weighted images (Figure 10). Furthermore, MRI is useful in the detection of extra-adrenal pheochromocytomas.

In conclusion, in adrenal masses presenting with attenuation values from +10 to +30 HU, chemical shift MRI is an efficient and accurate method, which may be applied for their characterisation instead of contrast media washout assessment with CT. The effectiveness of chemical shift MRI in differentiating adenomas from non-adenomas approaches 90%, and is thought to be only slightly lower than assessment of contrast media washout with CT (Figure 11).

Ultrasound

Ultrasound, compared to other techniques such as MRI and CT, is a relatively inexpensive and portable modality. Because of its wide prevalence, it is commonly used and often leads to the detection of non-symptomatic

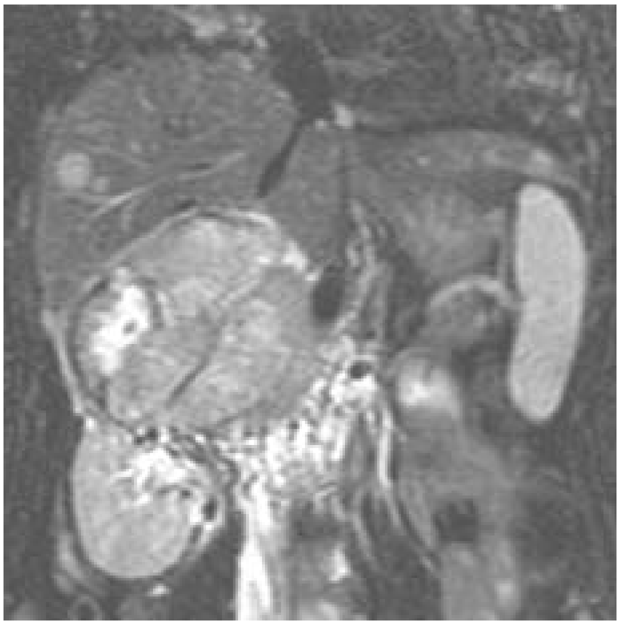

Figure 11. *T2-weighted MR image showing right adrenocortical carcinoma and metastatic lesions in the liver*

Rycina 11. *Rezonans magnetyczny, obrazy T2 zależne przedstawiają raka kory prawego nadnercza z przerzutami do wątroby*

Table I. *Adrenal pseudotumours in ultrasound examination*
Tabela I. *Pseudoguzy nadnerczy w badaniu ultrasonograficznym*

Bilateral lesions	Tumours of upper renal poles
	Cystic lesions of upper renal poles
Right adrenal field	Hepatic flexure
	Dilated inferior vena cava
	Focal liver lesion
Left adrenal field	Splenic lobe/accessory spleen
	Dilated, curved splenic vessels
	Splenic artery aneurysm
	Pancreatic tail
	Gastric diverticulum

adrenal tumours (incidentaloma). Non-symptomatic adrenal masses occur in 2–5% of the population. The sensitivity of this technique in the detection of adrenal masses is approximately 76%, with specificity around 92%. The sensitivity is lower in cases of masses located in the left adrenal gland, those smaller than 20 mm, and in obese patients.

The evaluation of the left adrenal gland with ultrasound is frequently difficult due to its location (posterior to the stomach and small bowel). Not infrequently, some anatomic structures may be demonstrated in adrenal fields and incorrectly diagnosed as adrenal masses (a false positive diagnosis) (Table I). In adults, normal adrenals are not visualised in the vast majority of patients and therefore small lesions are difficult to exclude, leading to a false negative diagnosis in some cases.

Ultrasound enables the measurement of larger masses (> 20 mm); however, differential diagnosis based solely on tumour size is impossible. Benign adenomas are usually small (< 50 mm), but some metastases and pheochromocytomas may be similar in size, which makes differentiation unfeasible.

Diagnostic difficulties especially concern patients with a primary extra-adrenal neoplasm accompanied by adrenal mass. Adrenal tumours visualised in these patients are as often metastases as benign adenomas; therefore their distinction is of the utmost importance and may be crucial for treatment planning.

When a larger adrenal mass (> 50 mm) is detected, metastases, pheochromocytomas, adrenocortical carcinomas as well as benign adenomas have to be taken into consideration in differential diagnosis. In malignant tumours and larger pheochromocytomas, low-echogenicity areas of necrosis may be present.

Because almost all adrenal masses are hypoechoic, this parameter is also not useful for their characterisation. A rare but important exception is hyperechoic myelolipoma, which requires differentiation from other retroperitoneal tumours containing fatty tissue, such as lipoma, liposarcoma and teratoma. Another adrenal lesion that may be hyperechogenic is adrenal haematoma. Its echogenicity depends on the time since haemorrhage. Early on, hyperechogenicity is characteristic, but later this lesion usually transforms into a hypoechogenic pseudocyst.

Another uncommon lesion, but with typical ultrasound appearance, is adrenal cyst, which has the appearance of a well-defined non-echogenic lesion with posterior acoustic enhancement. However, despite typical morphology, technical problems with adrenal visualisation in many patients mean that differentiation between a solid and a cystic adrenal mass may be difficult.

In conclusion, one of the main disadvantages of ultrasound is low sensitivity in the detection of adrenal masses smaller than 20 mm. Other disadvantages are: difficulties in assessment of adrenal fields in obese patients, and lack of accurate criteria for the discrimination of adrenal masses. The main advantage of ultrasound is its wide prevalence. Therefore it is considered to be a good modality for the follow-up (with size evaluation) of non-symptomatic lesions greater than 20–30 mm.

Nuclear medicine

Adrenal cortical scintigraphy is rarely useful compared to modern CT and MRI technology, which are far more sensitive in the detection of small masses. A primary radiopharmaceutical used in the differentiation of adrenal lesions is NP-59 (6-beta-iodomethyl-19norcholesterol), which is a cholesterol analogue effective in the identification of adrenocortical tumours secreting glucocorticoids, mineralocorticoids and androgens (non-symptomatic adenomas usually also secrete small amounts of hormones, therefore radiopharmaceutical uptake is also present). This diagnostic tool has a high sensitivity and specificity in the diagnosis of adrenal adenoma, thus lesions with no uptake are diagnosed as non-adenomas. However, adrenal cortical scintigraphy has many disadvantages: low effectiveness in the detection of masses smaller than 20 mm, thyroid blockage with Lugol's iodine, and high absorbed radiation dose [3].

In contrast to adrenal cortical scintigraphy, MIBG (Iodine-131 meta iodobenzylguanidine) is still very useful in the diagnosis of adrenal medullary neoplasms such as pheochromocytoma, paraganglioma, and neuroblastoma. Any uptake of MIBG by the adrenal gland is abnormal. This technique is especially useful in cases when pheochromocytoma is suspected, but no adrenal mass is identified on CT or MRI, meaning that extra-adrenal localisation is probable. MIBG scintigraphy may also be used to detect metastatic disease of any above-mentioned neoplasm or residual tumour after surgery. The disadvantages of this examination include thyroid blockage and a long time between radiopharmaceutical admission and examination (24–48 h) [12].

Positron Emission Tomography–Computed Tomography (PET–CT)

PET-CT is an imaging modality which combines Positron Emission Tomography (PET) and computed tomography (CT). Data from both devices is acquired simultaneously, in the same session and combined into a single image. Therefore functional imaging of radiopharmaceutical uptake, which shows the spatial distribution of metabolic activity in the body, can be correlated more precisely with anatomic imaging obtained by CT scanning.

It has been shown in multiple studies that malignancies are usually more metabolically active than benign tumours. For the purpose of differentiation of an adrenal mass, adrenal uptake of fluorodeoxyglucose (FDG) is compared to hepatic uptake if greater adrenal mass is considered to be of malignant origin. However, further differentiation between malignancies is impossible. Moreover, an adrenocortical carcinoma may be metabolically not active, and the results may be false-negative. The analysis of standardised uptake value (SUV) may also be combined with attenuation values assessment from unenhanced CT (with < 10 HU positive for adenoma). In addition, no significant difference was found in radiopharmaceutical uptake between lipid-rich and lipid-poor adenomas [13].

Increased FDG uptake in inflammatory adrenal lesions such as sarcoidosis, tuberculosis, adrenal endothelial cyst, some adrenal adenomas, periadrenal abnormality or adrenal cortical hyperplasia, may lead to a false positive diagnosis of malignancy. On the other hand, false negative results may be related to haemorrhage and necrosis in the metastatic tumour. Also, metastases from tumours that do not have FDG avid uptake, such as neuroendocrine tumours and bronchioloalveolar carcinoma, may yield false negative results on PET-CT [14].

In conclusion, FDG PET is a promising new technique which may be useful in differentiating between malignant (metastatic) lesions and benign adenomas in patients with known extra-adrenal malignancy; however, it does not allow differentiation between malignant lesions.

Adrenal vein sampling

Adrenal vein sampling is a procedure rarely performed in patients with primary aldosteronism. This diagnostic method is considered to be a difficult procedure. However, some authors believe that there may be an increased demand for such examination due to data showing that primary aldosteronism is more common than previously thought [15]. The examination technique is similar to venography, and consists of adrenal veins catheterisation and blood sampling after adrenocorticotropic hormone (ACTH) stimulation. CT examination performed prior to sampling is useful in procedure planning in terms of demonstrating the anatomy and positions of the adrenal veins.

Adrenal vein blood analysis may demonstrate unilateral or bilateral hormone secretion after ACTH stimulation, which allows differentiation between adrenal cortical hyperplasia and secreting adenoma. Secreting adenoma will cause a unilateral aldosterone secretion, whereas bilateral secretion will be present in adrenal cortical hyperplasia [16]. As adrenal cortical hyperplasia can demonstrate several appearances including macronodular, differential diagnosis with secreting adenoma in cases of primary aldosteronism is vital, mainly because patients with secreting adenoma may be offered surgery.

In conclusion, adrenal vein sampling is an invasive and demanding procedure. However, in selected cases there is no alternative for differentiation between primary adrenal lesion and adrenal hyperplasia. Performed in experienced institutions, it allows for differential diagnosis between these two.

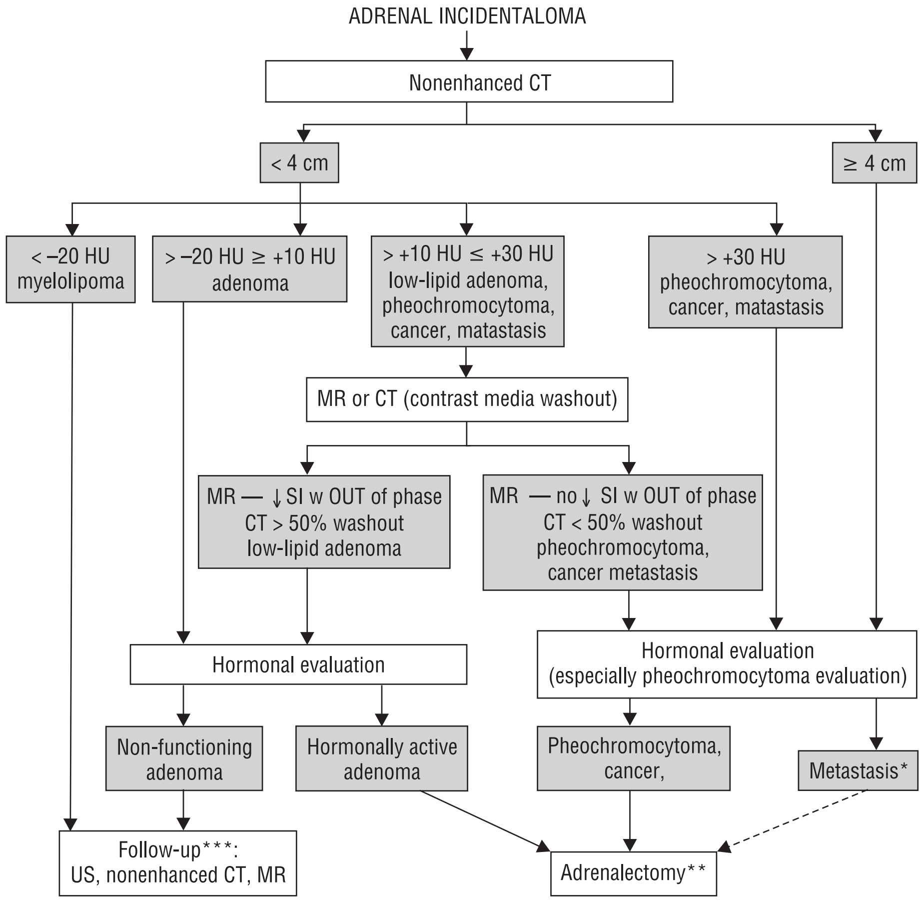

Figure 12. *Suggested evaluation of an adrenal incidentaloma [18, 19]; *metastasectomy should be considered in the case of an isolated adrenal metastatic lesion; **all hormonally active lesions (especially pheochromocytomas) require appropriate pharmacological treatment before surgery; ***there is no consensus on appropriate follow-up evaluation. The first imaging re-evaluation may be performed early (after 3–6 months). Afterwards, imaging re-evaluation may be performed annually for 2–4 years. Biochemical re-evaluation should be performed annually for 3–5 years. Should the tumour extensively grow or become hormonally active during follow-up, adrenalectomy should be considered; US — ultrasonography; CT — computed tomography; MR — magnetic resonance; HU — Hounsfield units*

Rycina 12. *Sugerowany schemat postępowania w przypadkowo wykrytych guzach nadnerczy [18, 19]; *w przypadku pojedynczego ogniska przerzutowego w nadnerczach należy rozważyć metastazektomię; **wszystkie guzy hormonalnie czynne (zwłaszcza guz chromochłonny) wymagają odpowiedniego leczenia farmakologicznego przed zabiegiem chirurgicznym; ***nie ma jednoznacznych ustaleń dotyczących dalszej obserwacji chorych. Kolejne badania obrazowe można przeprowadzić po niedługim czasie (po 3–6 miesiącach), a następnie powtarzać je corocznie przez 2–4 lata. Badania biochemiczne należy przeprowadzać raz do roku przez 3–5 lat. W przypadku gdy późniejsze badania wykażą wzrost guza lub gdy stanie się on hormonalnie czynny, należy rozważyć adrenalektomię; US — ultrasonografia; CT — tomografia komputerowa; MR — rezonans magnetyczny; HU — jednostki Hounsfield*

Biopsy

Adrenal biopsy is indicated especially in cases when an extra-adrenal tumour is present and a co-existing adrenal lesion cannot be accurately differentiated by CT, MRI or PET imaging. In such cases, the probability of metastasis is nearly as high as adrenal adenoma. Differentiation between those two lesions is vital for patients with no other metastasis confirmed [17].

Biopsy is an ultrasound-guided or CT-guided procedure performed with a thin needle (usually 22 G). Pheochromocytoma and coagulation disorders must be excluded before the procedure. For the right adrenal biopsy, a posterior or transhepatic approach is used, while for the left adrenal, a posterior or, rarely, transgastral approach is possible. The thin needle biopsy technique has a low complication rate. Complications that can appear are: bleeding, pneumothorax, pancreatitis and sepsis.

Summary

Non-contrast enhanced CT is a primary modality for the diagnosis of adrenal lesions (Figure 12). It allows detection of 95% of adrenal masses, and characterisation of most of them. Magnetic Resonance Imaging is a good modality for cases in which CT examination is unable to determine an adrenal tumour's character; we are here referring to masses with attenuation values from +10 to +30 HU at non-enhanced CT. Adrenal cortical scintigraphy has not received general recognition in the differential diagnosis of adrenal masses. However, nuclear medicine study with the use of MIBG is effective in the diagnosis of an extra-adrenal pheochromocytoma. PET-CT is considered a useful method for differentiating between malignant (metastatic) lesions and benign adenomas in patients with known malignancy history. Adrenal biopsy is indicated rarely in patients with known neoplastic disease and a co-existing adrenal lesion, which cannot be accurately differentiated by CT, MRI or PET imaging. Ultrasound, due to its availability and low cost, allows the detection of a large number of adrenal tumours. However, it has low sensitivity for the detection of small (< 2 cm) lesions, and is not capable of reliable characterisation of visualised masses. However, this technique plays an important role in the follow-up of non-hypersecreting adrenal lesions.

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