Ultrasound Diagnosis in Benign Thyroid Lesions

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Nodular goiter is a clinical concept that does not always coincide with a morphological definition. In clinical practice it is thought to mean a thyroid lesion of any size having a capsule that may be defined by palpation or by means of any imaging modality. A "multinodular goiter" is characterized by the presence of two or more nodules within the thyroid gland.

Thyroid nodules are detected in 4–15% of the population. The nodules are observed in more than 50% of patients with thyroid pathology; the incidence of nodules can reach 98.9% in endemic regions [1]. Thyroid nodules are identified in more than half of all autopsies [2]. The incidence of nodular goiter correlates with age.

Thyroid lesions include both colloid nodules and tumors. The latter are divided into the following groups according to the WHO histological classification (1988):

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1. Epithelial tumors
   a. Benign
      - Follicular adenoma
      - Others
   b. Malignant
      - Follicular carcinoma
      - Papillary carcinoma
      - Medullary carcinoma
      - Undifferentiated (anaplastic) carcinoma
      - Others
2. Nonepithelial tumors
   a. Benign
   b. Malignant
3. Malignant lymphomas
4. Miscellaneous tumors
5. Secondary tumors
6. Unclassified tumors
7. Tumorlike lesions

Thyroid lesions are assessed by the following US criteria:

1. Number of nodules
2. Location (in lobes and segments, in relation to the capsule, vascular bundles, or trachea)
3. Dimensions
4. Shape (roundish, oval, irregular)
5. Borders (smooth, rough)
6. Contours (well defined, indistinct)
7. Echodensity
8. Echostructure (the degree heterogeneity)
9. Calcifications (the dimensions, location, and presence of acoustic shadowing)
10. Fluid component (the dimensions and the ratio of fluid to solid components)
11. Peripheral halo
12. Posterior echo change (enhancement or shadowing)
13. Vascularity
14. Elasticity/rigidity with USE and SWE
15. Contrast enhancement, wash-in and wash-out with CEUS

Thyroid nodules may be solitary, multiple (two and more), or conglomeratic (when some nodules merge into one lesion).

The dimensions of nodules are measured in three mutually perpendicular planes. Each dimension (length, width, or depth) is the maximum between the opposite margins of the lesion. Nodule volume is calculated by the standard formula $V = (L \times W \times D) \times 0.52$, where L, W, and D are the length, width, and depth of the nodule, respectively [3]. The calculation of nodule volume in addition to its dimensions is important for precise dynamic follow-up of the thyroid lesions in cases of conservative treatment or minimally invasive modalities.

5.1 Nodular Goiter

Nodular goiter (colloid goiter, nontoxic nodular goiter, simple goiter) is a benign thyroid disease in the form of a nodule (nodules) containing ordinary cells and colloid. It is often associated with iodine deficiency and accounts for 60–75% of all thyroid lesions.

The basic US features of colloid nodules are as follows (Fig. 5.1):

- Oval (or roundish) shape
- Well-defined, smooth margins
- Intact thyroid capsule
- Decreased or unchanged echodensity in most cases
- Heterogeneous structure, often fluid inclusions
- Possible calcifications within the lesion and peripheral “egg-shell” calcification
- Hypoechoic surrounding halo
- Possible posterior echo enhancement
- A- or hypovascularity in CDI and PDI
- Medium elasticity with elastography and elastometry

Obligatory US features of colloid nodule are well-defined margins and intact capsule of both the nodule and thyroid gland. Long-lasting colloid nodules may contain coarse calcifications and shell-shaped or egg-shell peripheral impregnations. A calcium capsule may be observed in 2–4% of cases and can reach 2–3 mm thick (Fig. 5.2). The peripheral calcification significantly differs from microcalcifications and large echogenic inclusions, which are often detected in thyroid cancer.

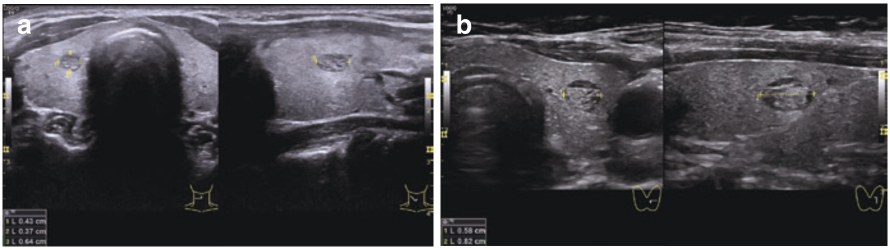

Fig. 5.1 (**a**, **b**) Colloid nodule. Grayscale sonography

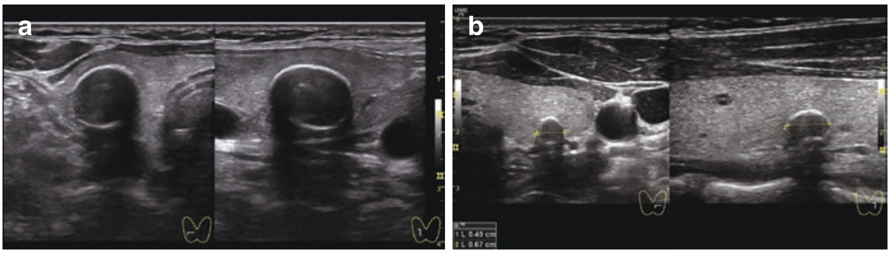

Fig. 5.2 (**a**, **b**) Colloid nodule. Grayscale sonography. “Egg-shell” calcification

Seventy to eighty percent of colloid goiters appear to be multinodular (Fig. 5.3). Multiple nodules often show identical echostructure. Combinations of colloid nodules with cysts, adenomas, or thyroid cancer are less common [4].

Colloid nodules show a peripheral pattern of blood flow with individual vascular signals in CDI in 40–50% of cases. This pattern is associated with the benign character of the nodules. According to Zubarev et al. [5] and Markova [6], CDI and PDI show rectilinear vascular structures that are normally distributed within colloid nodules (Fig. 5.4).

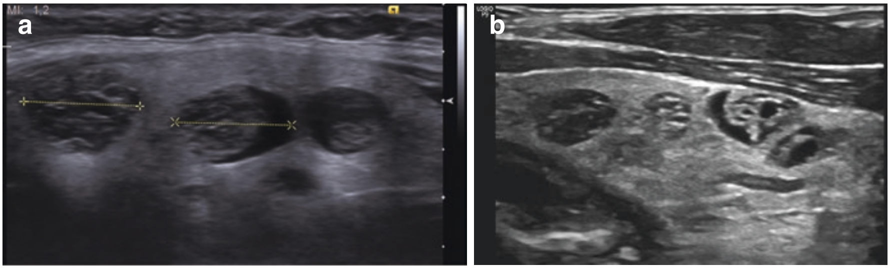

Fig. 5.3 (**a**, **b**) Multiple colloid nodules. Grayscale sonography

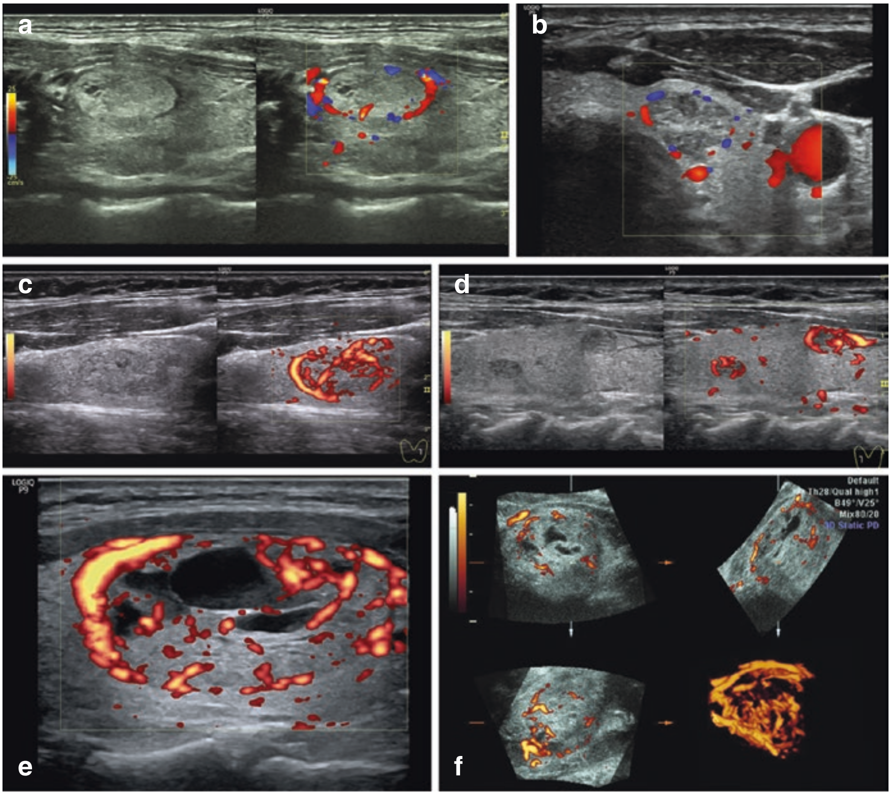

Fig. 5.4 Colloid nodule. Predominantly peripheral blood flow pattern. Sonograms. (**a**, **b**) CDI. (**c**–**e**) PDI. (**f**) 3DPD

Qualitative data of compression USE and quantitative parameters of elasticity (Young's modulus, strain-ratio index, share-wave velocity) in colloid nodes commonly reveal medium stiffness (elasticity), equal to the surrounding unchanged thyroid parenchyma (Fig. 5.5).

There is no need to use CEUS for typical colloid nodules. CEUS in colloid nodules commonly shows hypoenhancement, without any signs of hypervascularity and neoanogenesis (Fig. 5.6). Peripheral ring-shaped contrast enhancement is highly specific for benign thyroid nodules (sensitivity 83%, specificity 94%, positive predictive value 94%, negative predictive value 84%, overall accuracy of 88%) [7].

The specificities of US in grayscale, CDI, PDI, and 3D at diagnosing colloid nodules are 32.1, 47.6, 69.6, and 84.1%; their sensitivities are 70.7, 61.6, 65.5, and 75.7%; and their diagnostic accuracies are 53.1, 56.5, 70.3, and 79.8%, respectively [8]. According to Zubarev et al. [5], Doppler options and 3D reconstruction increase the sensitivity of sonography to colloid nodules by 5% (up to 75.5%), the specificity by 52% (up to 84.1%), and the diagnostic accuracy by 26.7% (up to 79.8%).

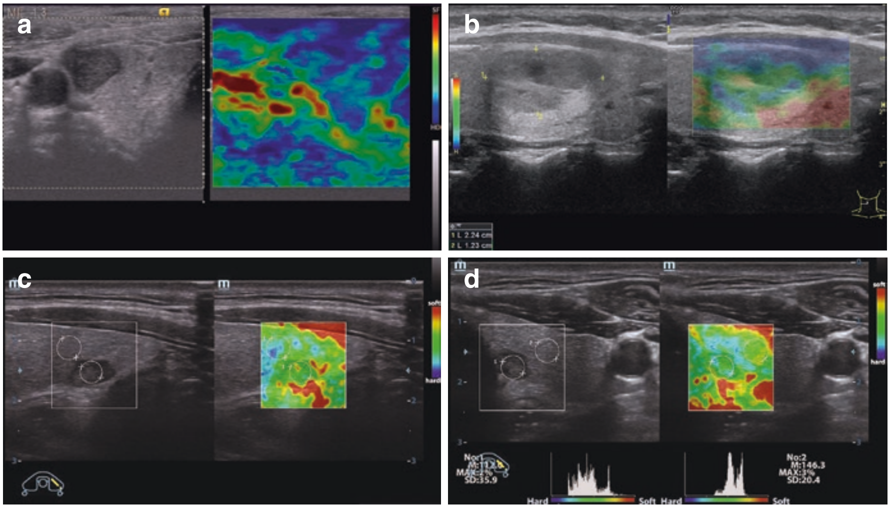

Fig. 5.5 Colloid node. (**a**, **b**) Compression USE. Color pattern similar to the surrounding thyroid parenchyma. (**c**, **d**) Strain-ratio index equal to normal thyroid tissue

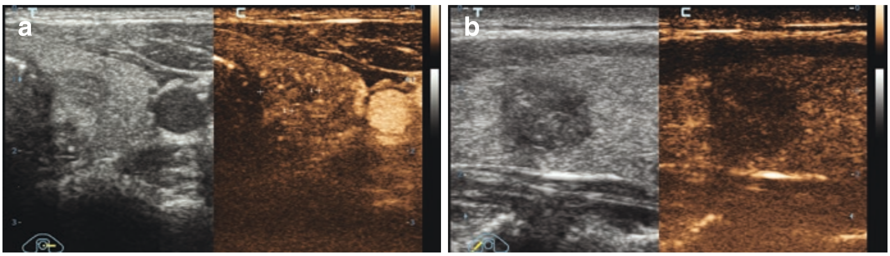

Fig. 5.6 (**a**, **b**) Colloid thyroid nodule. CEUS with SonoVue® 2.4 mL

The Example US Report in Colloid Goiter

- First name, middle initial, last name:
- Age:
- Date:
- The number of case history:
- US scanner:

The thyroid gland is typically located with regular well-defined margins and homogeneous isoechoic structure. The capsule is uniform and continuous on all extent.

The depth of the *isthmus*: 4 mm			
Right lobe		Left lobe	
Depth	16 mm	Depth	15 mm
Width	17 mm	Width	16 mm
Length	51 mm	Length	50 mm
Volume	6.6 cm^3	Volume	5.7 cm^3
The total volume 12.3 cm^3 does not exceed the upper limit			
A hypoechoic heterogeneous hypovascular nodule of 0.5 × 0.5 × 0.6 cm in size of roundish shape with well-defined regular margins, soft with USE, strain ratio 1.1, is located in the middle compartment of the lobe		A hypoechoic homogeneous avascular nodule of 0.8 × 0.7 × 0.9 cm in size with well-defined regular margins, soft with USE, strain ratio 1.1, is located in the inferior segment of the lobe	

The vascular pattern of the parenchyma is normal and symmetric with CDI and PDI. CPD is 10–15%.

The lymph nodes in the neck and supraclavicular areas are not enlarged.

CONCLUSION: Thyroid nodules, TIRADS 2.

US specialist:

5.2 Cyst

Thyroid cysts are thin-walled cavitary lesions filled with fluid (commonly, colloid). Cysts comprise up to 3–5% of all thyroid nodules. True cysts with flat epithelium lining make up <0.5% of all thyroid lesions and, as a rule, are represented by a single cyst. Fluid collections, which are often detected in thyroid nodules, are in most cases a consequence of colloid accumulation or degenerative changes.

Thyroid cysts are sonographically characterized by the following typical features (Fig. 5.7):

- Roundish or oval shape.
- Regular, well-defined margins.
- Anechoic homogenous inner structure; in rare cases the presence of echogenic inclusions or an isoechoic component is possible.
- Dorsal echo enhancement, especially intense in cysts over 5 mm in size.

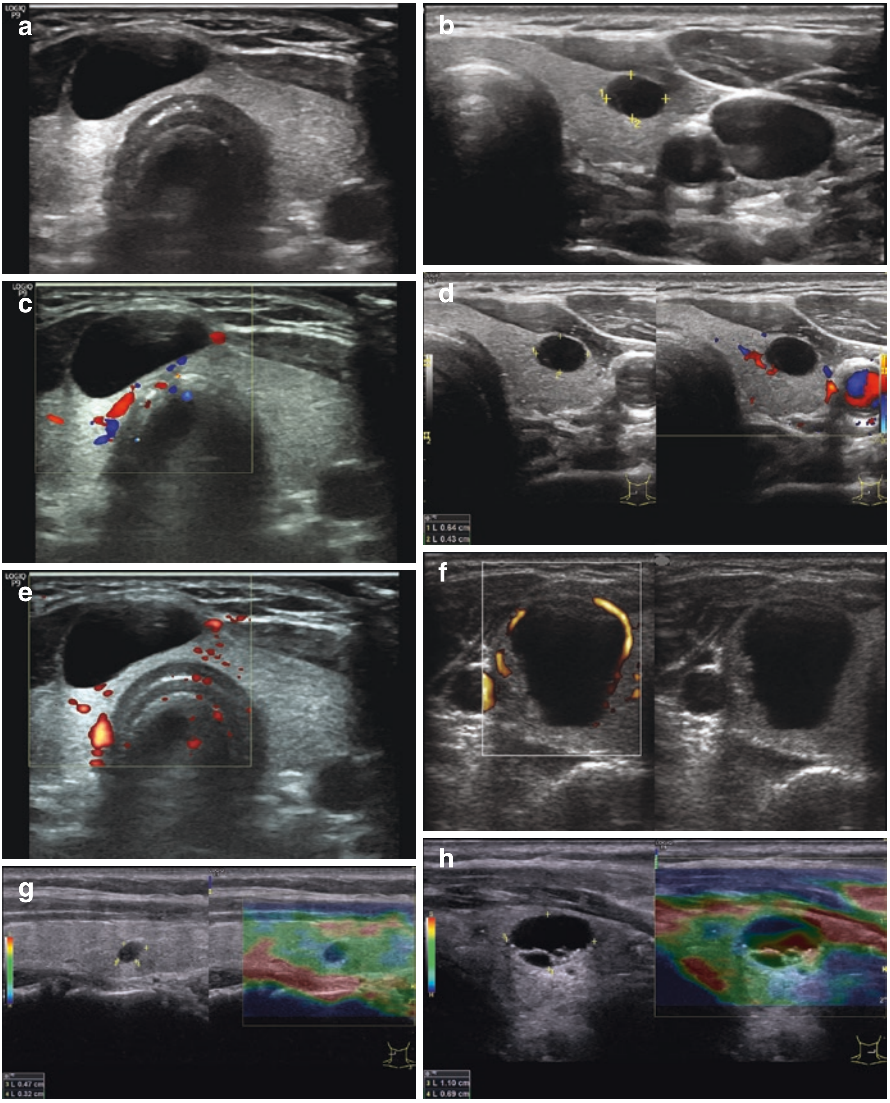

Fig. 5.7 Simple thyroid cyst. (**a**, **b**) Grayscale US. (**c**, **d**) CDI. (**e**, **f**) PDI. (**g**, **h**) Compression USE

- Lateral acoustic shadows, more often associated with cysts over 10 mm in size.
- Avascularity in CDI and PDI and in rare cases vascularization of a solid component.
- Compression US elastography reveals Score 1 according to Ueno-Itoh scale, which corresponds with either a homogeneous elasticity throughout the lesion or the image in three layers produced by reverberation artifacts. No color pattern is often observed. The average strain ratio is 0.5–2.
- Avascularity (perfusion defect) with CEUS.

Thyroid cysts differ in their origins and morphological structures. The following types can be defined [9]:

1. Simple colloid cysts
2. Complex cysts (Fig. 5.8)
   - Result from previous inflammatory processes in thyroid parenchyma
   - Filled with transudate
   - Contain the products of hemorrhages
   - The connective tissue component merges into the lumen
   - Have an epithelial component

Thyroid nodules that contain dense colloid may be observed as anechoic lesions and smooth, well-defined margins. They usually measure up to 1 cm in size and often show distinct point-like echogenic signals with a "comet tail," which

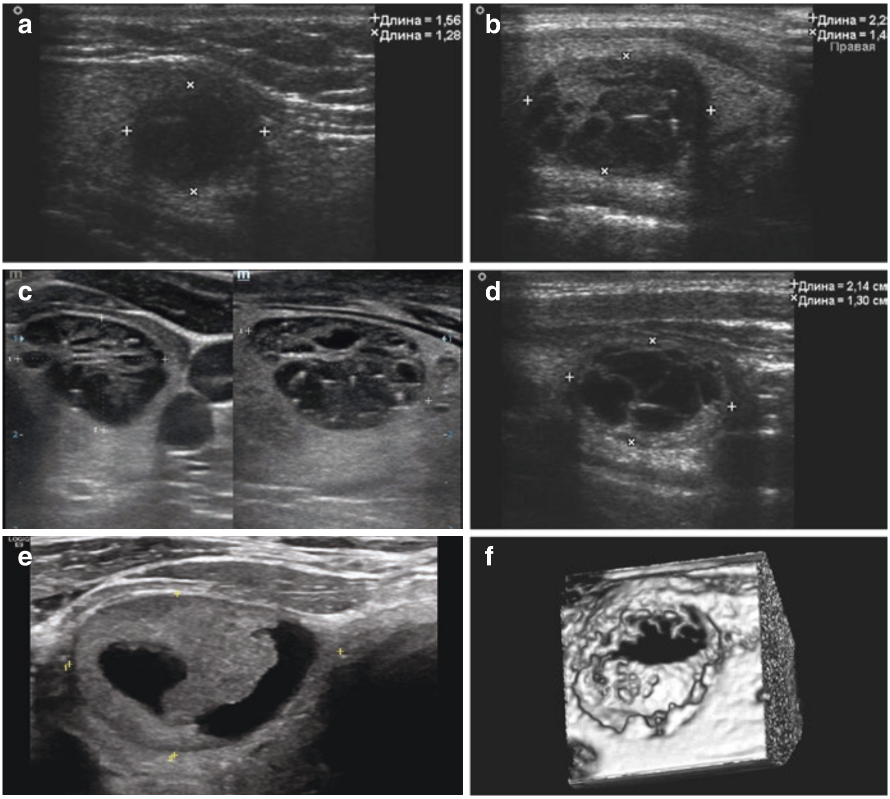

Fig. 5.8 Complex thyroid cyst. (**a**, **b**) Complex thyroid cyst containing products of hemorrhage. Grayscale sonography. (**c**, **d**) Complex thyroid cyst with connective tissue component. Grayscale sonography. (**e**) Complex thyroid cyst with epithelial component. Grayscale sonography. (**f**) 3D reconstruction

characterize dense colloid contents [10]. The “comet tail” is an acoustic phenomenon that results from ultrasound reverberation. It is observed when the US wave is caught between two or multiple reflecting surfaces. Reverberations occurring in grayscale sonography are detected as a short hyperechoic trace (“tail”) behind the source of the artifact (Fig. 5.9).

The abovementioned colloid lesions are normally multiple and correspond morphologically to enlarged follicles (macrofollicles) (Fig. 5.10). All cysts, including complex cysts, appear avascular in CDI and PDI (Fig. 5.11).

The incidence of malignancy in cystic lesions is about 7–19% [11]. Up to 20–30% of papillary thyroid cancers demonstrate fluid collections [12]. In cases

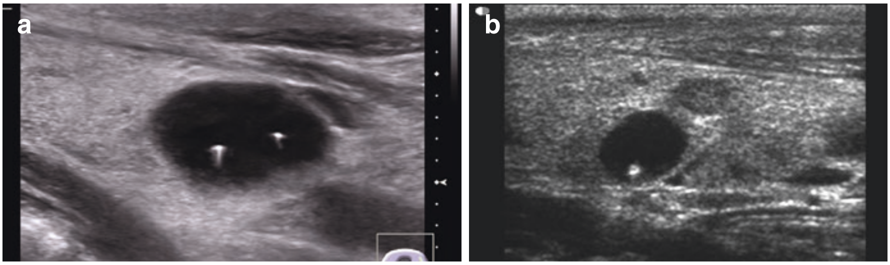

Fig. 5.9 (**a**, **b**) Colloid cyst. “Comet tail” sign. Grayscale sonography

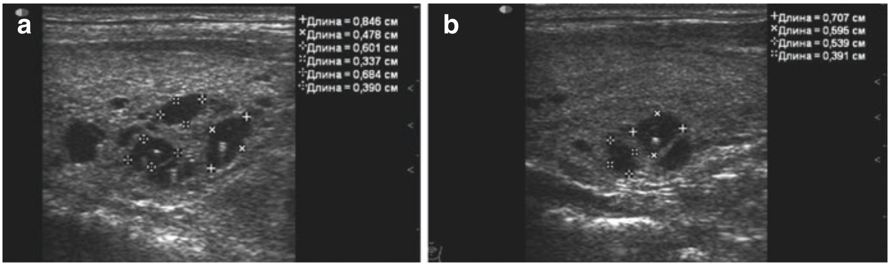

Fig. 5.10 Multiple colloid cysts (macrofollicles). (**a**, **b**) “Comet tail” sign. Grayscale sonography

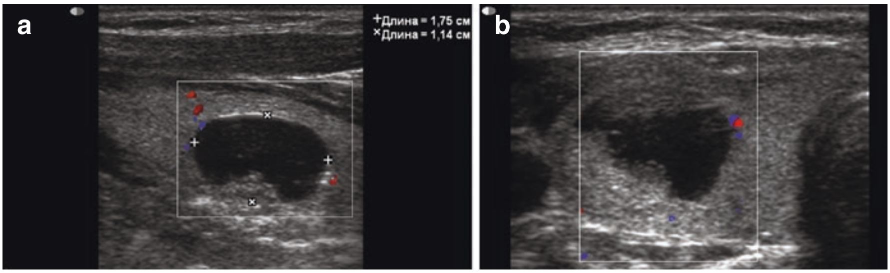

Fig. 5.11 (**a**, **b**) Complex cysts. Avascularity with CDI

with a solid component within the cyst, CDI and PDI are required. Increased vascularity of connective tissue septa and solid components demands further examinations (Fig. 5.12). Avascularity of septa is a reliable sign of a benign process. This is an important feature that permits nodule differentiation. CEUS is very sensitive in the detection of low-velocity blood flow in septa and solid component, thus contributing to differential diagnosis of complex cysts (Fig. 5.13). Solid component of complex thyroid cysts often exhibits the stiffness that is different from fluid component with compression US elastography and share-wave elastography (Fig. 5.14). However, the presence of fluid collections makes these options less reliable.

The specificities of US in grayscale, CDI, PDI, and 3D for thyroid cysts are 26, 63, 63, and 63%, with sensitivities of 96, 90, 90, and 90% and diagnostic accuracies of 64, 80, 80, and 80%, respectively [8].

Sonography permits not only cyst detection but also preliminary assessment of the nature of these lesions. However, it is often impossible to determine the

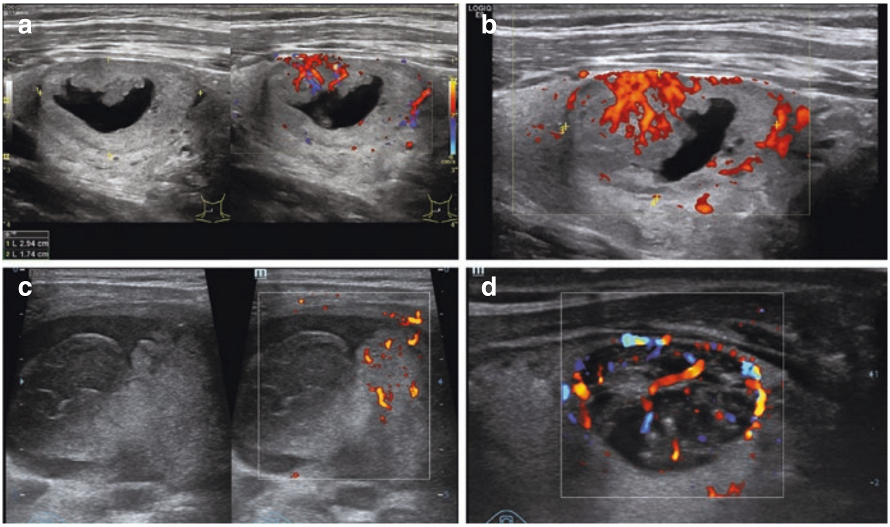

Fig. 5.12 (**a**–**d**) Papillary thyroid cancer with fluid component and hypervascular solid part. Echograms. Gray scale mode, CDI, PDI

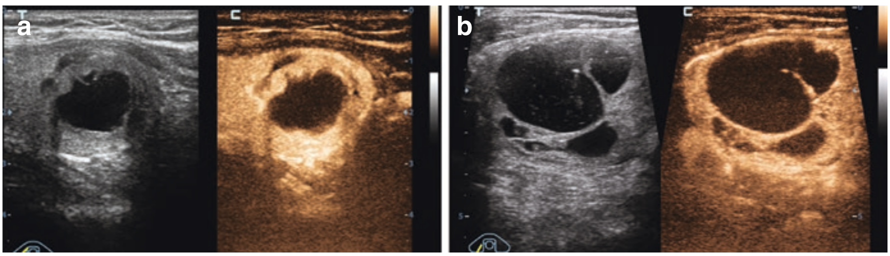

Fig. 5.13 (**a**, **b**) Thyroid lesion with fluid collections and vascularized solid component. Thyroid CEUS with SonoVue® 2.4 mL. FNAB returned colloid nodule, BSRTC 2

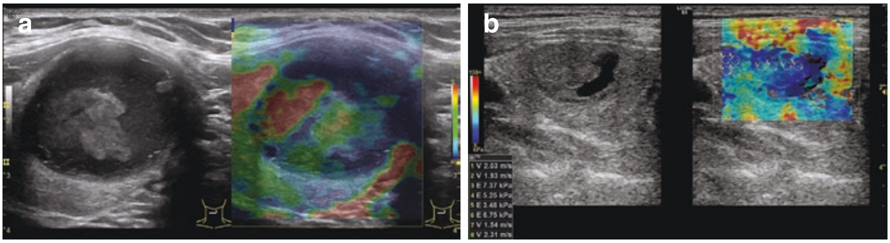

Fig. 5.14 Complex thyroid cyst. (**a**) Compression US elastography. (**b**) Quantitative parameters with share-wave elastography

morphological nature of the solid part of a complex cyst with a single US examination. Therefore, any suspicion of thyroid malignancy should be followed by US-guided FNAB.

The Example US Report in Thyroid Cyst

- First name, middle initial, last name:
- Age:
- Date:
- The number of case history:
- US scanner:

The thyroid gland is typically located with regular well-defined margins and homogeneous isoechoic structure. The capsule is uniform and continuous on all extent.

The depth of the *isthmus*: 3 mm			
Right lobe		Left lobe	
Depth	16 mm	Depth	15 mm
Width	17 mm	Width	16 mm
Length	51 mm	Length	50 mm
Volume	6.6 cm^3	Volume	5.7 cm^3
The total volume 12.3 cm^3 does not exceed the upper limit			
A homogenous anechoic avascular lesion of 0.9 × 0.8 × 0.5 cm in size of roundish shape with well-defined regular thin walls and posterior enhancement is located in the inferior segment of the lobe. Compression US elastography detects no color pattern, strain ratio is 1.0		A homogenous anechoic avascular lesion of 0.9 × 1.0 × 0.8 cm in size with well-defined regular margins and a single echogenic signal within its central compartment is located in the middle segment of the lobe. Compression US elastography detects no color pattern, strain ratio is 1.2	

The vascular pattern of the parenchyma is normal and symmetric with CDI and PDI. CPD is 10–15%.

The lymph nodes in the neck and supraclavicular areas are not enlarged.

CONCLUSION: Fluid (probably, colloid) thyroid lesions. TIRADS 2.

US specialist:

5.3 Adenoma

Adenomas are benign thyroid tumors, which develop as a result of local thyrocyte hyperplasia and proliferation due to genetic abnormality in a single precursor cell. Toxic adenomas (Plummer's disease) autonomously overproduce thyroid hormones and are accompanied by clinical symptoms of thyrotoxicosis.

Adenomas occupy 16–25% of all thyroid lesions [1]. They are typically represented by a solitary nodule. Multiple lesions are rare.

Thyroid adenomas are histologically typed according to the following classification [13]:

a. Follicular adenoma
   1. Simple adenoma (colloid macrofollicular adenoma)
   2. Microfollicular adenoma
   3. Fetal adenoma
   4. Embryonal (trabecular) adenoma
b. Papillary adenoma
c. Variants
   1. Oxyphilic (Hürthle cell) adenoma
   2. Clear cell adenoma
   3. Functioning adenoma (Plummer's disease, toxic multinodular goiter)
   4. Others

Various morphological types of adenomas cannot be sonographically differentiated. Follicular adenoma is the predominant benign thyroid tumor, accounting for over 85% of all benign neoplasms of the gland [14].

Typical US features of thyroid adenoma are as follows (Fig. 5.15):

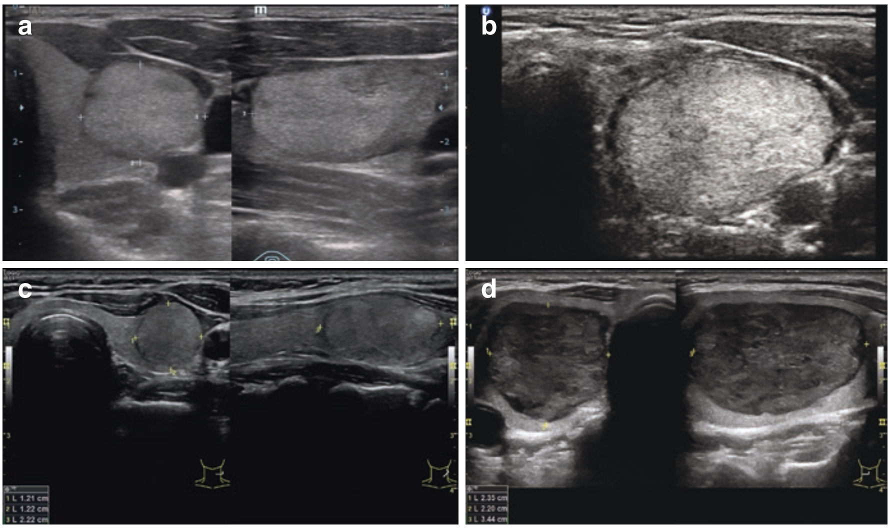

Fig. 5.15 Thyroid adenoma. (**a**–**d**) Grayscale US

- Oval or spherical shape.
- Low echodensity.
- Homogeneous or moderately heterogeneous echostructure.
- Regular, well-defined margins.
- Hypoechoic halo 1–3 mm in width.
- Intact thyroid capsule.
- Absence of calcifications.
- Hypervascularity with a mixed (central and peripheral) pattern and a regular distribution of vessels within the nodule in CDI and PDI is usually seen. A perinodular vascular ring corresponding to a halo is characteristic. Radial centripetal vessels connected to the peripheral ring (a "basketball basket" sign) are commonly detected.
- Compression USE reveals significant increase in lesion elasticity that is substantially different from the surrounding parenchyma. Elastometry detects strain ratio about 3.0 or higher.
- CEUS demonstrates hypervascularity with typical vascular halo and centripetal pattern.

Thyroid adenomas tend to grow fast, so they are normally large (over 2–3 cm in size) by the time they are diagnosed. The majority of adenomas show a peripheral hypoechoic ring (halo) in grayscale sonography. A halo is present in 87% of thyroid adenomas. It corresponds to histological capsule, edema of the surrounding normal parenchyma (especially in fast-growing lesions), or to nodule vessels. Thyroid adenomas show a typical vascular pattern in CDI and PDI (Fig. 5.16) with perinodular

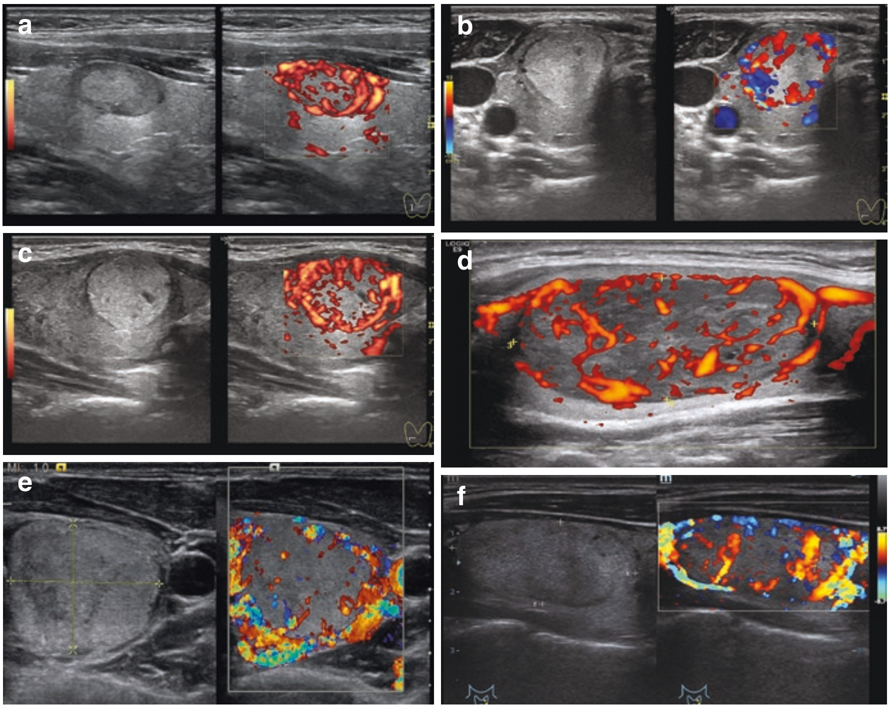

Fig. 5.16 Thyroid adenoma. Typical vascular pattern. (**a**–**f**) Grayscale US, PDI, and CDI

and intranodular hypervascularization: a perinodular vascular ring (corresponding to a halo, which is not always evident in grayscale) with centripetal radial vessels. This pattern was named "basketball basket." According to Sencha [15], this sign is observed in 25% of all thyroid adenomas. The vessels within adenomas appear visually dilated and wavy, with a centripetal direction. Regular vascular pattern without disorganization contributes in differentiation of adenoma from cancer.

Adenomas can undergo degeneration with cystic or hemorrhagic changes or calcination. Adenomas with a significantly decreased echodensity are often difficult to differentiate from colloid nodules and malignant tumors. Hypoechoic areas in adenomas are a consequence of hemorrhages into the nodule. The anechoic component in central or peripheral compartments of the lesion with typical fluid echostructure is thought to be associated with cystic degeneration (Fig. 5.17).

According to Struchkova [16], blood flow velocities in the main thyroid arteries and peripheral vessels of micro- and macrofollicular adenomas, as measured with PW Doppler, are increased compared with micro- and macrofollicular goiters (PSV = 19.3–40.1 cm/s vs. 10.9–30.6 cm/s, EDV = 5.6–13 cm/s vs. 3.3–10.8 cm/s, RI = 0.45–0.6 vs. 0.6–0.8, and PI = 0.8–1.2 vs. 0.7–1.1, respectively). Kotlyarov et al. [17] did not find any significant change in blood flow parameters in the vessels of adenomas with PW Doppler.

Compression USE commonly reveals intense staining of thyroid adenomas that is different from the surrounding parenchyma. The quantitative data of share-wave elastography prove abnormal elasticity of thyroid adenomas (Fig. 5.18).

The use of contrast agents fully demonstrates peripheral and central hypervascularization of thyroid adenomas. The wash-in phase is fast. It clearly reveals the characteristic "basketball basket" sign, which starts from the periphery of the lesion (Fig. 5.19). Follicular adenomas often exhibit the same microvascular architecture as follicular cancer.

According to Schleder et al. [18], thyroid adenomas and carcinomas with CEUS have statistically significant differences in temporal parameters of microvascularity. Thyroid adenomas exhibit very slow overall wash-out or central wash-out with persistent peripheral contrast enhancement in late phase. Thyroid carcinomas are characterized by complete washout. The evaluation of the dynamics of washout is of high diagnostic value (sensitivity, 81%; specificity, 92%; positive predictive value,

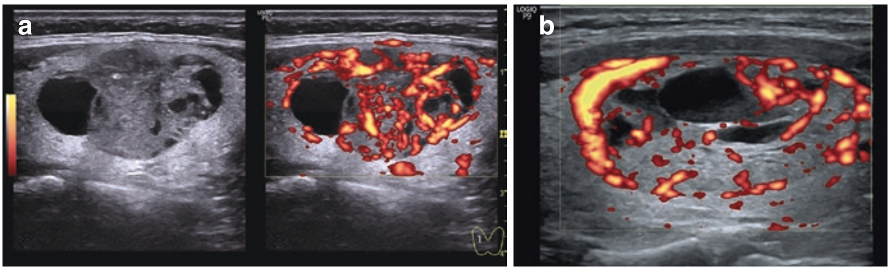

Fig. 5.17 Thyroid adenoma. Cystic degeneration. (**a**–**b**) Grayscale US and PDI

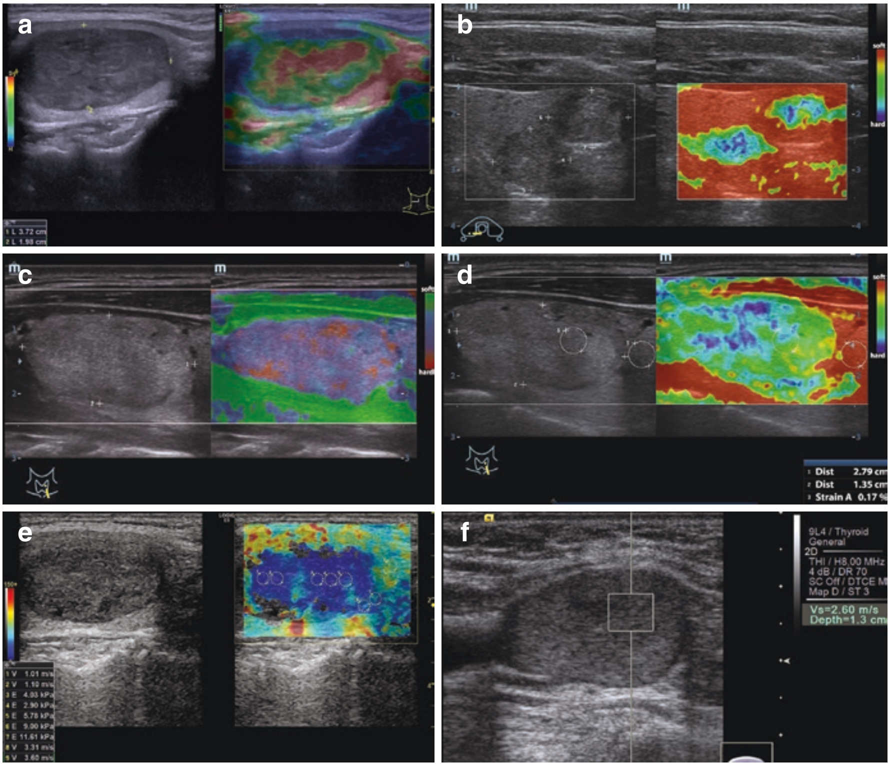

Fig. 5.18 Thyroid adenomas. (**a**–**c**) Compression USE. (**d**) Strain ratio. (**e**) Share-wave elastography. (**f**) ARFI

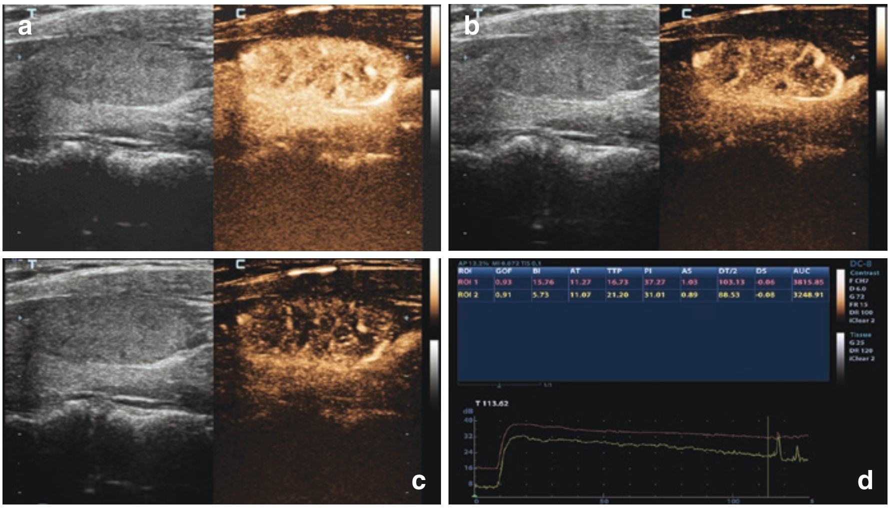

Fig. 5.19 Follicular adenoma of the thyroid gland. Thyroid CEUS with SonoVue® 2.4 mL. (**a**–**c**) Phases of contrast enhancement. (**d**) Time-intensity curve

97%; negative predictive value, 63%). It permits a more reliable differential diagnosis between adenomas and thyroid carcinomas [18].

The specificities of sonography in grayscale, CDI, PDI, and 3D in the diagnosis of thyroid adenomas are about 30, 56.6, 68.7, and 79.2%, with sensitivities of 79.9, 84, 89.5, and 93.4% and diagnostic accuracies of 38.2, 61.5, 72, and 82%, respectively [8]. According to Zubarev et al. [5], combining Doppler options with 3D increases the sensitivity of US to adenomas by 13.5% (up to 93.4%), its specificity by 49.2% (up to 79.2%), and its diagnostic accuracy by 43.8% (up to 82%).

The literature and our own experience prove that none of the features listed above can serve as an absolute criterion of the benign character of a thyroid nodule. Thyroid adenomas commonly belong to the category of TIRADS 4 or TIRADS 3. The role of US is often limited to the selection of the patients with nodules that are suspicious for a tumor and subsequent US-guided FNAB. The cytology often permits the benign nature of the obtained cells to be specified, but this is quite a problem in several cases, such as for follicular tumors and others.

The Example US Report in Thyroid Adenoma

- First name, middle initial, last name:
- Age:
- Date:
- The number of case history:
- US scanner:

The thyroid gland is typically located with regular well-defined margins and homogeneous isoechoic structure. The capsule is uniform and continuous on all extent.

The depth of the *isthmus*: 4 mm			
Right lobe		Left lobe	
Depth	19 mm	Depth	15 mm
Width	19 mm	Width	16 mm
Length	52 mm	Length	50 mm
Volume	9.0 cm^3	Volume	5.7 cm^3
The total volume 14.7 cm^3 does not exceed the upper limit			
A moderately heterogeneous slightly hypoechoic lesion of 1.8 × 1.8 × 3.2 cm in size of roundish shape with well-defined regular margins with halo is located in the lower half of the lobe. The lesion is hypervascular with predominantly peripheral blood flow and regularly distributed centripetal vessels. Compression US elastography detects hard pattern, strain ratio is 4.0		No lesions detected	

The vascular pattern of the parenchyma is normal and symmetric with CDI and PDI. CPD is 10–15%.

The lymph nodes in the neck and supraclavicular areas are not enlarged.

CONCLUSION: A lesion of the right thyroid lobe, suspicious for adenoma. TIRADS 4.

US specialist:

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