The Thyroid Nodule: From the Ultrasound Image to the Anatomopathological Diagnosis

T. González de la Huebra Labrador, A. Herrero Hernandez, C. Santos Montón, J. F. Ojeda Esparza, D. C. Cuellar, O. Padilla Campo; Salamanca/ES

Learning objectives

The purposes of this exhibit are:

- To review the different thyroid nodules, both benign and malignant.

- To describe the most common ultrasonography (US) features in each type of nodule (correlating it with its anatomopathological diagnosis), with special emphasis on the key aspects of the exploration which may shed light on the malignant nature of a nodule.

- To review the indications of fine-needle aspiration (FNA) biopsy in the study of thyroid nodules.

Background

Thyroid nodules are very common in the adult population (especially in elderly or female patients and in people with iodine deficiency or with a history of neck irradiation); however, the vast majority of them are benign. Just about 5% of thyroid nodules are malignant.

US is the first and the most sensitive imaging technique employed for the study of thyroid nodules and it may be used for guidance of FNA. Suspicious US features are useful for selecting patients for FNA biopsy.

Some basic concepts in US findings:

- The size of a thyroid nodule is not helpful for distinguishing a malignant from a benign nodule.

- The internal content of a nodule is categorized by the ratio between the cystic and the solid portions: solid, predominantly solid, predominantly cystic, and cystic.

- The parenchymal echogenicity of the thyroid gland is used as a reference for nodule echogenicity.

- Calcifications (in both benign and malignant nodules) include: **microcalcifications** Fig. 2 (tiny, punctuate echogenic foci of 1 mm or less, sometimes too small to produce posterior shadowing), coarse or **macrocalcifications** Fig. 5 (echogenic foci larger than 1 mm), and **rim**

calcifications (when a nodule has peripheral curvilinear or eggshell calcification).

- When punctuate echogenic foci are accompanied by reverberation artifacts, they are usually due to **colloid** materials Fig. 1 (easily differentiated from calcification on real-time US).

- Color and power Doppler US does not usually help are for distinguishing malignant and benign nodules (nonspecific findings).

Findings and procedure details

BENIGN NODULES:

Most thyroid nodules are benign nonneoplastic lesions that are anatomopathologically diagnosed either as **adenomatoid nodules** (with a variable amount of colloid or an increased number of follicular epithelial cells) or as **lymphocytic thyroiditis**.

Colloid materials are often seen as punctuate echogenic foci accompanied by reverberation (comet tail or ring-down) artifacts Fig. 1 .

The **spongiform appearance**, specific for benign nodule, is described as the aggregation of multiple microcystic components in more than 50% of the volume of the nodule.

A complete cystic lesion (**simple cyst**), a predominantly cystic or cystic nodule containing **colloid** artifacts Fig. 1 , a nodule with a **spongiform appearance,** and **isoechogenicity**, are findings which correspond to ***probably benign nodules*** (very specific for benignancy).

Sometimes a nodule shows an accompanying **hypoechoic halo** (a rim surrounding the nodule, a pseudocapsule caused by fibrous connective tissue and compressed thyroid tissue). A complete halo is a finding suggestive of benign nodule, but not specific.

Perinodular flow (on color or power Doppler US) is mainly a characteristic finding for benign nodules, but not specific.

MALIGNANT NODULES:

Risk factors for thyroid cancer include: family history of thyroid cancer, personal history of neck irradiation, male sex, age of less than 30 years or more than 60 years, and previous diagnosis of type 2 Multiple Endocrine Neoplasia (MEN).

The main pathologic types of thyroid **carcinoma** are: **papillary** Fig. 2 , **follicular** Fig. 3 (both with an excellent prognosis), **medullary** Fig. 4 (more aggressive), and **anaplastic** Fig. 5 (which has an extremely poor prognosis).

The most frequent malignant neoplasm is **papillary** carcinoma (psammoma bodies are

observed in the histologic diagnosis, seen as microcalcifications at US Fig. 2). The US findings for **medullary** carcinoma are almost the same Fig. 4 .

Although a cystic nodule is very rare for a thyroid malignancy, a mural solid component within the cystic nodule may be **papillary** thyroid carcinoma. Therefore, a small solid component in a predominantly cystic or cystic nodule should be carefully examined (and aspirated in case of presence of a suspicious malignant feature).

Hurthle cell carcinoma is a variant of **follicular** carcinoma Fig. 3 .

Thyroid **lymphoma** Fig. 6 is uncommon.

Metastases to the thyroid are rare and usually originate from primary lung, breast, and renal cell carcinomas Fig. 7 .

Sarcomas are extremely rare.

Aggressive local invasion is relatively common in **anaplastic** carcinoma Fig. 5 , **lymphoma** Fig. 6 and **sarcoma** (the nodule may cross the thyroid capsule and invade the adjacent structure such as trachea, esophagus and thyroid cartilage).

Thyroid **microcarcinoma** (small thyroid carcinomas) is defined as a tumour with a maximal diameter of less than or equal to 1 cm. Its diagnosis is very important because thyroid microcarcinomas may manifest with early lymph node metastasis Fig. 8 or extranodal invasion.

Mortality and rate of recurrence is directly proportional to the size of a thyroid tumor. However, even a **micropapillary** thyroid carcinoma has a substantial number of lymph node metastases Fig. 8 and recurrences.

Patients with multiple thyroid nodules have the same risk of malignancy as patients with solitary thyroid nodules. Multifocality and bilaterality is not uncommon even in thyroid microcarcinomas (therefore, multiple and bilateral nodules should not be regarded just as a multinodular goiter).

Intratumoral hypervascularity (evaluated by using Color or Power Doppler US) is observed in most of thyroid carcinomas, but it is a nonspecific finding.

The tissue of carcinoma is harder and firmer than that of the normal thyroid parenchyma or a benign nodule (helpful if we use US elastography, a new technique to measure the elasticity of tissue).

IMAGING FINDINGS SUGGESTIVE OF MALIGNANCY:

- A **taller-than-wide shape** (height that exceeds width).
- A **spiculated margin** (irregular or microlobulated).
- Marked **hypoechogenicity** Fig. 3 Fig. 4 Fig. 5 Fig. 7 .
- **Microcalcifications** Fig. 2 Fig. 4 Fig. 8 .
- **Macrocalcifications** Fig. 4 .

These are all findings with a specificity of over 90% for the diagnosis of malignancy. Therefore, the presence of at least one of them defines a nodule as a ***suspicious malignant nodule***.

Other US features that may be suggestive of malignancy include:

- Disruption of eggshell or rim calcification and a hypoechoic halo.
- Aggressive local invasion (direct tumor invasion of adjacent soft tissue).
- Solid nodule with intrinsic (intratumoral) vascularity.
- Metastasis lymph nodes Fig. 3 Fig. 6 Fig. 8 .

WHICH NODULES SHOULD BE BIOPSIED? GUIDELINES:

Fine-needle aspiration (FNA) biopsy is the most accurate and cost-effective method for diagnostic evaluation of thyroid nodules, with a high sensitivity and specificity for thyroid cancer detection. Furthermore, it is minimally invasive and safe (usually performed on an outpatient basis).

The results of FNA biopsy are operator dependent. Areas of fibrosis, calcification, and cystic degeneration should be avoided in order to have a better specimen adequacy; therefore, US-guided FNA is more likely to result in a correct diagnosis than palpation-guided FNA.

The threshold for biopsy of a thyroid nodule in a patient with risk factors for thyroid cancer should be lower than in a patient without risk factors.

A repeat FNA biopsy should be considered if: discordance between the findings at imaging and those at cytologic analysis, a growing mass, a recurrent cyst, or an inadequate FNA sample.

Indications for US-guided FNA (USFNA) biopsy and follow-up for thyroid nodules depend on the US findings.

The US findings allow us to divide thyroid nodules into three categories: ***suspicious malignant nodules***, ***probably benign nodules*** and ***indeterminate nodules*** (neither malignant nor benign features, without clear evidence of being benign or malignant).

When a single nodule is found, the presence of at least one malignant US finding necessitates USFNA regardless of the size of the nodule (but nodules smaller than 5 mm in size have a high rate of false positive US findings and a high rate of inadequate cytology). The **American Thyroid Association** (ATA) guideline recommends that a subcentimeter nodule should be biopsied only if the nodule has a suspicious finding or the patient has risk factors for thyroid cancer. For a nodule smaller than 5 mm, selective FNA can be done according to patient's risk factors and the experience of the radiologists (there is still debate concerning the fate and prognosis of microcarcinomas).

If a nodule has indeterminate findings on US and it is larger than 1 cm in diameter, then performing FNA is recommended (because possibility of malignancy cannot be excluded). If it is 1 cm or less in size, then an FNA biopsy is not necessary and follow-

up US would suffice.

If a benign appearing nodule (e.g., a spongiform nodule) is larger than 1 cm, performing follow-up US in two years and thereafter at 3-5 year intervals is recommended. If it is larger than 2 cm, then selective FNA biopsy can be done. Neither FNA nor follow up US is necessary for a spongiform nodule and a benign appearing nodule 1 cm or less in diameter.

In the case of multiple nodules of the thyroid, we should choose the nodules to be biopsied according to the US findings (not depending on the size criteria). According to the ATA guideline, in the presence of two or more nodules 1-1.5 cm or more in size, a FNA biopsy is recommended for nodules with suspicious US findings. If none of the nodules has suspicious US findings, then FNA should be done for the largest one. It is recommend aspirating at least one nodule for each lobe and at least one nodule (the largest) among multiple nodules that have similar US findings.

The size change criteria adopted from the ATA guideline recommend an FNA biopsy if an indeterminate nodule is growing. If a benign nodule is growing, then performing an immediate FNA biopsy is not recommend in every incidence. At least one more follow-up US exams can be selectively advised.

When a malignant lymph node is suspected, it is necessary to biopsy it in the lateral neck area as well as a thyroid nodule regardless of the nodule's size and features. Central neck dissection is performed in almost all the patients with thyroid papillary carcinoma; however, lateral neck dissection (levels II-V) is selectively done for patients who have a preoperative diagnosis of lymphatic metastasis. Therefore, USFNA for suspicious lymph nodes may be important for surgical management.

When the initial US findings are probably benign, FNA biopsy is not necessary; follow-up US or clinical observation is advisory for a nodule's change.

Conclusion

The major teaching points of this exhibit are:

- The morphological characteristics of the thyroid nodules allow us to suggest their probable nature.

- The presence of microcalcifications is an example of highly specific finding of malignancy.

- It is important to know the imaging findings suggestive of malignancy and make a FNA biopsy when they are observed in order to reach an anatomopathological diagnosis.

References

1. Moon WJ, Baek JH, Jung SL, Kim DW, Kim EK, Kim JY, Kwak JY, Lee JH, Lee JH, Lee YH, Na DG, Park JS, Park SW. Ultrasonography and the Ultrasound-Based Management of Thyroid Nodules: Consensus Statement and Recommendations. KJR. 2011; 12(1):1–14.
2. Kim MJ, Kim EK, Park SI, Kim BM, Kwak JY, Kim SJ, Youk JH, Park SH. US-guided Fine-Needle Aspiration of Thyroid Nodules: Indications, Techniques, Results. RG. 2008; 28:1869–1889.
3. Hoang JK, Lee WK, Lee M, Johnson D, Farrell S. US Features of Thyroid Malignancy: Pearls and Pitfalls. RG. 2007; 27:847–865.

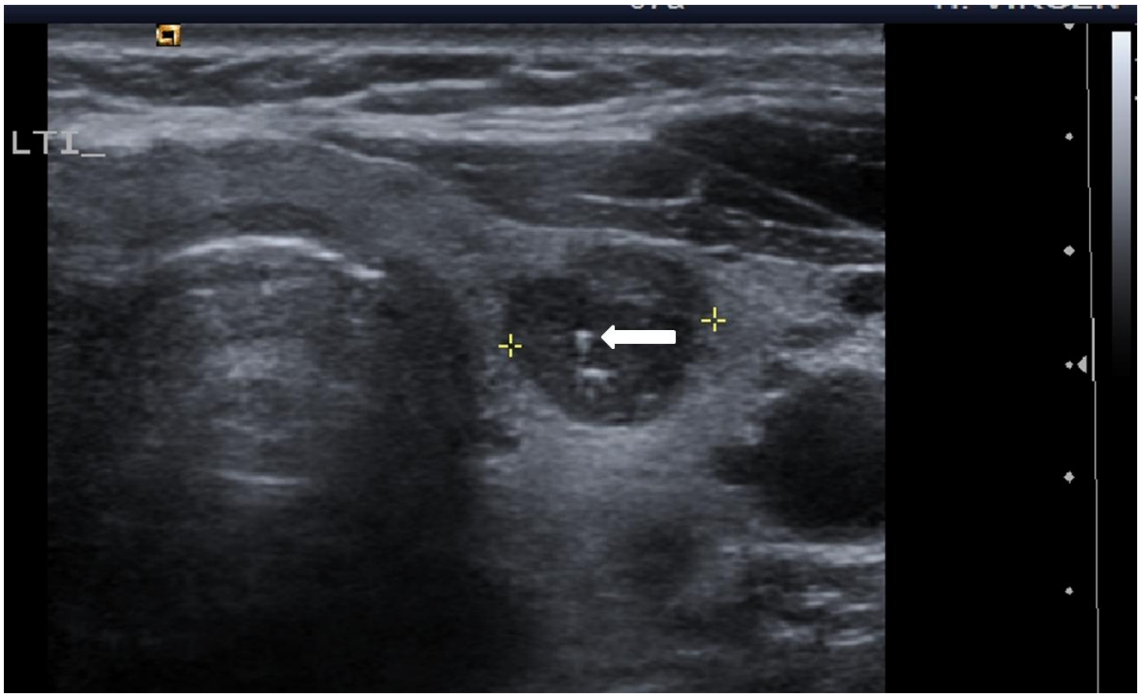


Fig. 1
Annotation:
Benign thyroid nodule: Transverse sonogram of the left lobe of the thyroid shows a predominantly cystic nodule (between calipers) with punctuate echogenic foci and reverberation artifacts (arrow), a finding indicative of inspissated colloid.

Origin and source of image:

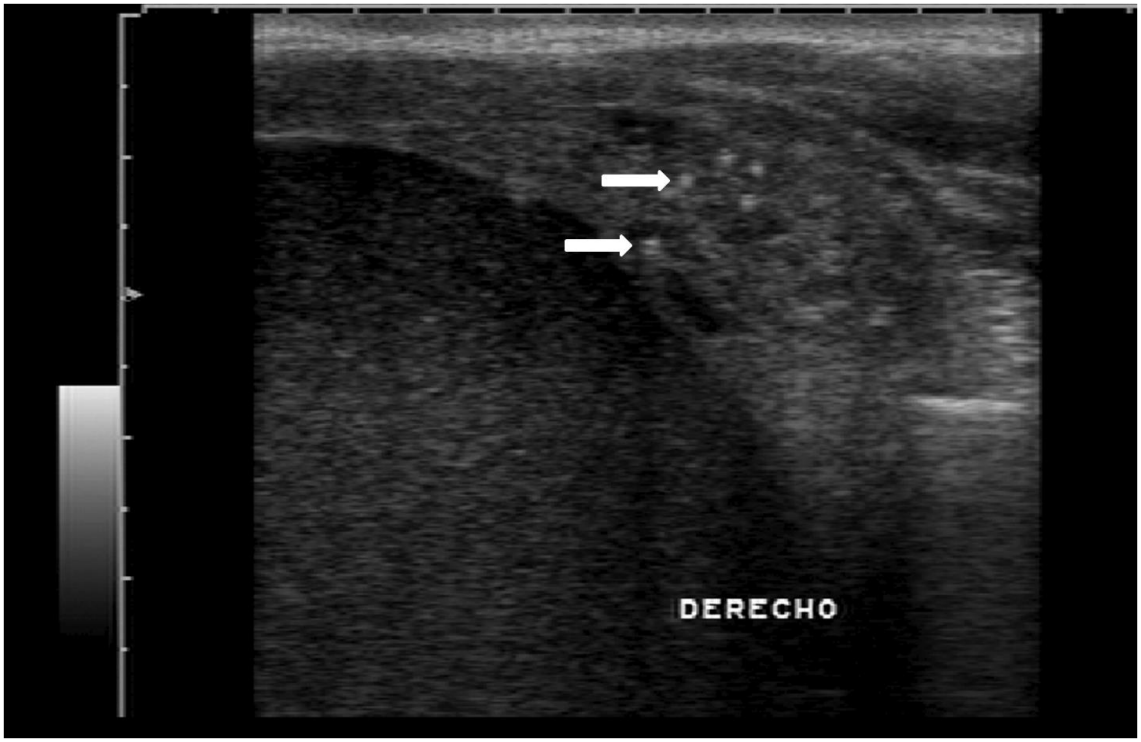


Fig. 2
Annotation:
Papillary thyroid carcinoma: Sonogram of the right lobe of the thyroid demonstrates punctate echogenic foci with and without posterior acoustic shadowing, findings indicative of microcalcifications (arrows) in the solid nodule. (The other nodule, the big one, was histologically benign).

Origin and source of image:
© - Salamanca/ES

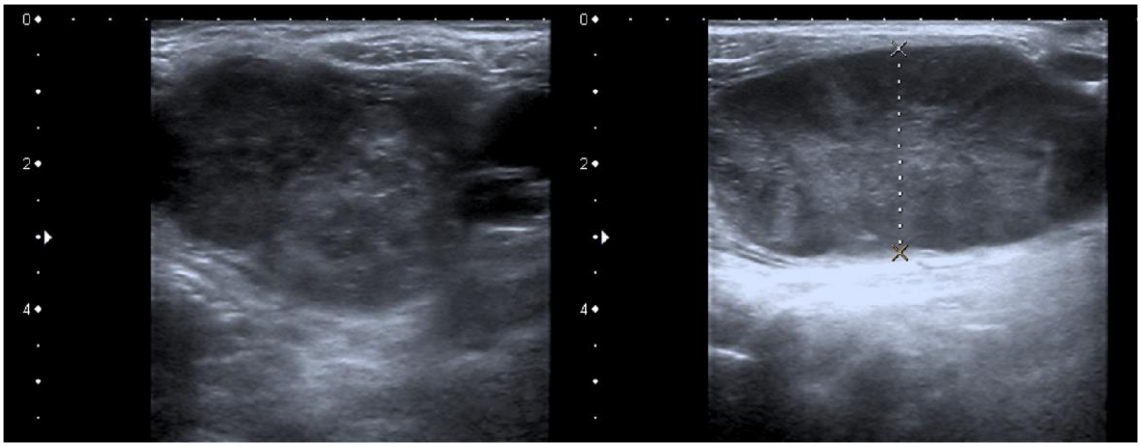


Fig. 3
Annotation:
Hürthle cell (follicular) carcinoma: Transverse sonogram of the left lobe of the thyroid shows a hypoechogenic solid nodule (left image). Sonogram of the left neck shows lymph node metastasis (between calipers, right image).

Origin and source of image:

© - Salamanca/ES

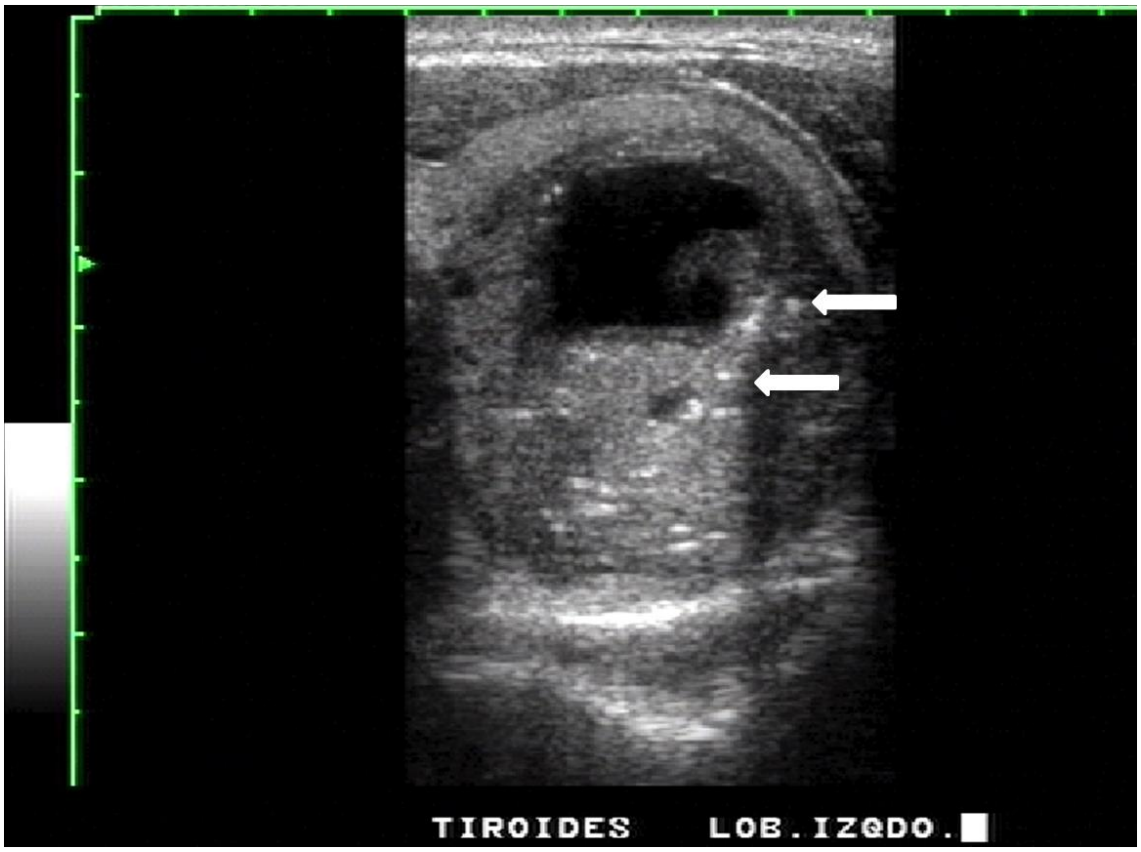


Fig. 4
Annotation:
Medullary thyroid carcinoma: Transverse sonogram of the left lobe of the thyroid shows a predominantly solid and hypoechogenic nodule with microcalcifications (arrows).

Origin and source of image:
© - Salamanca/ES

Fig. 5
Annotation:
Anaplastic thyroid carcinoma (left lobe) developed on a papillary thyroid carcinoma (right lobe): Longitudinal sonogram of the right lobe shows a nodule with macrocalcifications, which corresponded to a papillary thyroid carcinoma. Longitudinal

sonogram of the left lobe shows multiple hypoechogenic nodules with macrocalcifications, which corresponded to a anaplastic thyroid carcinoma. CT confirmed calcifications and showed muscular invasion, as well as pulmonary metastasis (not showed).

Origin and source of image:
© - Salamanca/ES

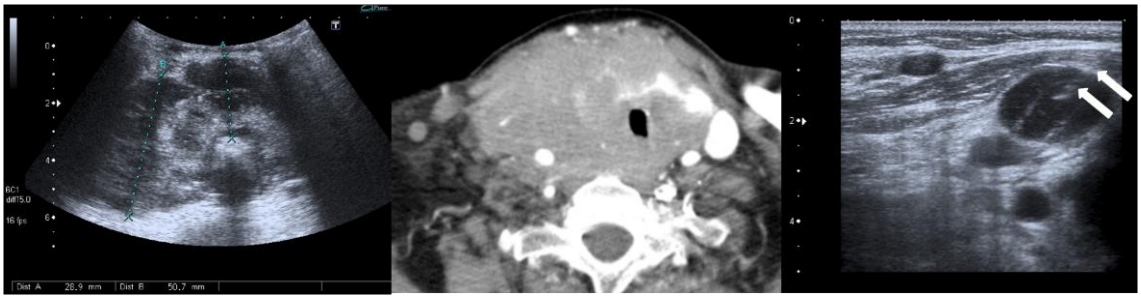


Fig. 6
Annotation:
Thyroid lymphoma: Transverse sonogram of the thyroid shows a large heterogeneous mass (between calipers) with marked hypoechogenicity areas (left image). Contrast-enhanced CT confirmed the US findings and showed aggressive local invasion (middle image). A US-guided FNA biopsy of a lymph node metastases was performed to have the anatomopathological diagnosis (right image, the arrows show the needle).

Origin and source of image:
© - Salamanca/ES

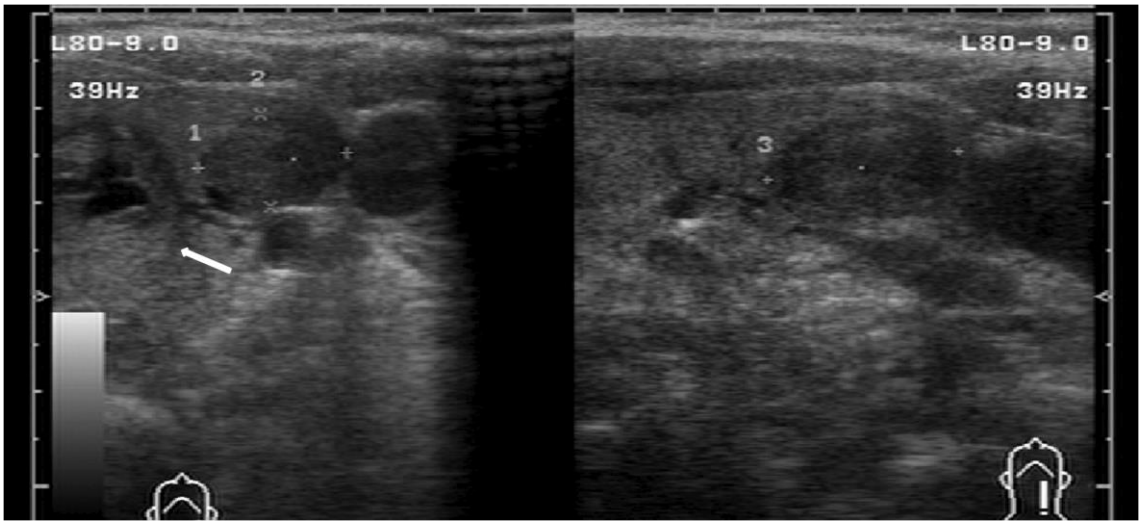
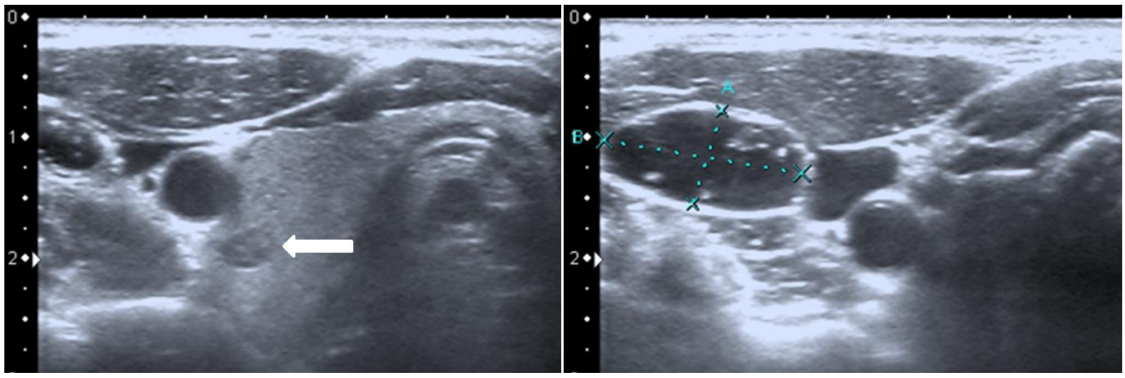


Fig. 7
Annotation:
Renal cell carcinoma metastases to the thyroid: Transverse (left) and longitudinal (right) sonograms of the left lobe of the thyroid show a round hypoechoic nodule (between calipers). Note that there is also a bigger nodule (arrow) which anatomopatological diagnostic was benign.

Origin and source of image:
© - Salamanca/ES



a. b.

Fig. 8
Annotation:
Lymph node metastasis from Papillary thyroid microcarcinoma: (a) Transverse sonogram of the right lobe of the thyroid shows a small nodule with microcalcifications (arrow). (b) Transverse sonogram demonstrates a cystic lymph node metastasis with microcalcifications (between calipers) identified in the internal jugular chain on the ipsilateral side.

Origin and source of image:
© - Salamanca/ES