



EXPERT'S CORNER: A PERSONAL APPROACH

Controversies in medicine: Thyroid nodules ‘‘head or tails’’



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Undoubtedly, thyroid nodules are one of the most common pathologies a physician faces in clinical practice. Not only the endocrinologist, but also the internist and the first contact physician, this situation obeys to the fact that this thyroid gland alteration is highly prevalent amongst the general population. Statistics on the prevalence of this pathology vary from series to series. However, the numbers indicate that between 4% and 7% of the general population present one or more nodules on their thyroid and, as in all diseases related to this organ, they are more frequent in females. Nevertheless, these numbers evidently underestimate the prevalence, since studies of autopsies conducted in people who have died of causes unrelated to their thyroid, show that the prevalence of the nodules can reach up to 50% or more. This simple fact is the best demonstration that this pathology of the gland has a very high prevalence, and is an asymptomatic problem with low morbidity and mortality, since these people, who died of different causes and were not aware of their gland problem, definitely had a completely asymptomatic thyroid disease, perhaps for many years.

When the nodule, or nodules, are discovered by the patient or a physician during a physical examination, it causes a great deal of anxiety in the patient and concern in the physician. Anxiety on behalf the patient due to the

fact that the presence of a tumor in any part of the body implicitly brings the possibility of cancer. On the other hand, the physician's concern comes from the uncertainty of the nature of the lesion and the lack of methods which may allow us to know with absolute accuracy and certainty whether the nodule is benign or malignant and if treatment should be conservative or if the lesion ought to be removed. There are other statistics worth knowing and keeping in mind: thyroid cancer represents 15% of all cancers, in other words a significantly high number. However, the mortality rate of thyroid cancer is 0.2 per 100,000 in men and 0.52 per 100,000 in women. In total, it is 0.36 per 100,000 for both genders. That is to say, a significantly low number compared to other malignant diseases. Furthermore, in 13% of autopsies, there were unsuspected findings of thyroid cancer. These numbers indicate that thyroid cancer is relatively frequent, yet with a low morbidity and mortality.

Here is where thyroid nodules become a ‘‘heads or tails’’ situation. Should patients with thyroid nodules or multinodular goiter undergo medical treatment, or should they all turn to surgical removal of the nodules? Naturally, neither one nor the other. It is necessary to thoroughly study each patient, know their clinical history and use the diagnostic resources available nowadays with responsibility and sensibility, in order to try to classify every patient as a high or low thyroid cancer risk. Some years ago, the decision was made almost at random, ‘‘heads or tails’’; today, this would be unacceptable and inexcusable. Careful analysis of all diagnostic elements should lead to a significantly accurate presumptive diagnosis. Family background is important,

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since certain types of tumors may have a family tendency, such as medullary thyroid cancer, or medullary cancer which are part of the pluriglandular diseases. It is necessary to know if the patient is from or has lived for some time in a geographically goitrogenic area with a iodine deficiency. We know that the incidence of cancer is higher in these areas. Incidence is higher as well if the patient has received radiation in the face or neck due to some condition such as acne or a lymphoma, or if the patient has been exposed to an environment where he/she was exposed to ionizing radiation. All this background information increases the possibility of thyroid cancer.

Thyroid nodules, in their majority, are asymptomatic. However, there are some that, due to their location or size, may cause compression to adjacent organs. Thus, on occasion, causing dysphagia when the esophagus is compressed, or dyspnea when the compression is on the trachea. Others may cause dysphonia by compressing the laryngeal recurrent nerves. Pain is not a frequent symptom unless there is bleeding in the nodule, which may occur and is generally accompanied by a fast growth of the tumor. Habitually, thyroid function remains normal, in such a way that there is not any data of hypo or hyperthyroidism, except when dealing with an overactive nodule. In that case, the nodule is in fact a toxic thyroid adenoma, which may course with thyrotoxicosis and, statistically, has a very slim probability of being malignant.

On the other hand, the physical examination of the gland provides us with valuable information. In order for the nodule to be palpable, its diameter must be greater than 1–1.5 cm. In other words, nodules under these dimensions, usually cannot be felt. In addition, through careful palpation of the neck, it is possible to find two or more surrounding nodules, and we must take advantage of this examination to look for grown lymph nodes throughout the neck, mainly in the carotid chains. Statistics have established that small nodules under 1 cm have fewer possibilities of being malignant. In contrast, larger nodules (3–4 cm) more frequently carry a cancer in their interior. Nodule consistency should be recorded, given the fact that the higher the consistency, the higher the possibility of the nodule being malignant. The same occurs if they have an extremely irregular surface or if they are adhered to the shallow or deep planes. Another important piece of information is the speed of growth of the lesion. Extremely aggressive cancers, such as anaplastic ones, grow rapidly.

The information in the previous paragraphs clearly shows the fact that a good clinical history, with proper background information, a good record of the symptomatology and physical examination of the lesion, can lead us closer to a correct diagnosis of the nature of the lesion and contributes decisively to the classification of the patient under low or high risk of cancer.

In recent years, cytopathological and imaging laboratory studies have also helped us in risk classification and complement the clinical study so the physician can make a proper decision regarding the best treatment.

It is not the objective of this review to go into detail about all laboratory diagnostic procedures. Thus, we will focus on the most utilized and most efficient of them. We believe that in the near future, we will have better procedures, with fewer "false positives" and "false negatives", which

currently impede us from selecting patients who should undergo surgery and those who should undergo treatment with a conservative management with better accuracy. I will only list three procedures: laboratory analysis, ultrasound, and fine-needle aspiration cytology. All of these are useful, but none are completely reliable.

Most of the time, the thyroid profile is totally normal because the thyroid function is not altered and the rest of the gland around the nodule or nodules works properly. Only rarely do patients present a toxic thyroid adenoma, thus presenting thyrotoxicosis and whose possibility of a malignant lesion is statistically very low. Antithyroid antibody determination, especially anti-peroxidase or anti-microsomal, allows for diagnosis of an autoimmune chronic thyroiditis or Hashimoto. Its presence in high levels impedes being able to depend on the determination of thyroglobulin; the latter, in absence of antibody elevation, works as a marker of thyroid cancer. However, its false positive-negative rate is high and we must interpret this result with caution.

Ultrasound is without a doubt the most utilized imaging study, and provides us with valuable information. Nevertheless, just as with other assays, it is not infallible. In this study, we are able to accurately appreciate the size of the lesion, the presence, if any, of other accompanying nodules, the texture of the thyroid tissue, the nodule's position and its form, regularity of its margins, content, echogenic and vascular pattern.

It is well known that approximately 70% of nodules are solid, 20% cystic and the remaining mixed. Out of the solid nodules, approximately 20% are malignant, while amongst the mixed the number decreases to 13%, and amongst the cystic the number decreases to 7%. Cysts larger than 4 cm in diameter have a greater possibility of malignancy. When the pattern is anechogenic it is more probable for the nodules to be benign. Benign adenomas are generally surrounded by a well-defined capsule, which turns the nodule in some sort of bull's-eye. Malignant nodules show the existence of an incomplete peripheral halo, signs of an absent bull's-eye, irregular margins and the presence of micro calcifications in its interior. The incidence of malignancy is 55% in solitary nodules with calcifications, compared to 23% when there are not any calcifications.

The use of fine-needle aspiration cytology has become popular over the last 30 years. According to studies with very large series of patients, this procedure has a specificity of 96% and a sensitivity of 93% for a diagnosis of malignancy, when the material sent to the lab is adequate for the cytological study. It is a simple procedure and practically painless, with very scarce complications. The fear of having the needle disseminating malign tumors has completely disappeared, since there have been no reported cases.

In my opinion, with a smart use of the obtained data through a proper clinical history, ultrasound and a fine-needle aspiration cytology, we are able to reach a high-predictive value regarding the benignity or malignity of a nodule, thus avoiding unnecessary surgery and considering monitoring or substitution treatment with thyroidal hormones as a therapeutic alternative, even if the latter has not proven great efficacy in multiple studies. Nevertheless, if used with responsibility and caution, we are able to

separate all diagnostic instances of patients into high or low risk of cancer categories, thus avoiding the old ‘‘heads or tails’’.

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Recommended reading

1. Ovalle-Berumen F, Zúñiga-Guajardo S, Alanis-Castillo R, et al. El uso de varios métodos diagnósticos en la evaluación preoperatoria del Nódulo Tiroideo. *Rev Investig Clín.* 1984;36:333–7.
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