Thyroid Nodular Evaluation and Treatment in Elderly Patients

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The management of thyroid nodules in the elderly patient involves paying specific attention to risk factors for malignancy. Certainly, patients over 45 years of age have a higher risk of harbouring a malignancy than younger patients. When a decision is made for intervention, one must keep in mind comorbidity issues balanced against the risk of surgery for a potential malignant tumour of low biological activity.

Key words: thyroid, risk factors, comorbidity, malignant tumour.

Introduction

The clinical detection of thyroid nodules is increasing in our population, especially due to greater awareness and the use of imaging modalities in the neck. Thyroid nodules are clinically present in 5% of the population, and this prevalence increases considerably with the use of neck ultrasound.[1]

The incidence of malignancy in clinically apparent thyroid nodules varies from 5–20%, and women are more affected than men by a ratio of 3:1.[2-4] When properly treated, it is quite unusual for patients to die of thyroid malignancy. In the United States, there are approximately 1,300 deaths from thyroid malignancy per annum; the figure in Canada is about one-tenth of that.[5]

In this article, we will describe the management of thyroid nodule, with an emphasis on management in the elderly patient (over 65 years of age), within the full context of thyroid nodular disease and malignancy.

Incidence

Thyroid nodular disease spans all ages, yet the incidence of malignancy is most prevalent in the very young (less than 20 years) and seems to escalate beyond the age of 45 years.[6] Certainly, aggressive thyroid disease occurs more frequently in the older patient.

There are definite patient factors that increase the risk of malignancy. Certain geographical areas show a greater prevalence of thyroid cancer. There is a significant increase in the incidence of thyroid malignancy in Hawaiians, Filipinos and Ukrainians, especially in the area surrounding Chernobyl. The risk associated with these areas may be due to exposure to nuclear waste as a result of nuclear weapon testing and leakage from nuclear sites.[7]

Radiation *per se* has always been a risk factor in the development of malignancy. The use of radiation was highly prevalent in the 50's and early 60's, and may have been administered for the treatment of skin disorders, tonsil disorders and the management of scars. The latency period for the development of cancer in the thyroid is usually between 15 and 40 years after radiation. Increasingly, we are seeing patients who have been treated with radiation for other entities, including lymphoma, breast cancer or head and neck malignancies. In these cases, the lower doses on the isodose curves were applied to areas around the lower neck, and thus exposed these patients to the potential development of thyroid malignancy.

A family history of thyroid cancer is significant, especially if there is a possibility of medullary thyroid cancer history or of multiple endocrine neoplasia.

Pathological Classification

Benign thyroid nodules may be hyperplastic nodules which represent colloid storage disorders, inflammatory disease or true neoplasms such as adenomas. Thyroid malignant disease may be classified in those tumours derived from follicular cells, parafollicular cells, as well as others.

By far the most common tumour of follicular cell origin is papillary thyroid cancer. Pathologically, this is characterized by morphological features of papillae formation and certain cellular features such as crowding and nuclear pseudoinclusions. A subset of papillary thyroid cancer is the follicular variant, which does not have the morphological features of papillary cancer but does display the

Table 1
Clinical Indicators Suggestive of Malignancy

Tumour Factors
Hard, fixed nodule
Vocal cord paralysis
History of head and neck irradiation
Distant metastases
Regional metastases
Rapid growth
Pressure effect
Recurrent cyst
Patient Factors
Age (very old or very young)
Gender (male)
Ethnicity or residence of individual

cellular features. In the past, this type of tumour was probably diagnosed as follicular cancer; however, a true follicular cancer does not have the nuclear features of papillary cancer, has a predominately follicular pattern of cellular morphology, and is characterized by capsular and / or vascular invasion.

Hurthle cell cancers, also of follicular cell origin, are composed of oncocytic cells that are rich in mitochondria but display capsular and / or vascular invasion. Anaplastic cancers, the most virulent of the follicular cell cancers, microscopically demonstrate many of the features of aggressive, high grade malignancies such as nuclear pleomorphism, bizarre forms and invasiveness.

Medullary thyroid cancer (MTC) is derived from the parafollicular or C-cells, and this neoplasm may be sporadic or may show hereditary patterns. It may be part of the Multiple Endocrine Neoplasia Type 2 constellation with coexisting pheochromocytoma and / or hyperparathyroidism. Pathologically, the cells are irregular and epithelioid, and are usually arranged in nests in a fibrous stroma with varying amounts of amyloid. The cells typically stain for calcitonin. Patients with hereditary MTC may show seropositivity for ret oncogene as well as calcitonin and carcinoembryonic antigen (CEA), which represent biological markers for diagnosis and follow-up.

Other less common malignant tumours that occur are lymphomas, sarcomas, melanomas and metastatic lesions from distant sites.

Clinical Evaluation

Most patients that present with thyroid nodular disease have had serendipitous detection of nodules by either themselves or their family physician. Less commonly, patients present with cosmetic deformities, airway or foodway compromise due to large goiters, or vocal problems. Even less frequently, patients present with evidence of regional or distant metastatic disease.

In the evaluation of patients presenting with thyroid nodules, it is

Evaluation of the Patient with a Thyroid Nodule

FNA: Fine needle aspiration
U/S: Ultrasound

important in the elicitation of the history to determine how long the nodule has been present, whether or not there are symptoms resulting from the nodule, a family history, a history of radiation and certainly the place of birth and where the patient grew up.

Evaluation of the elderly in this particular scenario should involve determination of comorbidity factors, such as concomitant central nervous system, cardiac, respiratory, renal and other diseases. This will greatly influence the decision for surgical intervention—if the nodule has a low risk of being malignant, the presence of comorbidity factors may dissuade the clinician from aggressive intervention.

In the physical examination, it is important to ascertain size and location of the nodule as well as other concomitant nodules in the neck suggestive of regional metastatic disease. Evaluation of the vocal cords is of paramount importance if surgical intervention is being contemplated, since vocal cord impairment may signify invasion of the recurrent laryngeal nerve. Furthermore, the status of vocal cord mobility needs to be known if there is impairment postoperatively.

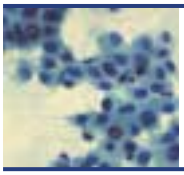
In managing the elderly, a general physical examination to determine the patient's general performance level and their ability to withstand surgery is also important.

Investigations

Patients presenting with thyroid nodularity should have, in their initial workup, a fine needle aspiration (FNA) biopsy (Figure 1). The results of this test are a good indication of the pathology of the mass. However, the drawbacks of this technique are that the aspirate may be insufficient to make a diagnosis or the nodule may be technically inaccessible. Furthermore, the specificity of the test if read benign may be only 80%, which may preclude absolute clinical decision making.[8]

A thyroid nodule that is impalpable and inadvertently found on routine ultrasound for another reason is generally known as an "incidentaloma". Unless there are other overriding factors indicating that intervention is necessary, incidentalomas usually are not clinically significant and can be managed with yearly ultrasounds to determine growth.[9] Otherwise, significant and palpable thyroid nodules should undergo FNA and patients also should have a sensitive thyroid-stimulating hormone (TSH) test to determine their thyroid metabolic status.

With larger nodules that may have significant mediastinal extension or nodules that are accompanied by possible regional metastatic disease, CT scanning without contrast, as this may interfere with subsequent radioactive iodine (I131) administration, should be done to map extensive local disease and determine the extent of regional and mediastinal metastatic disease.



Significant, palpable thyroid nodules should undergo FNA.

Indications for Intervention

The indications for intervention in patients with thyroid nodular disease must take into account a range of patient- and tumour-related risk factors (Table 1), as FNA often may be insufficient for absolute diagnosis. That certain risk factors predispose malignancy has been well established by researchers from Memorial Sloan-Kettering Cancer Center.[10] Certainly, age is one of them—patients older than 45 have a greater risk of having malignancy in a thyroid nodule than those younger than 45. Other patient-related risk factors for malignancy are gender (male), history of radiation, ethnicity (Filipino), place of birth (Chernobyl area) and family history.[11]

Tumour-related risk factors include size (greater than 4cm), hardness, presence of vocal cord paralysis, presence of regional or distant metastatic disease, and suspicious or positive fine needle aspirate for cancer. These risk factors can be critically assessed and patients may be categorized into low, intermediate or high risk. An example of a low-risk patient with nodular disease would be a young female with a small nodule, whereas an example of a high-risk patient would be an elderly male with a large nodule and a highly suspicious fine needle aspirate.[12]

In dealing with elderly patients, particularly those who present a low risk and have many significant comorbidities, management should differ from younger patients without such factors, given that many thyroid malignancies are only mildly aggressive. This should be taken into consideration in the case of elderly infirm patients, who should be observed for signs of progressive disease rather than unnecessarily treated surgically. However, the whole clinical picture must be taken into account, especially in this day and age in which thyroid surgery is expeditious and carries low operative morbidity in skilled hands.

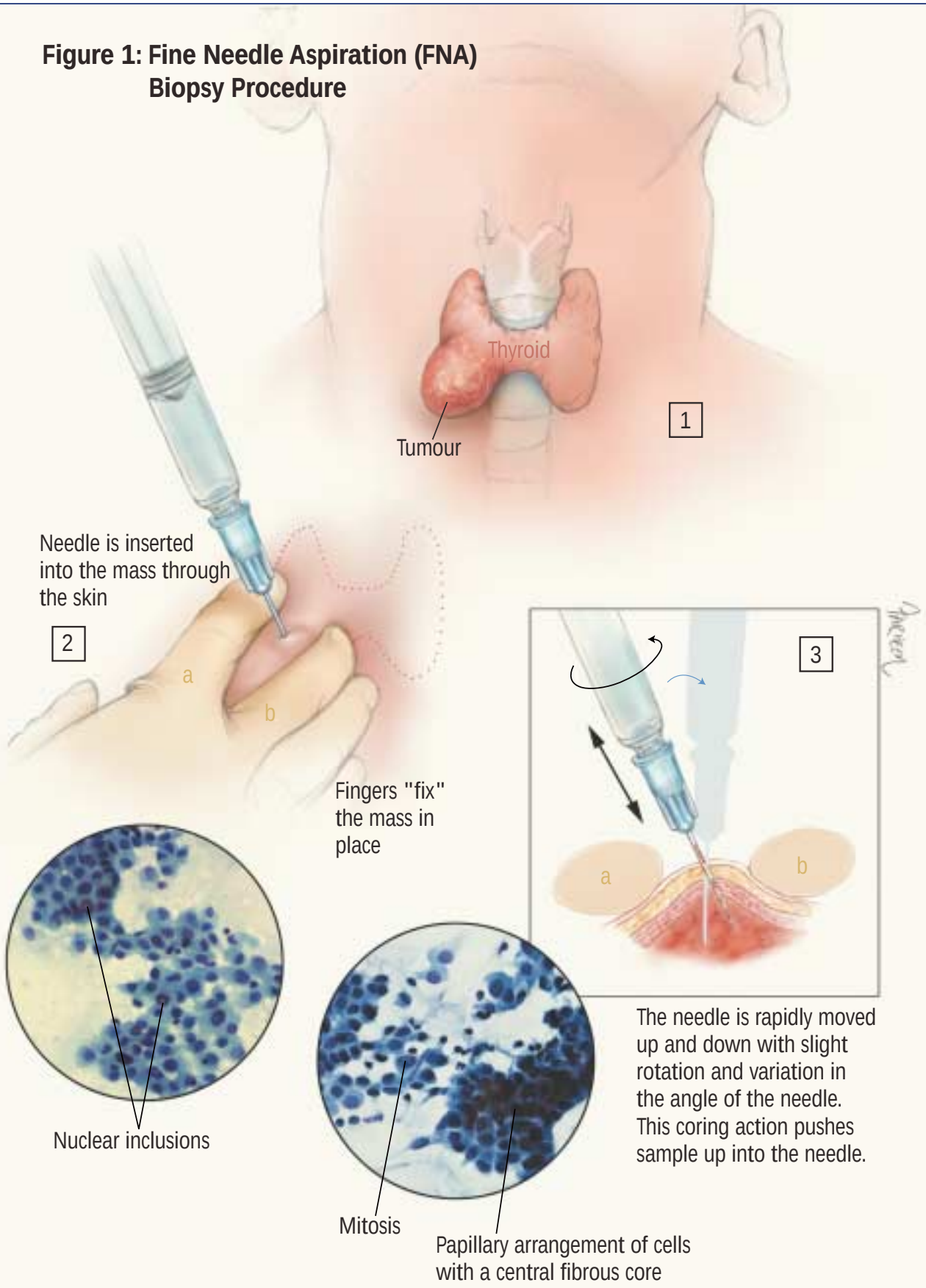
Treatment

The treatment of thyroid cancer is surgical, and often adjunctive radioactive iodine is given since some studies have shown that this regimen reduces the incidence of recurrence and increases survival rates.[13] A solitary thyroid nodule that does not show definite malignancy in a high-risk patient should be managed with a partial thyroidectomy, with the option to go on to total thyroidectomy if intraoperative pathology shows suspicion for malignancy.[14]

Although we believe that the surgical management of known thyroid cancer should be a total thyroidectomy, partial thyroidectomy is certainly an option for small lesions in low-risk patients. The controversy over whether total or partial thyroidectomy is the appropriate treatment for differentiated thyroid cancer continues to rage, and there is valid evidence supporting both sides of the argument.

The management of metastatic neck disease is by regional neck dissection or

Figure 1: Fine Needle Aspiration (FNA) Biopsy Procedure



Biopsy slides courtesy of Dr. Yvan Bedard, Department of Pathology, Mount Sinai Hospital, Toronto, ON.

more extensive dissection as determined by the extent of the metastases.

The management of medullary thyroid cancer is total thyroidectomy plus regional neck dissection to include the central compartment of nodes around the thyroid gland as well as regional nodes.

Anaplastic carcinoma is usually an inoperable disease if it is highly infiltrative with gross involvement of adjacent structure; affected patients are usually treated palliatively. With minimal invasion or localized anaplastic disease, surgical extirpation is a worthwhile endeavor since survival is a possibility (up to 20% five-year survival rates).

Post-surgical management of most well-differentiated thyroid cancers involves the application of adjunct I131 treatment. As mentioned above, usually this is administered to all patients with follicular cell-derived malignancies, apart from the low-risk patients.[13]

External beam radiation is generally reserved for patients with gross residual disease after surgery or evidence of significant invasion of adjacent structures. Medullary thyroid cancers are usually treated with surgery only; in certain cases with extensive and / or infiltrative disease, external beam radiation is administered.

At times, within the surgical specimen there are occult foci of differentiated thyroid cancer in an otherwise benign thyroid. These are managed with close postoperative observation. The prevalence of such occult foci may be up to 20% in the normal North American population.[15]

Follow-up

Follow-up of patients with differentiated thyroid cancer involves clinical evaluation, determination of serial serum thyroglobulin (a serological marker for presence of possible thyroid malignancy) and the determination of adequacy of hormonal levels by sensitive TSH monitoring.[16] Although some clinicians follow patients with serial ultrasounds, their routine use is not recommended because they are highly sensitive and may pick up benign nodules that present a dilemma for the investigator.

High-risk thyroid cancer patients should have I131 scanning at intervals post-definitive management. In the past, this has necessitated withdrawal from thyroxine for about three weeks, with the inconvenience of rendering the patient hypothyroid. With the availability of recombinant TSH, however, this problem is now avoided.[17]

Patients with medullary thyroid cancer should be followed with, in addition to a clinical evaluation, serum calcitonin and carcinoembryonic antigen (CEA) measurements, as these may provide good biological markers for recurrent disease. With this cancer, it is important to rule out the familial variant, so first-degree relatives should be tested with ret oncogene to determine whether they are at risk of developing this disease.

It has been shown that there are several prognostic factors with respect to thyroid malignancy. They are age, grade, extent of tumour, gender and size of nodule. Therefore, age plays a significant role in prognosis. Patients older than 45 years have diminished rates of survival compared to adults younger than the age of 45.[12]

Conclusion

We have given our overview of the management of thyroid nodular disease. Age factors that play a role in the diagnostic context of cancer are:

1) higher incidence of malignancy in older age groups and;
2) comorbidity related to age.

These two factors play a large role in making the decision for surgical intervention. If the patient with thyroid malignancy has been treated for malignancy, age is a significant parameter in determining prognosis. ◆

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