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Perplexing issues in the management of thyroid nodules

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Nodules of the thyroid, is one of the commonest problems in endocrinology and endocrine surgery world over. The prevalence of nodules varies with the modality employed to detect nodules. When clinical methods are used for detection the prevalence is around 4-7% [1]. This may be higher in areas of iodine deficiency [2]. The prevalence in image based studies and postmortem studies is much higher [3, 4 & 5]. There appears to be an increasing prevalence of thyroid nodules world over. It is debatable whether this is a true increase or a reflection of sophisticated and highly sensitive diagnostic methods. The latter is the more likely reason for the increase. There is an increase in the prevalence of nodules with age [6].

Nodules of the thyroid cause concern as the commonest presentation of a thyroid cancer is a solitary nodule of the thyroid. Even though fear of cancer is a concern only about 5-15% of thyroid nodules are truly malignant [7]. Easy access to imaging modalities detects very small nodules of the thyroid which may not in reality, cause any increase in morbidity or mortality. Even when a nodule is palpable easily, confirming the malignant nature of a nodule remains a difficult prospect in some patients due to the indeterminate nature of the cytology report. Follicular lesions of the thyroid still cause issues as the distinction between an adenoma and carcinoma cannot be decided on cytology.

Several methods have been tried to overcome this handicap but no single test has yet emerged as a reliable guide. The patients still need a hemithyroidectomy to determine the histological nature of the nodule in follicular lesions.

While classifications such as Bethesda classification [8] and the THY classification [9] have improved the diagnostic accuracy a great deal, there are about 10-20% of lesions classified as AUS/FLUS lesions. (Atypia/ follicular lesions of unknown significance). Caution is needed in dealing with these lesions, because only about 20% of these AUS/FLUS lesions will turn out to be a true malignancy even though the rate of malignancy varies between institutions [10]. To compound the problem, if the FNAC is repeated in an AUS/FLUS lesion the diagnostic accuracy is not improved [10].

If caution is not exercised the tendency would be to over treat to allay the fears of the patient and the anxiety of the physician. To overcome these difficult problems new molecular tests have been developed to evaluate malignant potential in thyroid nodules. These will hopefully improve the diagnostic accuracy of thyroid nodules. These molecular tests, available as



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mutation panels, which can be performed on cytology specimens are likely to enable clinicians to make better decisions in managing thyroid nodules, in the near future [11].

Even if a small nodule is deemed to be definitely malignant there is sufficient evidence to suggest that sub centimeter (less than 1cm) cancer may only need surveillance [12 & 13]. These cancers are mostly papillary microcarcinoma which behave in a very indolent manner and rarely become overt disease and cause morbidity. Clinicians must be cautious not to over treat these patients as the evidence suggests that patients under surveillance do much better [12 & 13]. Though evidence points to the contrary in the era of information technology, expectations and the anxiety of the patients pose dilemmas in the management of these lesions.

It is well known that some thyroid nodules function autonomously, giving rise to the phenomenon of autonomously functioning thyroid nodule (AFTN). AFTN is a diagnosis rarely made in clinical practice as most patients will remain euthyroid. Clinicians must be cognizant of this entity to diagnose and treat it properly. Evidence guided management strategies will enable clinicians to offer the best possible treatment for the patients.

To make decision making easier thyroid nodules can be divided into, nodules that are more than 1 cm and nodules smaller than 1 cm. Nodules below 1 cm are not palpable clinically and hence would be image detected lesions, making it easier to develop management algorithms. Evidence supports this subdivision as smaller nodules do not seem to cause much morbidity or mortality.

Perusal of the literature shows that the American Thyroid Association (ATA) Thyroid Guidelines [14] recommends that only nodules >1 cm diameter merit further investigations unless there are specific suspicious features, such as a positive family history for thyroid cancer, history of radiation exposure etc. The features that raise the possibility of malignancy are well established [15]. This indicates that, nodules not palpable clinically, but detected incidentally on imaging do not warrant further investigations. The only investigation that may be considered is a repeat US Scan after a sufficient period of time (6 Months). Nodules that are palpable need complete assessment.

One other option that needs to be considered especially in a developing economy is the development of a predictive score of malignancy such a score will take into account, clinical features, sonographic features and cytological features in predicting a malignancy. Radiomics (rad- score) is a new tool used in oncology, which extracts large amount of quantitative features from medical images using data-characterization algorithms enabling the development of a score [16]. Some centres have developed a score such a Radiomics Score for thyroid nodules [17]. Due to the variability of expertise and resources each country/region will need to develop its own score. This

will be good tool to develop for Sri Lanka as it is cost effective and will help reduce unnecessary interventions.

Some patients request screening tests for thyroid cancer. An US Scan combined with a fine needle aspiration appears to be the obvious method to detect early thyroid cancer. There have been seminal studies on this, and the evidence completely negates such an approach [18]. The authors of the much quoted Korean study on screening ultrasonography made an earnest plea that “Concerted efforts are needed at a national level to reduce unnecessary thyroid ultrasound examinations in the asymptomatic general population” [18]. This advice must be heeded to by all endocrinologists, endocrine surgeons and any doctor dealing with a thyroid disorder. It must be remembered that thyroid cancer has very good prognosis. It has been clearly demonstrated that detecting small cancers does not improve survival [18].

There is a tendency to ‘over rely’ on investigations in modern medicine. This is definitely not favourable in a cash deprived health system. This is not cost effective and does not improve health status [19]. In addition the laboratory services are overburdened leading to inefficiency. This is very important to remember in Sri Lanka as the health system is already overburdened. Hormone assay, US Scan and a Fine needle Cytology (FNAC) are essential investigations in any thyroid disorder. Other investigations have a limited role in the routine assessment of a thyroid nodule. The use of other investigations must be for specific reasons e.g. an Isotope scan for an AFTN. The request for investigations must be, as in all other instances, evidence guided to ensure the best outcome for the patient and to make the use cost effective.

While it is acknowledged that management of a thyroid nodule still has areas of contention, there is sufficient evidence available to assist the clinicians in making decisions evidence guided. The more difficult task is to get the balance between inaction and overtreatment, right. The development of molecular markers and other genetic information including hopefully a single marker for thyroid malignancies combined with more clinical acumen will enable clinicians of the future to deal with thyroid nodules better.

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