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ELSAYED, YASSER ALI (2002) "THE DILEMMA OF CLINICALLY APPARENT SOLITARY THYROID NODULE : NOW, A SOLVED PROBLEM," *Mansoura Medical Journal*: Vol. 31 : Iss. 2 , Article 7.

Available at: <https://doi.org/10.21608/mjmu.2002.127100>

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THE DILEMMA OF CLINICALLY APPARENT SOLITARY THYROID NODULE : NOW, A SOLVED PROBLEM

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ABSTRACT

This study was done on (56) patients with clinically apparent solitary thyroid nodule (S.T.N). They were treated in Mansoura Endocrine Surgery Unit (M.E.S.U) during the period from January 2001-January 2002 inclusive . All our patients were presented by palpable single nodule in the thyroid gland either in right lobe, left lobe or isthmus . Patients with malignant nodule were mainly presented by rapid recent increase in size of the nodule and some presented with early hoarseness of voice or dysphagia. Those with toxic nodule were presented with or without thyrotoxicosis and those presented by simple (benign) nodule were presented by accidentally discovered thyroid swelling or bad cosmetic appearance specially in females . All patients were submitted to adequate history taking,

clinical examination and indirect laryngoscopy. Different methods of investigations were done that included measurement of thyroid hormones THS, neck ultrasound, C.T& MRI (in certain cases when needed) and thyroid scan using Technitium ninety nine (Tc99). Histopathological examination was done using FNAB, if failed trucut needle biopsy and if failed frozen section was done. According to the result of pathology whether: a) Malignant (papillary, follicular, Medullary) b) Simple (benign) c) Toxic, Adequate treatment was done that varies in every case ranging from total lobectomy in benign lesion up to total thyroidectomy and block dissection or cherry picking (berry picking) in medullary or papillary cancer respectively.

Conclusion :

S.T.N may become now a solved

surgical problem after following our proposed protocol in management.

INTRODUCTION

Solitary thyroid nodule is a common clinical problem. In the United States, the prevalence of palpable thyroid nodules is about 0.5% of which about half are solitary nodules (1). In Egypt and according to statistics from Mansoura Endocrine Surgery Unit, the incidence of S.T.N is about 0.7%. When ultrasonographic or necropsy data are used to estimate prevalence, the prevalence is about 10 Fold higher (2). There are three clinical circumstances in which the presence of a thyroid nodule generates special concern. The first is one in which the clinical features of the nodule, such as rapid growth, hardness, fixation to adjacent structures, or the presence of regional lymphadenopathy, suggest thyroid carcinoma. The second clinical circumstance is the presence of thyroid nodule in a patient with a history of radiation to the head, neck or chest (3). Finally a patient with Graves' disease with the presence scintigraphically hypofunctioning nodule and Further, thyroid carcinoma in this setting is more aggressive than in euthyroid individual(4). The vast

majority of patients with thyroid nodules, however do not fall into any of the foregoing clinical categories. Rather, the nodule is discovered incidentally by the patient or is detected during a routine evaluation. In the past, such a patient would have undergone ultrasonographic examination(5). Although Fine-needle Aspiration Cytology or Biopsy (FNAC) or (FNAB) of thyroid nodules was first reported more than 60 years ago, this procedure began to gain general acceptance only in the 1980s. Consequently, FNAC is now widely used in the evaluation of patient with a thyroid nodule(6). Cytodiagnosis is designated as benign, malignant or indeterminate. An indeterminate cytodiagnosis refers to smears containing little colloid and many follicular cells or Hurthle cells in a pattern suggestive of a neoplasm(7). Cystic lesions, such as simple cysts or degenerating adenomas, are most often responsible for inadequate smears because of a paucity of cells (8). Because of its accuracy, simplicity and low cost, FNAC has virtually replaced ultrasonography and radio-nuclide as the primary diagnostic tool in the evaluation of euthyroid with a thyroid nodule (9). If the cytodiagnosis is clearly benign, the patient

should be followed and the clinical characteristics of the nodule observed (10). Although suppressive therapy with levothyroxin is often used in this circumstance, prospective studies have demonstrated that such therapy does not reduce the size of the nodule (11). Moreover, suppressive doses may have adverse effects on the heart and skeleton (12). Some thyroidologists recommend Surgical resection of the nodule (13). Total thyroidectomy has been recommended for patients who have papillary cancer of the thyroid. Modified neck dissection was recommended in patients with palpable lymphadenopathy (14). For benign S.T.N total lobectomy or total thyroidectomy may be done according to many factors (15).

This work aims at solving the problem of S.T.N as much as possible by trying to describe a specific, strict and ideal protocol for diagnosis and treatment to end that dilemma.

PATIENTS & METHODS

This study is a prospective study that included (56) patients with clinically apparent S.T.N. All our patients were submitted to careful history taking & clinical examination.

A) History :

Included age of the patients, sex, occupation, whether the nodule is of short or long duration or accidentally discovered, rapid recent increase in size, development of pain either local or referred to the ear, dyspnea, hoarseness of voice, progressive dysphagia, subsequent development of lymph node enlargement in the neck. Special stress on history of intake of antithyroid drugs (dose & duration), history of irradiation to the neck history of pathological fractures, bone aches, haemoptysis, consanguinity, hereditary diseases, genetic disorders and similar conditions affecting other members of the same family. History taking also included asking all our patients about toxic manifestations such as insomnia, irritability, nervousness, intolerance to hot weather, palpitation, loss of weight inspite of increased appetite, and muscle twitches.

B) Clinical examinations :

All our patients were submitted to thorough & complete clinical examination that included both general and local examination:

- i. general examination: body build, nervous state, look of the patient, vital signs (pulse, blood pressure,

temperature), facial expression, tremors, hand exam, lower limb exam., heart, chest, abdomen and skeletal system.

- ii. Local examination: classical local exam of the thyroid was done & included: inspection, palpation, percussion, auscultation & transillumination. The comment on S.T.N. included its size, site, shape, surface, pulsation, movement with deglutition, consistency, mobility, overlying skin (dilated veins, sinuses, scar of previous operation), relation to surrounding structures. This was followed by lymph node examination in the neck (central & lateral nodes). Percussion of the swelling followed by direct percussion over the sternum to detect retrosternal extension. Auscultation was done over the swelling for any continuous machinery murmur (toxic nodule). Transillumination was done to detect whether the swelling is translucent or transopaque. Local exam was ended by E.N.T. examination and assessment of mobility of the vocal cords. After careful history taking and examination, I preliminarily classified our patients into: malignant, benign (simple) & or toxic nodule.

Further steps (investigations) were taken to confirm the diagnosis. Our investigations included:

A) *Laboratory tests* : (1) Thyroid function tests (serum T3, T4 & serum T.S.H). (2) Complete blood picture. (3) Liver function tests (4) serum creatinine (as a profile for renal functions).

B) *Neck ultrasound* : by using a special probe, it was a very useful tool in determining whether the swelling is solid or cystic and also detected enlarged lymph nodes in the neck .

C) *Thyroid Scan* : was done in cases of S.T.N. using Technitium ninety nine pertechnetate (Tc99). It was very useful in mapping of the thyroid and functioning thyroid metastases in the neck. The most important value of scan was detection of the nature of the nodule (cold, hot, warm or cool). Cold nodule means cyst or malignant. Hot nodule means hyperfunctioning nodule & if > 4cm in size it is called toxic adenoma. Toxic adenoma is radiological term that may or may not be associated with clinical manifestations of thyrotoxicosis. Warm nodule means increased activity of a nodule with some activity of the remaining thyroid tissue. Cool nodule means hypofunctioning adenoma. It is to be known that warm &

cool nodules are not uncommon entity.

D) Computerized Tomography (C.T) and Magnetic Resonance imaging (M.R.I) : both modalities could give clear definition of anatomy of the S.T.N, metastases to lymph nodes in the neck, and the relation to surrounding structures (C.T was done for 2 patients & MRI was done for 1 patient only).

E) Doppler ultrasound : was done for 2 patients only with large S.T.N to differentiate between actual invasion and / or just displacement of the carotid & Jugular vessels. In both patients there was only just displacement of the above-mentioned vessels.

F) Pathological diagnosis : cytodiagnosis of S.T.N was a step of utmost importance to confirm the diagnosis whether the nodule is malignant, benign (simple) or toxic. The result of histopathological exam, in addition to another criteria such as: age, sex, intraoperative detection of other nodules & the presence of regional lymph nodes, were important factors affecting the strategy of treatment and the extent of resection. Pathological diagnosis was done depending on the size of the clinically apparent S.T.N. If the nodule was less than 4 cm in its

greatest dimension FNAC was done & If the nodule was more than 4 cm, then trucut needle biopsy done guided by ultrasound or C.T which could localise the swelling adequately and avoided injury of big vessels in the neck or in the thyroid gland. This technique was done easily with no special tactics, except that the sample was put in a formalized saline. FNAC was done by using a disposable 23-gauge needle attached to a syringe holder without local anaesthesia and three or four aspirations were performed. The aspirated material was expelled onto glass slides & smeared. I used the alcohol-fixed technique stained by the papanicolaou method. If cyst fluid is obtained, it must be concentrated by filtration before processing. Interpretation of the slides by an experienced cytopathologist is of paramount importance. Lastly, if pathological diagnosis is undetermined by FNAB or trucut, I did surgical resection of the nodule. Intraoperative frozen section was done in all patients to confirm previously given pathological data. That type of biopsy succeeded in diagnosis of all papillary & medullary cancer (as they are non architectural diagnosis) . Also succeeded in diagnosis of 80% of follicular cancer but the pathologist should take differ-

ent multiple cuts to detect angio invasion & capsular invasion (as it is architectural diagnosis). Frozen section could diagnose perfectly all simple & toxic nodules.

Surgical Strategy :

I believe that " there is unanimity of opinion that surgical extirpation of the S.T.N is the ideal treatment so long as there is an efficient endocrine surgeon" (thyroidectomist). The question to me was the extent of resection. In papillary carcinoma I did total lobectomy in (6 patients) (their ages below 40 years), and total thyroidectomy in (6 patients) (their ages above 40 years). If there was lymph node enlargement I did total thyroidectomy & cherry (berry) picking of lymph nodes (2 patients). In follicular carcinoma I

did total thyroidectomy (2 patients), and total thyroidectomy with block dissection (1 patient) with enlarged lymph nodes. In medullary carcinoma, I did total thyroidectomy with classical (formal) block dissection (3 patients) as there was ipsilateral lymph nodes enlargement . In benign (simple) nodule, I did total lobectomy (4 patients) & total thyroidectomy (in 16 patients) according to the circumstances present & detection of other nodules in the contralateral lobe. In toxic nodule : if the adenoma (radiological) not associated with the clinical manifestations of thyrotoxicosis I did total lobectomy (4 patients) & if adenoma was associated with the clinical manifestations of thyrotoxicosis, then total thyroidectomy was the solution (12 patients).

Table (1): Relation between pathological types and sex.

	Males	Females	Total
Malignant	12 60%	8 40%	20 35.7%
Benign	12 60%	8 40%	20 35.7%
Toxic	14 87.5%	2 12.5%	16 28.6%
Total	38 67.9%	18 32.1%	56 100.0%

$$P= 0.37134$$

Table (2): Relation between pathological types and pattern of increase in the size of the nodule .

	No	Gradual	Sudden	Total
Malignant	6 30.0%	6 30.0%	8 40.0%	20 35.7%
Benign	0.0 0.0%	12 60.0%	8 40.0%	20 35.7%
Toxic	6 37.5%	6 37.5%	4 25.0%	16 28.6%
Total	12 21.4%	24 42.9%	20 35.7%	56 100.0%

P= 0.29403

Table (3): Relation between pathological types and hoarseness of voice.

	No hoarseness	Hoarseness	Total
Malignant	4 20%	16 80%	20 35.7%
Benign	20 100%	0 0%	20 35.7%
Toxic	16 10.0%	0 0%	16 28.6%
Total	40 71.4%	16 28.6%	56 100%

P= 0.0123

Table (4): Relation between pathological types and dysphagia.

	No dysphagia	Dysphagia	Total
Malignant	14 70.0%	63 30.0%	20 35.7%
Benign	14 70.0%	6 30.0%	20 35.7%
Toxic	4 25.0%	12 75.0%	16 28.6%
Total	32 57.1%	24 42.9%	56 100.0%

P= 0.09418

Table (5): Relation between pathological types and dyspnea.

	No dyspnea	Dyspnea	Total
Malignant	16 80.0%	4 20.0%	20 35.7%
Benign	8 40.0%	12 60.0%	20 35.7%
Toxic	4 25.0%	12 75.0%	16 28.6%
Total	28 50.0%	28 50.0%	56 100.0%

P= 0.04979

Table (6): Relation between pathological types and presence of hot nodules.

	No hot nodules	Hot nodules	Total
Malignant	20 100.0%	0.0 0.0%	20 35.7%
Benign	14 70.0%	6 30.0%	20 35.7%
Toxic	16 100.0%	0.0 0.0%	16 28.6%
Total	50 89.3%	6 10.7%	56 100.0%

P= 0.04861

Table (7): Relation between pathological types and presence of cold nodules.

	No cold nodules	Cold nodules	Total
Malignant	16 80.0%	4 20.0%	20 35.7%
Benign	14 70.0%	6 30.0%	20 35.7%
Toxic	4 25.0%	12 75.0%	16 28.6%
Total	34 60.7%	22 39.3%	56 100.0%

P= 0.04507

Table (8): Relation between pathological types and ultrasound examination.

	Solid	Solid and cystic	Total
Malignant	6 30.0%	14 70.0%	20 35.7%
Benign	2 10.0%	18 90.0%	20 35.7%
Toxic	2 12.5%	14 87.5%	16 28.6%
Total	10 17.9%	46 82.1%	56 100.0%

P= 0.45325

Table (9): Relation between pathological types and fine needle diagnosis.

	Negative	Positive	Total
Malignant	4 20.0%	16 80.0%	20 35.7%
Benign	0 0.0%	20 100.0%	20 35.7%
Toxic	2 12.5%	14 87.5%	16 28.6%
Total	6 10.7%	50 89.3%	56 100.0%

P= 0.345.7

Table (10): Relation between pathological types and trucut diagnosis.

	Negative	Positive	Total
Malignant	2 10.0%	18 90.0%	20 35.7%
Benign	0 0.0%	20 100.0%	20 35.7%
Toxic	2 12.5%	14 87.5%	16 28.6%
Total	4 7.1%	52 92.9%	56 100.0%

P= 0.53836

Table (11): Relation between pathological types and Surgical operations.

	TL	TT	TT&BD	TT&CPLN	Total
Malignant	6 30.0%	8 40.0%	4 20.0%	2 10.0%	20 35.7%
Benign	4 20.0%	16 80.0%	0 0.0%	0 0.0%	20 35.7%
Toxic	4 25%	12 75.0%	0 0.0%	0 0.0%	16 28.6%
Total	14 26%	36 64%	4 7%	2 3%	56 100%

P= 0.29403

TL = Total Lobectomy
 TT = Total Thyroidectomy
 TT & BD = Total Thyroidectomy & Block Dissection
 TT & CPLN = Total Thyroidectomy and Cherry Picking of Lymph Nodes.

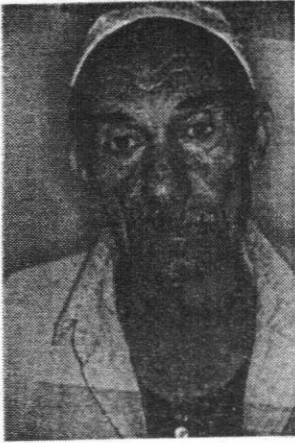


Figure (1) : Male patient aged 50 years presented with S.T.N in the left lobe.



Figure (3) : A child female aged 10 years presented with S.T.N in the left lobe and isthmus.



Figure (2) : Female patient aged 30 years presented with S.T.N in the isthmus.

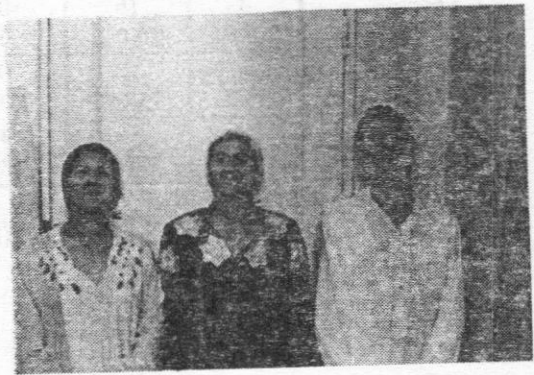


Figure (4) : Three members in the same family presented with S.T.N proved later on to be medullary carcinoma .

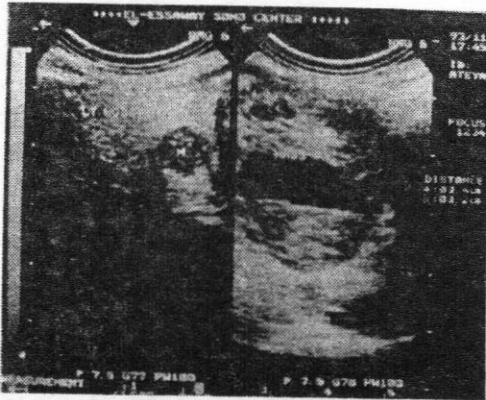


Figure (5) : Thyroid ultrasound shows solid and cystic lesions.

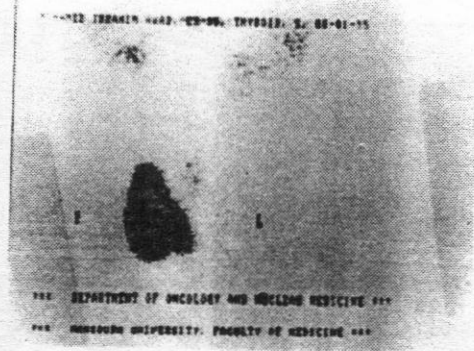


Figure (7) : Thyroid scan (Tc99) shows toxic adenoma.

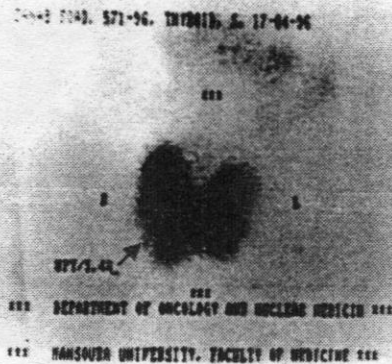


Figure (6) : Thyroid scan (Tc99) shows cold nodule in the right lobe.

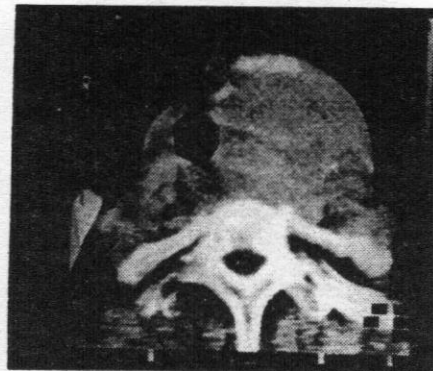


Figure (8) : C.T. scan of the neck shows large (left S.T.N) shifting the trachea to the right side.

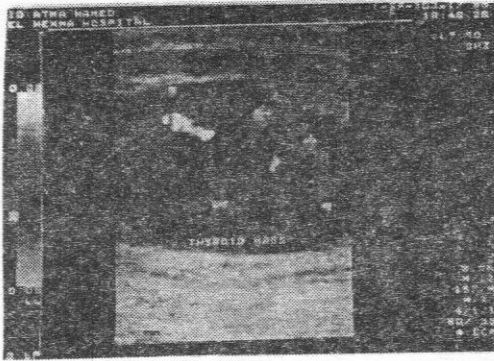


Figure (9) : Duplex scan shows thyroid mass without infiltration of carotid or jugular vessels.



Figure (11) : The same patient in (fig. 10) ten days after operation.



Figure (10) : Reported case of a female aged 65 years with huge left S.T.N.

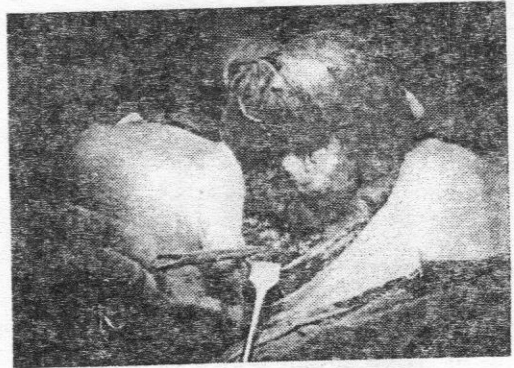


Figure (12) : Intraoperative photograph shows last step of removal of the huge S.T.N.



Figure (13) : Removed thyroid specimen from the patient in (fig. 10) weight (750 grams).

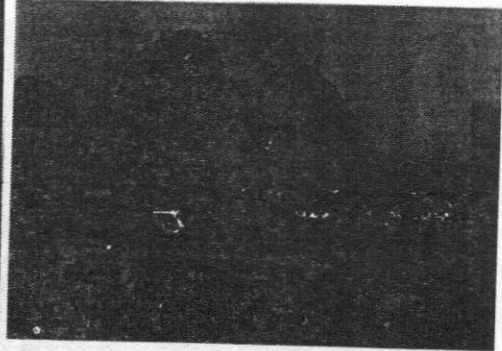


Figure (15) : Specimen shows total thyroidectomy.

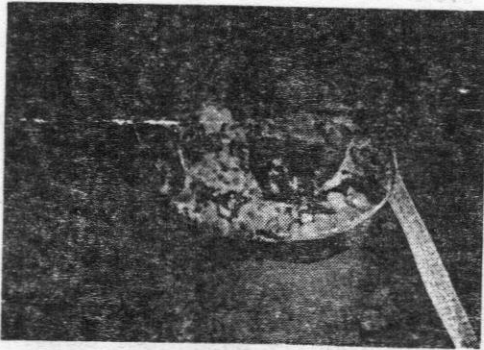


Figure (14) : Cut section in the huge S.T.N shows solid and cystic areas with haemorrhage inside.

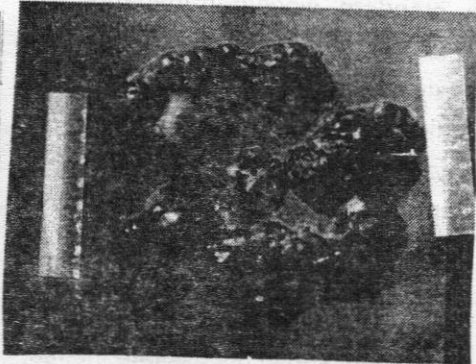


Figure (16) : Specimen shows cherry picking of lymph nodes.

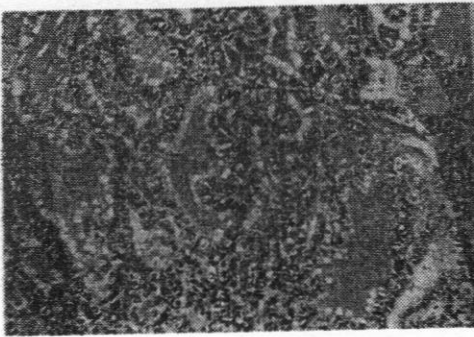


Figure (17) : M/E shows mixed papillary and follicular carcinoma.

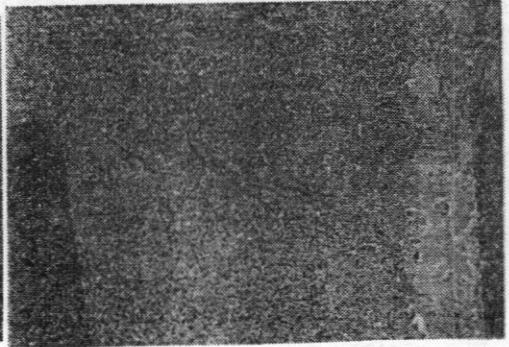


Figure (18) : M/E shows medullary carcinoma (note: amyloid deposits in the right side of the field).

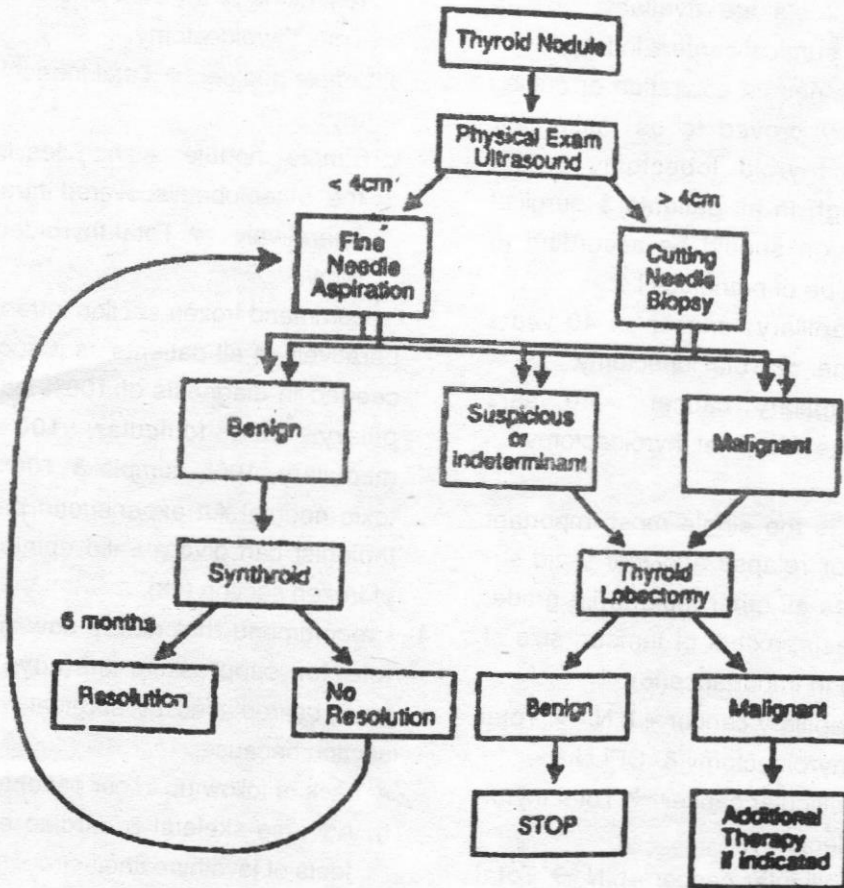
DISCUSSION

(Howkin's et al., 1987), described a standard workup in management of S.T.N. The initial step in patient evaluation was history taking and clinical examination determining the size and location of the nodule. Careful palpation was required to detect Jugular, supraclavicular, and submandibular nodes. Hoarseness, difficulty swallowing liquids, or dyspnea with exertion may necessitate indirect laryngoscopy. Fine needle aspiration cytology is the primary diagnostic

procedure for smaller lesion (<4cm). Ultrasound is used to measure exact lesion size before suppression and to ensure that no other thyroid masses or suspicious lymph nodes have been missed. If the lesion appears totally cystic on ultrasound, aspiration may completely eliminate it. If the thyroid nodule is large (>4cm), cutting needle biopsy is the preferred diagnostic maneuver. Therapeutic intervention is based on biopsy results. If the fine-needle aspiration cytology or biopsy is benign, ultra-

sound used to measure the nodule and thyroid suppression is started. If the results are suspicious or malignant, surgical resection is indicated. During TSH suppression for benign tumours, the responsible physician must be certain that TSH levels are actually suppressed by the dose of levothyroxine sodium. If the nodule

remains unchanged or decreased without resolution after 6 months, repetition of aspiration cytology is indicated. If the nodule increases in size, surgical resection is indicated. Nodule size can be accurately re-evaluated by physical examination and thyroid ultrasound. The entire scheme is outlined.



I considered the above mentioned scheme as a basic scheme in management of S.T.N, but in fact, I disagree with it in many points :

- 1- Cutting needle biopsy if the nodule (>4cm) should be guided by ultrasonography or C.T for adequate localisation of the nodule and avoidance of injury of any vital structures in the neck specially that both tools are available now in most surgical centers in Egypt.
- 2- If fine needle aspiration or cutting biopsy proved to be malignant, then thyroid lobectomy is not enough in all patients & surgical decision should be according to the type of pathology i.e:
 - a. Papillary cancer < 40 years age → Total lobectomy.
 - b. Papillary cancer > 40 years age → Total thyroidectomy.

Age is the single most important factor for relapse and mortality superseding all other factors (i.e grade, metastasis, extent of tumour, size of tumour) in importance(16).

- c. Papillary cancer + L.N. → Total thyroidectomy & CPLN.
- d. Follicular cancer → Total thyroidectomy.
- e. Follicular cancer +L.N → Total thyroidectomy & Total (radical)

BD .

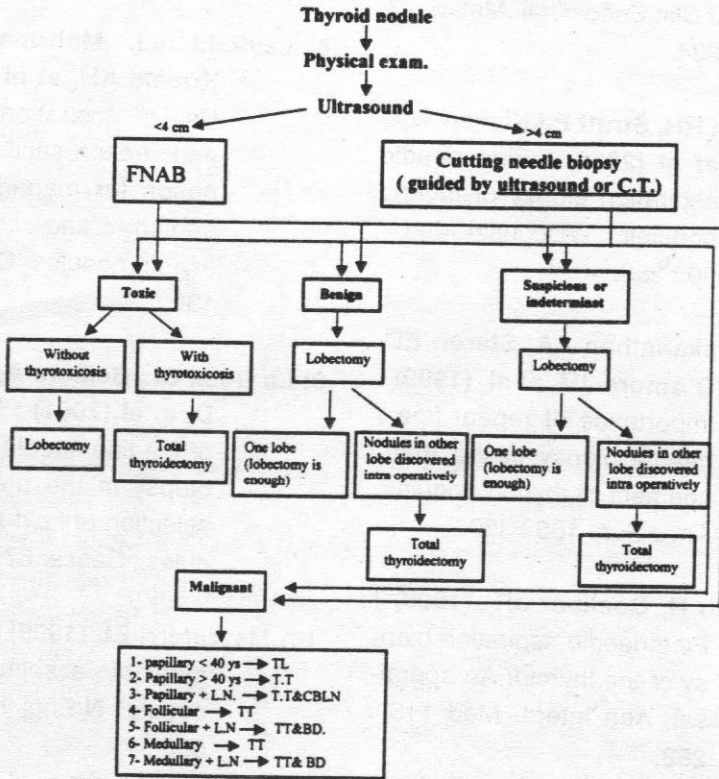
- f. Medullary cancer → Total thyroidectomy.
 - g. Medullary cancer + L.N → Total thyroidectomy & Total (radical) BD .
 - h. Toxic adenoma without clinical manifestations of thyrotoxicosis → Total lobectomy.
 - i. Toxic adenoma with clinical manifestations of thyrotoxicosis → Total thyroidectomy.
 - J. Simple nodule → Total lobectomy
 - k. Simple nodule + nodules in the other lobe discovered intraoperatively → Total thyroidectomy.
- 3- I recommend frozen section intraoperatively in all patients as it succeeded in diagnosis of 100% papillary, 80% follicular, 100% medullary, 100% simple & 100% toxic nodule. An experienced pathologist can give a valid opinion of frozen section (18).
- 4- I recommend that nearly now no role for suppressive therapy & must be replaced by surgical resection because:
 - a. Lack of follow up in our patients.
 - b. Adverse skeletal & cardiac effects of levothyroxine.
 - c. In experienced hands, the oper-

ative morbidity is extremely small and it is universally recognized that there is no place now for "occasional thyroidectomist" (18).

- d. Great advances and wide safety measures in anaesthesia.
- e. I. restrict suppressive therapy

for very minimal group of patients who are absolutely refusing surgical interference inspite of many trials to convince them to do surgery and warning them of hazards of adverse effects of suppressive therapy.

The proposed scheme of Mansoura Endocrine Surgery Unit (M.E.S.U)



N.B: Frozen section is mandatory after every step of surgical resection.

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الملخص العربي

يعتبر الورم المنفرد العنقودي للغدة الدرقية من أهم المشاكل الجراحية وذلك لعدم وجود نظام جراحى محدد لتشخيص وعلاج هذه المشكلة. ويشمل الورم المنفرد العنقودى كل أنواع أمراض وتضخمات الغدة سواء كانت حميدة أو خبيثة أو تسمية أو التهابات. أجريت هذه الرسالة على (٥٦) مريض فى الفترة من يناير ٢٠٠١ إلى يناير ٢٠٠٢. تم تصنيف هؤلاء المرضى لمجموعات وتنوعت الفحوصات والتحاليل المعملية للوصول لتشخيص محدد. بعد الوصول لتحديد نوع التضخم باثولوجيا يتم علاج المريض على أساس نوع العينة المأخوذة من الغدة. كان نتيجة هذا البحث أن توصلنا لجدول محدد لكيفية تشخيص وعلاج مثل هذه الحالات المحيرة جراحياً. ويعتبر كل مريض بهذا النوع من التضخم حالة منفردة وتختلف عن الحالات الاخرى سواء فى طرق التشخيص أو العلاج. ونأمل فى نشر البروتوكول الذى توصلنا له فى مراكز علاج الغدة الدرقية للعمل به فى علاج المرضى .