นิพนธ์ต้นฉบับ

Ultrasound and aspiration cytology or needle biopsy in the diagnosis of single thyroid nodule

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A prospective study was carried out in 116 patients with clinically diagnosed single thyroid nodule to evaluate the diagnostic accuracy of ultrasound and aspiration cytology or needle biopsy. All patients had an operation for the final pathological diagnosis. Carcinoma was found in 8 per cent of patients. Ultrasound (in 93 patients) had an accuracy of 93 per cent in predicting the physical characteristics of the nodules, and was 86 per cent accurate in detecting the number of nodules; it did not detect 12 of 15 cases with multiple nodules : Cytology or needle biopsy (in 96 patients) detected 6 of 7 carcinomas, having a sensitivity of 86 per cent. A specificity of only 52 per cent was due to the relatively high false positive reports, which could improve with experience. The potential role of both investigations in the management of single thyroid nodule is discussed.

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ผู้ป่วยที่เป็นก้อนเดี่ยวในต่อมไทรอยด์จำนวน 116 คน ได้รับการศึกษาด้วยอุลตราซาวนด์และ aspiration cytology หรือ needle biopsy ผู้ป่วยทุกรายได้รับการผ่าตัดและมีผลพยาธิของก้อนสำหรับประเมินผลของการวินิจฉัย พบว่า 8% ของผู้ป่วยกลุ่มนี้เป็นมะเร็ง

อุลตราซาวนด์ (ในผู้ป่วย 93 ราย) มีความแม่นยำถึง 93% ในการบอกลักษณะของก้อนว่าเป็นถุงน้ำหรือเนื้อ หรือเนื้อปนน้ำ และมีความแม่นยำ 86% ในการสำรวจจำนวนก้อนในต่อมไทรอยด์

Aspiration cytology ร่วมกับ needle biopsy (ในผู้ป่วย 96 ราย) สามารถวินิจฉัยมะเร็งได้ 6 ใน 7 ราย คำนวนเป็น sensitivity ได้ 86% แต่มี specificity เพียง 52% เนื่องจากมี false positive ค่อนข้างสูง

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The single thyroid nodule is a common clinical problem and its surgical removal represents the commonest elective operation at the Chulalongkorn Hospital. Apart from pressure symptoms caused by a large nodule, the main reason for operation is that the nodule may be malignant. Since the incidence of carcinoma in patients with a single thyroid nodule from a previous study at this hospital was only 8 per cent[1], it is evident that the majority of patients does not require an operation which has its own risk and attending high cost. However, before deciding to treat a single thyroid nodule conservatively, such as with longterm thyroid suppression, one should be fairly certain that it is not malignant.

Until recently non-operative methods of distinguishing between benign and malignant thyroid nodules have been unsatisfactory. Clinical criteria of malignancy, such as a history of cervical irradiation, a hard fixed mass, and palpable cervical lymph nodes are found only in a minority of patients[2]. Early and well-differentiated carcinomas usually cannot be distinguished from benign nodules clinically[3]. Isotope scan of the thyroid is also unsatisfactory since most benign nodules as well as carcinomas are non or hypofunctioning[4]. Developments in ultrasound have enabled the physical characteristics and number of thyroid nodules to be accurately determined[5]. Needle biopsy and more recently, aspiration cytology have become more widely used in the diagnosis of thyroid nodules[6,7]. Claims have been made as to the efficacy of both cytology and needle biopsy in distinguishing between benign and malignant nodules, with a corresponding reduction in the number of patients requiring operation[8-10].

This preliminary study was carried out to determine the accuracy of ultrasound and aspiration cytology or needle biopsy in the diagnosis of single thyroid nodule in a hospital with limited experience in these procedures.

Material & Methods

All patients with clinically diagnosed single thyroid nodule were admitted into the study if they consented to have surgery. Preoperative ultrasound of the thyroid was carried out using a static B-scanner with a 5 MHz short-focus transducer. The number, size, and physical characteristics of the nodules were recorded by the radiologist. Physical characteristics were classified as solid, cystic, or complex (mixed solid and cystic components). Isotope scan was not done routinely.

Aspiration cytology or needle biopsy was carried out twice per patient, preoperatively and during operation, in order to assess the surgeons' sampling accuracy. Cytology was generally preferred to needle biopsy although the latter method was sometimes employed in large and hard nodules. The first specimen was obtained percutaneously in the operating room after the patient had been anaesthetized and the neck extended in the "thyroidectomy" position. The needle was introduced into the nodule in a plane parallel to the trachea and great vessels to avoid injuring these structures. The second specimen was obtained during operation by direct puncture of the nodule after the thyroid had been fully exposed. Aspiration cytology was carried out using a No.20 needle on a 20 ml wet glass syringe for stronger suction. At least 4 smears were made from each nodule on glass slides, fixed in 95% alcohol, and stained with Papanicalaou

stain. Needle biopsy was carried out using a 14-gauge Vim-Silverman needle. The specimens were fixed in 10% formalin and subsequent paraffin sections were stained with haematoxylin and eosin. Interpretation of both cytology and needle biopsy was done by an experienced pathologist, but who had no previous experience in the cytology of the thyroid. Slides and biopsy specimens were coded so that the pathologist had no knowledge of the true pathology of the nodules. Cytology results were classified as benign, malignant, borderline, and negative when there were inadequate cells for interpretation. The following cytological features were considered malignant : cells with large hyperchromatic nuclei and clear intranuclear inclusion bodies, papillary arrangement of cells, and the presence of psammoma bodies. The following features were considered borderline : hypercellularity, variation in nuclear size, and papillation or pseudopapillary pattern.

After cytology or needle biopsy, thyroidectomy was performed in the routine fashion. Frozen-section biopsy was carried out if there were any doubts of malignancy. The thyroid specimens were sent for routine histopathological examination. The gross appearance and number of the excised nodules as well as the final pathological diagnosis were used as standards to assess the accuracy of ultrasound, cytology, and needle biopsy.

Results

Between February 1982 and June 1983, 116 patients with clinically diagnosed single thyroid nodule were studied. There were 108 females and 8 males. The patients' ages ranged from 15 to 74 years, with a mean of 35.7 years. Age distribution is shown in figure 1. Duration of the nodules varied from one week to 20 years, mean 1.9 years. Seventy-three nodules were in the right lobe, 40 in the left lobe, and 3 in the midline. Sizes of the nodules varied from 1 to 10 cm, mean 3 cm. Isotope scan had been carried out in 47 patients; 41 nodules were cold, 4 warm, one hot and a 1 cm nodule was not detected. Four carcinomas all showed up as cold nodules in the isotope scan. Thyroid suppression with thyroxin or thyroid extract had been tried in 35 patients for a period of 1 month to 6 years, mean 10.6 months. However, some of the patients did not have regular treatment. Thirty-one nodules were unchanged in size and 4 became larger. Two papillary carcinomas were unchanged in size after 3 and 8 months of thyroid suppression.

Preoperative ultrasound was done in 93 patients, and cytology or needle biopsy in 96 patients. Seventy-three patients had both investigations performed. At operation, 97 patients were found to have true single thyroid nodules and 19 patients multiple nodules. Gross appearance of the dominant nodules consisted of 51 solid, 19 cystic, and 46 complex or mixed nodules. Frozen-section biopsy was done in 19 patients; 3 malignant and 15 benign nodules were correctly diagnosed, but a follicular carcinoma with lymphocytic infiltration was incorrectly diagnosed as benign. There was no operative mortality or serious morbidity in this series.

The final pathological diagnosis is shown in table 1. All the 9 carcinomas were in females; 5 were papillary, 3 follicular, and one Hürthe-cell. All malignant nodules were solid except one papillary

carcinoma which showed mixed solid and cystic components. Carcinomas were found in 8 of 51 solid nodules (16 per cent) compared with one of 46 complex nodules (2 per cent). Two carcinomas were associated with multiple nodules. Three carcinomas were locally invasive, 2 of which also had cervical lymph node metastasis although the nodes were not palpable. Twelve patients in this series were suspected clinically to have carcinoma, including 5 patients who had palpable cervical lymph nodes; but all were proven to have benign nodules after surgical excision.

Results of ultrasound are shown in table 2. The overall accuracy in identifying the number of nodules was 86 per cent. Only 3 of 15 cases with multiple nodules were detected by ultrasound. Detected nodules averaged 2.9 cm (1-8 cm) in diameter whereas undetected nodules averaged 0.7 cm (0.3-1.5 cm) in diameter. Ultrasound was 93 per cent accurate in determining the physical characteristics of the nodules. Five solid and one complex carcinomas were correctly identified, but another solid carcinoma was incorrectly interpreted as cystic.

Eighty-seven patients had aspiration cytology and 11 had needle biopsy of their nodules, 2 patients had both procedures performed. The results were pooled because of the small number of needle biopsies (table 3). Twenty-five of the specimens, all from benign nodules, were reported as negative; 18 of these were from cystic or predominantly cystic nodules. Assuming that a malignant or borderline report was an indication for surgery, cytology and needle biopsy correctly diagnosed 6 of 7 carcinomas, a sensitivity of 86 per cent. The single false negative report occurred in a follicular carcinoma with lymphocytic infiltration; frozen-section biopsy in this case was also reported as benign and the final diagnosis was made only after metastatic follicular cells were found in the excised lymph nodes. When negative results were excluded, cytology and needle biopsy correctly diagnosed 33 of 64 benign nodules, a specificity of 52 per cent. By comparing the results of percutaneous and operative cytology or needle biopsy in each case, the surgeons' sampling accuracy in the first and second half of the study period was 91 per cent and 96 per cent respectively ($P > 0.05$).

Discussion

The pathology of clinically single thyroid nodules, with an 8 per cent incidence of carcinoma, was similar to a previous study from this hospital[1]. The results also confirmed that the majority of carcinomas were relatively early, well-differentiated, and could not be distinguished from benign nodules clinically.

Ultrasound had a 93 per cent in determining the physical characteristics of the nodules. The accuracy of 86 per cent in identifying the number of nodules was not quite as good. The detection of 3 out of 15 cases with multiple nodules was only slightly better than palpation alone. Admittedly the sizes of the undetected nodules were small, averaging 0.7 cm in diameter, but results may improve with experience. The limitation of ultrasound is that it only provides information on the physical characteristics and number of the nodules. Although the majority of carcinomas presented as single and solid nodules, 2 of 9 cases in this series were

multiple and one was partially cystic. The reported incidence of cystic or partially cystic carcinomas also varied considerably, but could be as high as 33 per cent[11]. We feel that although ultrasound is a noninvasive procedure, it is only an indirect diagnostic method and its ability in distinguishing benign from malignant nodules is probably limited. Ultrasound has been used in conjunction with cytology to select the size of aspiration needles[12]. Others have suggested that serial ultrasound may be used to follow the size of nodules during thyroid suppression therapy[13].

The 86 per cent sensitivity of cytology and biopsy in diagnosing carcinoma was comparable to other reports[12, 14]. The only false negative interpretation was from a difficult case in which the final diagnosis was established only after histological examination of the excised lymph nodes. The specificity of only 52 per cent was due to 13 benign nodules being incorrectly reported as malignant and 20 borderline interpretations in which only 2 carcinomas were ultimately found. Greater experience could reduce this relatively high false positive rate. However, the limitation of cytology and needle biopsy in differentiating a highly cellular adenoma from a well-differentiated follicular carcinoma is well recognised; the diagnosis usually requires histological examination of the whole specimen for evidence of capsular or vascular invasion[7]. For this reason, operation is usually advised for cellular follicular tumours[7, 15]. About 25 per cent of cytological specimens were negative. Although these were mainly from cystic or predominantly cystic nodules, a more thorough sampling technique could possibly obtain more positive results.

The comparable sampling accuracy, particularly of aspiration cytology, in the first and second study periods suggested that a great deal of experience was not required. The safety of aspiration cytology and needle biopsy could not be determined in this series because they were performed immediately before and during operation. Other reports have found that both procedures are safe if properly performed[6, 7]. Needle tract spread of carcinoma is a very rare complication of needle biopsy[16], but has not been reported in aspiration cytology which employs a smaller needle[7].

Cytology, combined with needle biopsy when necessary, may have an important role in the management of single thyroid nodule for it provides direct information on the cellular morphology of the nodule. However the accuracy, particularly the false positive interpretation, needs to be improved. Nodules which are reported as malignant should obviously undergo surgical resection. Borderline nodules should also have surgery unless there are medical contraindications[7, 15]. The borderline group should include cellular follicular tumours and Hürthle-cell neoplasms because of the latter's uncertain behaviour[17]. Nodules interpreted as benign could be treated with thyroxin suppression and reevaluated at regular intervals. Pressure effects, clinical suspicion of carcinoma, and failure to diminish in size or enlargement after thyroxin therapy are indications for surgical intervention. Cases reported as negative could undergo reaspiration or rebiopsy if the nodules persist or recur. With this general policy, and judging from our preliminary results, the initial number of operations for single thyroid nodule could be reduced by 37 to 63 per cent, depending on the

outcome of cytologically negative nodules. A further prospective study with longterm follow-up of unoperated cases is required. If all nodules are to have cytology or needle biopsy then ultrasound is probably not routinely necessary.

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Figure 1 : Age Distribution in 116 Patients with Clinically Single Thyroid Nodule

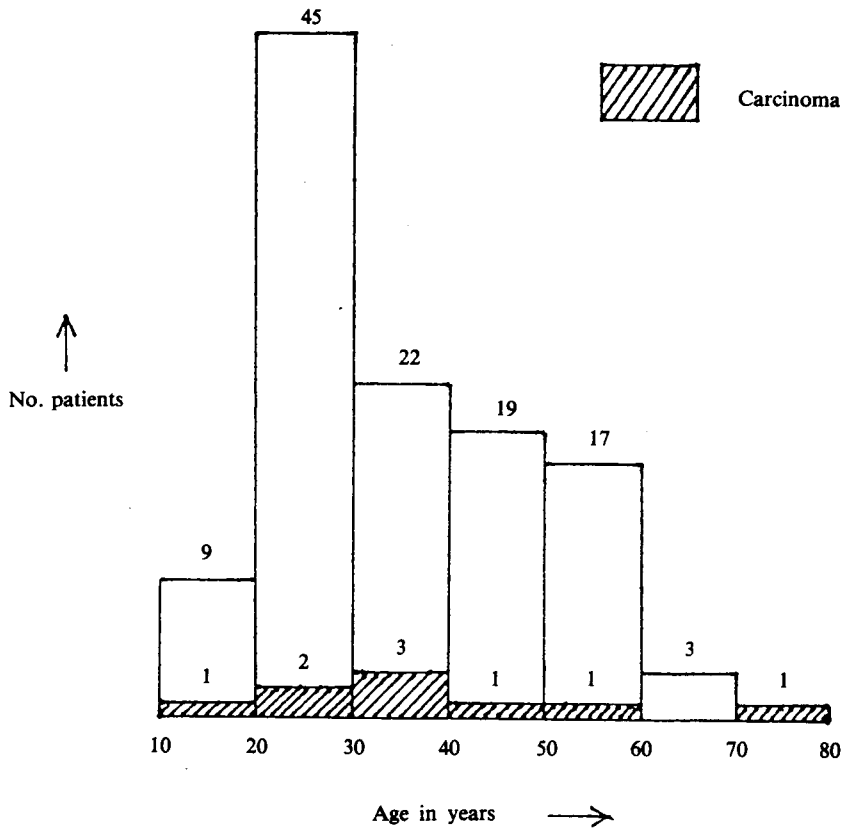

Table 1 : Final Pathological Diagnosis in 116 Patients

	No. patients	Per cent
Adenoma	80	69
Adenomatous goitre	24	20
Carcinoma	9	8
Cyst	3	3

Table 2 : Results of Ultrasound in 93 Patients

Operative findings	Total cases	Ultrasound	
		Correct	Incorrect
No. of nodules			
Single	78	77	1
Multiple	15	3	12
Physical characteristics			
Solid	39	37	2
Cystic	17	15	2
Complex	37	34	3

Table 3 : Results of Cytology and Needle Biopsy in 96 Patients

Pathological diagnosis	Total cases	Cytology/biopsy diagnosis			
		Benign	Malignant	Borderline	Negative
Carcinoma	7	1	4	2	-
Benign	89	33	13	18	25
Adenoma	68	26	11	14	17
Adenomatous goitre	19	6	2	4	7
Cyst	2	1	-	-	1

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