Original articles

Management options for solitary thyroid nodules in an endemic goitrous area

AK Sarda, Anju Gupta, PK Jain, S Prasad

Summary

An analysis of management of 546 cases of solitary thyroid nodules in an endemic area is presented. None of the evaluating procedures could effectively isolate benign from malignant disease. Of 508 cases considered clinically to be benign, 42 harboured malignancy on histological examination whereas of the 38 cases suspected clinically to be malignant, 21 were histologically benign. ¹³¹I-Thyroid scanning also lacked sensitivity in identifying malignant nodules since the prevalence of malignancy in cases which were 'cold' (44/316) was not significantly different from that amongst the 'uniform' cases (15/142). Fine-needle aspiration cytology, although the most sensitive and specific evaluating modality, did not decrease the number of operations for solitary thyroid nodules nor did it increase the incidence of malignancy amongst the operated cases, because of its limitations in differentiating benign from malignant follicular neoplasms. The conditions under which surgery was advocated are described.

Keywords: thyroid neoplasms, fine-needle aspiration cytology, goitrous areas

In the management of solitary nodules of the thyroid gland various evaluating procedures are utilised in an effort to differentiate between benign and malignant nodules and avoid unnecessary surgery. However, despite the use of different diagnostic modalities, it is practically impossible to exclude nodules which might not harbour malignancy. This dilemma is compounded in endemic goitrous areas where large numbers of patients with thyroid swellings may feel well and be able to perform normal work without bothering about the neck swelling which is prevalent amongst relatives and friends. This presents severe difficulties for the physician who regards all such swellings as neoplastic disorders, requiring active management. Further, the higher percentage of thyroid cancer, with a preponderance of follicular cancers in endemic areas,¹ precludes the use of fine-needle aspiration cytology (FNAC) as a reliable diagnostic tool as it cannot differentiate between benign and malignant follicular neoplasms.^{2,3} Reports that even early stages of thyroid cancer in these areas pursue an unrelenting clinical course,¹ make it mandatory that an objective pre-

operative evaluation is undertaken, so as to isolate cancers amongst the thyroid disorders managed in the out-patient department. In India, where 120 million people are estimated to live in iodine-deficient areas, of which one-third are goitrous,⁴ the problem assumes great clinical significance. We present our experience with the management of clinically benign solitary thyroid nodules in patients from the sub-Himalayan belt, which is a recognised endemic goitrous area.⁴

Materials and methods

The case records of 546 solitary thyroid nodules were analysed. The solitary thyroid nodule was a single nodule of either lobe or isthmus of the thyroid gland without any associated features of malignancy. The recorded proformas included clinical features with special emphasis on the rate of growth of the swelling, any change in voice, pressure symptoms, and any clinical evidence of hyperthyroidism. The thyroid hormonal profile (thyroxine, tri-iodothyronine, thyroid-stimulating hormone) was estimated by radioimmunoassay. A thyroid scan was recorded using a rectilinear scanner 24 hours after administration of 15 μ Ci of ¹³¹I. The scans were designated 'cold', 'uniform' or 'hot' depending on whether they were hypo-, iso-, or hyper-functioning. Thus, in patients under study there were 316 'cold' 142 'uniform' and 88 'hot' scans. FNAC was performed in 113 patients by the technique described earlier.² FNAC results were reported as benign (56 cases plus 18 cases with acellular aspirate), follicular neoplasms or suspicious (32 cases), or malignant (seven cases) depending on the cell characteristics. Cystic swellings were diagnosed on the basis of aspiration of at least 3 ml of fluid and an effort was always made in such cases to empty the cyst completely by gentle pressure on the gland.

Until the advent of FNAC, all 'cold' solitary thyroid nodules were advised surgery (243 cases); subsequently, patients with FNAC reports of follicular neoplasms or malignancy have been advised operation (39 cases). Indications for surgery are listed in box 1.

Hemithyroidectomy was performed in patients with a pre-operative diagnosis of a benign nodule; in 20 patients a completion (near-total) thyroidectomy was performed on receipt of the histological diagnosis of malignancy. In patients with a definitive diagnosis of cancer established by FNAC, near-total thy-

Department of
Surgery, Maulana
Azad Medical
College and
Associated Lok
Nayak Hospital,
New Delhi, India
AK Sarda
A Gupta
PK Jain
S Prasad

Correspondence to
Dr AK Sarda, 27, RPS,
Triveni-I, New Delhi-110
017, India

Accepted 29 January 1997

Indications for surgery*'Cold' solitary thyroid nodule*

- FNAC +ve for malignancy/suspicious
- cosmesis
- large size, especially with pressure symptoms
- clinical suspicion of malignancy on the basis of recent rapid growth, pain, hoarseness, firm-to-hard on palpation
- male sex
- not responsive to suppressive therapy with thyroxine

Cystic nodule

- recurs after one complete aspiration
- residual swelling persists
- aspirated fluid cytologically +ve for malignancy

'Hot' solitary thyroid nodule

- hyperthyroid
- euthyroid: size > 3 cm, age > 40 years, duration > 3 years

Box 1

roidectomy was performed as described earlier.^{3,4}

Statistical significance was calculated using the chi-square test.

Results

The prevalence of malignancy in solitary thyroid nodules in the present study was 10.8% (59/546). There was no significant difference in the prevalence of malignancy in patients below and above 40 years of age. There was a higher prevalence in male patients; although the overall male to female ratio was 1:2.1, the ratio was 1:0.9 amongst those with malignant nodules. In females, the prevalence of malignancy was significantly higher in patients above 40 years (11/92) than those below 40 years (17/280) ($p < 0.005$). However, no such difference was encountered in male patients (18/105 patients below 40 years had malignancy compared to 13/69 patients above 40 years).

On the basis of clinical features (table 1), malignancy was suspected in 7% (38 cases). However, history and clinical examination cannot be considered good predictors of malignancy since 86.2% of the malignancies occurred in nodules with a history of slow growth (50/521). Further, of the 38 cases clinically suspected to be malignant, only 44.7% (17 cases) were shown histologically to be cancers.

¹³¹I-Thyroid scanning was the main screening procedure used in the present study. Of the 316 'cold' scans, 44 (13.9%) were malignant; of the 142 'uniform' scans, 15 (10.6%) were malignant, while none of the 88 'hot' scans were malignant. The difference in the prevalence of malignancy between the 'cold' and the 'uniform' scans was not statistically significant ($p < 0.5$), even when correlated for patients below and above 40 years of age or separately in the two sexes. Thus, although scanning could assess the functional status of

Table 1 Modes of presentation of 546 solitary thyroid nodules

Presentation	Total	Malignant
Growing neck mass:		
gradual	521	50
rapid	15	9
Pain	19	6
Voice change	16	7
Pressure symptoms	8	3
Hyperthyroid	60	0
Clinically benign	508	42
Clinically suggestive of malignancy	38	17

Investigations for solitary thyroid nodules*Clinical suspicion (poor predictor)*

- clinically benign ($n=508$): 42 malignant on histology
- clinically malignant ($n=38$): 28 benign on histology

FNAC (sensitive and specific)

- 56 cytologically benign: 2 carcinoma histologically
- 7 cytologically malignant: 5 carcinoma, 2 follicular adenoma on histology
- limited role in endemic area due to inability to differentiate between benign and malignant follicular neoplasms

¹³¹I-Thyroid scan (lacks sensitivity)

- malignancy in cold scans: 44/316
- malignancy in uniform scans: 15/142

Box 2

the nodule, it lacked sensitivity in discriminating benign from malignant nodules.

FNAC, which was performed in 113 cases, had a sensitivity of 76.9%, specificity of 71.0%, and an overall accuracy of 71.7%. The false-negative rate was 4.1% and 2/7 were falsely reported as positive (table 2). Of the 32 aspirates reported as follicular neoplasms, 21.9% were malignant. Although a specific cytologic diagnosis helped in planning a definitive operative procedure, there was no decrease in the number of operations nor was there an increase in the prevalence of malignancy in the surgically treated cases (44/433 before the introduction of FNAC and 15/113 since, with a p -value of < 0.5). Another advantage of FNAC lay in its ability to differentiate purely from partially cystic lesions. Thus, 10/28 cysts were 'cured' because they subsided after aspiration and did not recur during the two-to-three-year follow-up period.

Histologic findings in the operated cases are given in table 3.

Discussion

In the present study, 10.8% of the 546 cases of solitary thyroid nodules were found to be malignant. A history of exposure to radiation, extremes of age, male sex, recent rapid growth

Table 2 Correlation of FNAC and histopathology in patients with solitary thyroid nodules

Cytology	Number	Histopathology		
		Follicular adenoma	Adenomatous goitre	Carcinoma
Benign	56	20	34	2
Follicular neoplasm	32	19	6	7
Carcinoma	7	2	0	5
'Acellular' fluid	18 (4*)	3	10	1

*Reported histologically as simple cysts

Table 3 Histopathology of 546 solitary thyroid nodules

	Total number	'cold' (n=316)	'uniform' (n=142)	'hot' (n=88)
Follicular adenoma	247	134	55	58
Adenomatous goitre	202	112	62	28
Carcinoma*	59	44	15	0
Cysts	18	15	3	0
Thyroiditis	15	7	6	2
Tuberculosis	2	2	0	0
Abscess	2	2	0	0
Parathyroid adenoma	1	0	1	0

*papillary 38; follicular 12; medullary 4; anaplastic 3; other 2

of the nodule, pain and pressure symptoms, and hard physical character of the nodule have been reported to be predictive of malignancy in 20–60% of patients.⁵ History and examination can be regarded as poor predictors of malignancy, however, in the present study, since in only 7% of nodules could a suspicion of malignancy be harboured on the basis of clinical examination, and of these less than half were malignant. We did find, however, that nodules occurring in males of all age groups and in females above 40 years of age should be viewed with a higher degree of clinical suspicion for malignancy.

Radionuclide thyroid scanning was previously employed extensively to screen for malignancy. In 'cold' scans, the prevalence of malignancy was reported to be up to 31%,⁶ while 'hot' scans were rarely malignant. The main limitation of the scanning procedure is that it cannot distinguish benign from malignant nodules and, since the majority of surgically treated 'cold' nodules are benign histologically, this evaluating modality cannot be considered a sensitive or specific diagnostic option. It is also not cost effective⁷ and has been reported to be associated with the risk of radiation exposure.⁸ It is significant that, in the present study, the prevalence of malignancy in 'cold' nodules was not statistically different from that occurring in the 'uniform' scans. Thyroid nuclide scanning was, therefore, not a sensitive discriminant of malignancy.

FNAC has been recognised as a sensitive, specific, and cost-effective diagnostic aid in selecting solitary thyroid nodules for surgery.^{2,7–14} Routine use of the procedure has been reported to decrease the cost of treatment, decrease the number of operations performed and increase the number of surgically proven cancers.^{2,14} However, these findings were not corroborated by the present study. Firstly, the study underlined the main limitation of FNAC, especially pertinent in

endemic areas with a higher percentage of follicular neoplasms, ie, its inability to differentiate benign from malignant follicular tumours.^{2,9–14} A suspicious cytologic finding always needs surgical treatment since 10–50% (21.9% of the 32 suspicious cytologic reports in the present study) are histologically malignant.¹⁵ Secondly, the number of operations performed did not decrease in the present series, nor was there any significant increase in the number of surgically proven cancers. A possible explanation for this discrepancy could be the reasons, outlined above, for advising surgery in our patients; the reported virulent behaviour of thyroid cancers, even in their early stages, in endemic goitrous areas,⁴ also dictates that nodules with a clinical suspicion of malignancy be removed surgically. Patients presenting late in the course of the disease with large nodules, with or without pressure symptoms, account for a substantial number of operations performed.

Thus, of all the evaluating procedures employed, FNAC was found to be the most reliable and safe modality, providing more specific information than was attainable with the other techniques. However, especially in endemic goitrous area, FNAC cannot be regarded as a complete answer and it is suggested that a combination of diagnostic procedures should be employed to differentiate between benign and malignant tumours, with clinical judgement forming an essential evaluating step in decision making.

A therapeutic decision for a patient presenting with a solitary thyroid nodule, based on the investigative modalities described above, is outlined in the figure. Surgery for solid 'cold' and 'uniform' nodules was advised if the cytologic report suggested cancer and in large nodules producing pressure symptoms; other indications for operation were cosmesis, a clinical suspicion of malignancy, and male sex.

Figure Management of solitary thyroid nodules

Thyroid suppression has been used as a diagnostic and therapeutic modality such that, following three to six months of therapy, if the tumour decreases in size it can be regarded as benign and can be managed with life-long hormone suppression.^{7-10,16} However, in the present study it was not common practice to subject patients to hormone suppression, primarily due to the fact that since both benign and malignant nodules may respond to such therapy, a decrease in the size of the nodule may not always signify its benign nature.^{16,17} Besides, not all the patients in these areas were available for regular assessment of change in the size of the nodule.

Management of the cystic thyroid nodule has been facilitated by the diagnostic and therapeutic application of FNAC. Our approach to such lesions is guided by the findings in an earlier study in which 44.7% of the cysts were cured after one aspiration. Surgery was advised if the cysts recurred after one aspiration, when the cytology of the aspirated fluid was positive for malignancy, or if, after aspiration, a residual swelling persisted.²

Surgery is advocated for 'hot' nodules in hyperthyroid patients. Surgery for euthyroid 'hot' nodules may be suggested on the basis

of reports that hyperthyroidism occurs more frequently in such lesions in males¹⁸ and in older age groups.^{18,19} The level of function is roughly proportional to nodule size,¹⁸⁻²⁰ and hyperthyroidism is reported to occur when the solid component exceeds 3 cm.^{18,20} Even in larger nodules, hyperthyroidism was more frequent in patients over 40 years of age.¹⁹ A follow-up study has also shown that euthyroid patients with 'hot' nodules become hyperthyroid within 1-15 years.^{18,20} Hyperthyroidism has also been reported to be twice as common in nodules present for more than three years from the time they were first noticed, especially in patients over 40 years of age.

Thus, surgery for solitary thyroid nodules should be performed if there is any cytologic suspicion or evidence of malignancy or for hyperthyroidism. In endemic goitrous areas, however, more thyroidectomies are performed on the basis of a clinical suspicion of malignancy, as it is recognised that even early cancers behave virulently³ and the treating surgeon does not want to miss any cancer in solitary nodules in patients from socio-economically backward and remote areas who are likely to be lost to follow-up.

- Pandav CS. Towards the eradication of iodine deficiency disorders in India (editorial). *Indian J Comp Med* 1986; 11.
- Sarda AK, Bal S, Duttagupta S, et al. Diagnosis and treatment of the cystic disease of the thyroid by aspiration. *Surgery* 1988; 103: 593-6.
- Sarda AK, Kapoor MM. Thyroid carcinoma—a report of 206 cases from an area with endemic goitre. *Acta Oncol* 1990; 29: 863-7.
- Sarda AK, Bal S, Kapoor MM. Near-total thyroidectomy for carcinoma of the thyroid. *Br J Surg* 1989; 76: 90-2.
- Burch HB. Evaluation and management of the solitary thyroid nodule. *Endocrinol Metab Clin North Am* 1995; 24: 663-710.
- Oomen R, Walter NM, Tulasi NR. Scintigraphic diagnosis of thyroid cancer: correlation of thyroid scintigraphy and histopathology. *Acta Radiol* 1994; 35: 222-5.
- Jossart GH, Clark OH. Well differentiated thyroid cancers. *Curr Prob Surg* 1994; 12: 933-1024.

- Burrow GN. The thyroid: nodules and neoplasia. In: Felig P, Baxter JD, Broadus AE, Frohman LA, eds. *Endocrinology and metabolism*. New York: McGraw-Hill Book Co, 1987; pp 473-510.
- Silverman JF, West RL, Larkin EW, et al. The role of fine-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasia. *Cancer* 1986; 57: 1164-70.
- Ashcraft MW, van Herle AJ. Management of thyroid nodules: II. Scanning techniques, thyroid suppressive therapy, and fine needle aspiration. *Head Neck Surg* 1981; 3: 297-322.
- Gharib H, Goellner JR. Fine needle aspiration biopsy of the thyroid: an appraisal. *Ann Intern Med* 1993; 118: 282-9.
- Lenquist S. The thyroid nodule. Diagnosis and surgical treatment. *Surg Clin North Am* 1987; 67: 213-32.

- 13 Backdahl M, Wallin G, Lowhagen T, *et al.* Fine needle aspiration biopsy cytology and DNA analysis: their place in the evaluation and treatment of patients with thyroid neoplasms. *Surg Clin North Am* 1987; **67**: 197–212.
- 14 Frable WJ. The treatment of thyroid cancer. The role of fine-needle aspiration cytology. *Arch Otolaryngol Head Neck Surg* 1986; **112**: 1200–3.
- 15 Rojeski MT, Gharib H. Nodular thyroid disease. Evaluation and management. *N Engl J Med* 1985; **313**: 428–36.
- 16 Clark OH. TSH suppression in the management of thyroid nodules and thyroid cancer. *World J Surg* 1981; **5**: 39–47.
- 17 Hill LD, Reebe HG, Hipp R, *et al.* Thyroid suppression. *Arch Surg* 1974; **108**: 403–5.
- 18 Hamburger JI. Evolution of toxicity in non-toxic autonomously functioning thyroid nodules. *J Clin Endocrinol Metab* 1980; **50**: 1089–93.
- 19 Sarda AK, Padhy AK, Bal S, *et al.* Autonomously functioning thyroid nodules. *South Med J* 1989; **82**: 206–9.
- 20 Blum M, Shenkman L, Hollander CS. The autonomous nodule of the thyroid: correlation of patient age, nodule size and functional status. *Am J Med Sci* 1975; **269**: 43–50.