

East African Medical Journal Vol. 78 No. 5 May 2001

THYROID CARCINOMA AT KING EDWARD VIII HOSPITAL, DURBAN, SOUTH AFRICA

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T.V. MULAUDZI, P.K. RAMDIAL, T.E. MADIBA and R.A. CALLAGHAN

ABSTRACT

Background: Western literature depicts papillary carcinoma as the most common thyroid malignancy followed by follicular carcinoma.

Objective: To assess the clinical pattern of thyroid carcinoma among African and Indian patients.

Setting: King Edward VIII Hospital, Durban, South Africa.

Design: A retrospective study.

Subjects: One hundred patients with thyroid carcinoma treated at a tertiary teaching hospital between 1990 and 1997.

Results: Seventy seven patients were Africans and 23 were Indians. The male to female ratio was 1:6. Ninety eight patients presented with goitre with or without regional lymph node involvement or distant disease. The duration of symptoms ranged from one to 360 months. The mean age at presentation was 48.6 ± 16.0 years. Follicular carcinoma was the most common malignancy among African patients (68%), followed by papillary carcinoma (16%), anaplastic carcinoma (13%) and medullary carcinoma (2.6%). Papillary carcinoma was the most common malignancy among Indian patients (57%) followed by follicular carcinoma and medullary carcinoma. There was no anaplastic carcinoma among Indian patients. Fifty five patients underwent lobectomy with 32 undergoing subsequent completion thyroidectomy. Nine patients had near total thyroidectomy, 27 were offered total thyroidectomy as primary surgery and eight had biopsy only. The in-hospital mortality was 8%. Recurrence rate was 8%.

Conclusion: Most patients present long after the development of symptoms. Follicular carcinoma is the most common thyroid malignancy among Africans. Further studies are required to explain this phenomenon.

INTRODUCTION

Thyroid cancer is uncommon, representing 1% of all malignancies(1). Papillary thyroid carcinoma is the most frequent histological subtype followed by follicular carcinoma(1-3). Thyroid carcinomas are two to four times as frequent in women as in men and the median age at diagnosis is 45-50 years(4).

This study was undertaken to document differences in clinical pattern of thyroid carcinoma among African and Indian patients at King Edward VIII Hospital, Durban, South Africa. This hospital traditionally treated African and Indian patients from the days when health care was segregated in South Africa(5,6). Despite the abolition of racial discrimination by the new government in 1994, patient demographics in this hospital have remained generally unchanged. Consequently only these two population groups could be studied.

MATERIALS AND METHODS

The medical records of all patients treated for thyroid carcinoma from 1990 upto 1997 were retrieved from medical records and retrospectively analysed. Demographic data, clinical

presentation, management and outcome were all documented. Data regarding follow up were obtained from outpatient records.

The protocol regarding the management of differentiated thyroid carcinoma in our institution is as follows: Patients presenting with a thyroid nodule undergo fine needle aspiration biopsy (FNAB) during work-up. If the FNAB shows malignant cells then patients are stratified into low and high risk groups according to the "AMES" criteria as described by Cady *et al* in 1979(7). Low risk patients are offered lobectomy (+ isthmusectomy) and total thyroidectomy is reserved for those at high risk. Where the diagnosis of carcinoma is made postoperatively on paraffin section after lobectomy, the "AGES" criteria are used as described by Hay *et al* in 1987(8) to decide if the patient requires re-operation and completion thyroidectomy. High-risk patients undergo total thyroidectomy. The presence of nodal metastases necessitates modified neck dissection. After total thyroidectomy in patients with follicular carcinoma a radioactive iodine(I^{131}) uptake scan is done to screen for metastases. If these are present, the patients are offered a therapeutic dose of radioactive iodine.

RESULTS

There were 100 patients (Table 1), of whom 86 were females (male to female ratio 1:6). Their ages ranged from

17 to 89 years (mean 48.62±16.00, median 53). Seventy seven patients were Africans (68 females and nine males) and 23 patients were Indians. Female preponderance was noted in both African and Indian patients, but it was more marked in African patients.

Table 1

Patient's profile

	Overall	African	Asian
Total	100	77	23
Males	15	9	7
Females	86	68	16
M:F ratio	1:6	1:8	1:2
Age (years) range	17-89	18-89	17-63
Mean	48.62±16.00	50.91±16.11	43.19±14.04

The duration of goitre ranged from one month to 360 months (mean 46±61 months). Twenty one patients presented with associated complications of goitre, namely: voice changes(sixteen), dysphagia(ten), stridor(four), loss of weight(four) and thyrotoxicosis(two). Some patients had more than one complication. The histological pattern is shown in Table 2. Follicular carcinoma was the most common, followed in a descending order by papillary carcinoma, anaplastic carcinoma and medullary carcinoma. One patient had metastatic squamous carcinoma of the oesophagus.

Table 2

Distribution of thyroid carcinoma

Type	African n=77	Asian n=23	Overall n=100	p value
Papillary	12 (16%)	13 (57%)	25	<0.0001*
Follicular	52 (68%)	8 (35%)	60	0.005*
Medullary	2 (3%)	2 (9%)	4	0.226+
Anaplastic	10(13%)	0	10	0.111+
Secondary	1 (1%)	0	1	

*Chi-squared test

+Fisher's exact test

African patients: The duration of goitre ranged from one month to 360 months. Disease was confined to the thyroid gland in 48 patients including the patient with secondary oesophageal carcinoma. There was associated cervical lymph node involvement in ten patients. Out of the 17 patients who presented with associated distant disease, two did not have clinical evidence of goitre. Follicular carcinoma was the most common malignancy (68%) followed by papillary carcinoma (16%), anaplastic carcinoma (13%) and medullary carcinoma (2.6%).

There were 12 patients with papillary carcinoma. Of eight patients who underwent lobectomy, three proceeded to total thyroidectomy. One patient who was offered thyroidectomy defaulted prior to surgery. A decision was made in the other four patients not to subject them to

completion thyroidectomy. In one patient with an irresectable tumour, only a biopsy could be performed at surgery. There were 52 patients with follicular carcinoma. Thirty underwent lobectomy, 20 of whom proceeded to completion thyroidectomy. Five patients underwent near-total thyroidectomy and seventeen underwent total thyroidectomy. Two patients with medullary carcinoma underwent lobectomy and subsequent completion thyroidectomy. Of the twelve patients with anaplastic carcinoma, three underwent lobectomy (one of whom required completion thyroidectomy); one underwent near-total thyroidectomy and one underwent total thyroidectomy. Seven had irresectable tumours, in which biopsy only was possible.

Two patients with papillary carcinoma received a therapeutic dose of radioactive iodine following total thyroidectomy. Twenty eight patients with follicular carcinoma received a therapeutic dose of radioactive iodine. Six patients with follicular carcinoma received external beam radiation. All patients with anaplastic carcinoma were given external beam radiotherapy.

The median follow up was five months (range 1-120). All six recurrences were follicular carcinoma. Eight patients died in hospital (anaplastic 3, follicular 4, papillary 1), giving an in-hospital mortality of 10%. Six patients re-presented with recurrence (8%), all with follicular carcinoma. Twenty two patients (42%) had disease at last follow-up (follicular 17, anaplastic 3, papillary 2).

Indian patients: The duration of goitre ranged from three months to 156 months. Disease was confined to the thyroid gland in 15 patients (papillary 10, follicular 4, medullary 1). There was associated cervical lymph node involvement in four patients (papillary 2, follicular 1, medullary 1). Four patients presented with associated distant disease (papillary 1, follicular 3).

Papillary carcinoma was the most common malignancy, followed in order by follicular carcinoma and medullary carcinoma. There were no cases of anaplastic carcinoma among Indian patients. There were 13 patients with papillary carcinoma. Six patients underwent lobectomy, two of whom went on to have total thyroidectomy. A decision was made in the other four patients not to subject them to total thyroidectomy, as they were low risk categories. Three patients underwent subtotal thyroidectomy and four underwent total thyroidectomy. There were eight patients with follicular carcinoma. Six underwent lobectomy, four of whom went on to have total thyroidectomy and two patients were considered low risk and were not offered total thyroidectomy, the other two patients underwent total thyroidectomy. The two patients with medullary carcinoma underwent total thyroidectomy. Six patients with follicular carcinoma received therapeutic doses of radioactive iodine.

The median follow up was 12 months (range 1-114 months). There were two recurrences (9%), one papillary and one follicular. Six patients (26%) had residual disease at the last follow up (papillary 2, follicular 3, medullary 1). There were no in-hospital deaths.

Whole group: Complications associated with surgery were hypocalcaemia (transient and permanent) in 19% of cases, hypothyroidism (6%), hoarseness (5%), wound infection (2%) and haematoma (2%). The overall complication rate was 34%.

DISCUSSION

Papillary thyroid carcinoma is reported in the literature to be the most common histological sub-type of thyroid carcinoma accounting for 60-70% of cases (1,3,9) followed by follicular carcinoma (15-25%) (1,3). In this study, follicular histology was more frequent than papillary carcinoma in the whole group but predominated significantly in Blacks while papillary histology predominated in Indian patients. Decker (10) found in 1974 in Johannesburg, South Africa, that follicular morphology predominated. We believe that this is merely due to chance. Kalk *et al* (5) also noted in 1997 that there was a national predominance of follicular carcinoma in South Africa. They also noted that the incidence of thyroid carcinoma was higher in Whites compared to Africans. In that study the follicular to papillary ratio was 2:3 in the whole group, was 3.7:1 in Africans and was 0.68:1 in Whites. In this study it was 2.4:1 overall, 4:1 among African patients and 1:1.6 among Indian patients.

There is convincing evidence that nutritional iodine status influences the morphology of thyroid cancers both within and between population groups (5,11-14). These studies have shown that papillary cancers predominate in iodine-replete areas while follicular and anaplastic types were commonest in iodine deficient populations.

The female preponderance and the mean age at diagnosis was similar to that in the West (1-3). The most common presenting symptom was goitre (98%) with most patients presenting long after the beginning of symptoms. Twenty one per cent of these patients presented because there were complications associated with the presence of goitre.

Controversy exists in the surgical management of differentiated thyroid carcinoma. The proponents of total thyroidectomy (2,15) recommend its use in differentiated thyroid carcinoma because it reduces the small but significant chance of a well-differentiated thyroid carcinoma undergoing anaplastic transformation, allows the measurement of serum thyroglobulin to be used as screening test for recurrent or persistent disease, reduces recurrence rate and eliminates multifocal disease. Those who advocate less than total thyroidectomy (1-3,8,16) cite the high complication rate associated with total thyroidectomy (parathyroid and recurrent laryngeal nerve injury) coupled with lack of improved survival rates.

Cady *et al* (7) in 1979 made a practical rating system called "AMES" which is based on the age of the patient, the presence of remote metastases, the extension of the primary tumour beyond the thyroid capsule and the size of the primary tumour. This helped grade patients into high and low risk groups. In 1987 Hay *et al* (8) proposed a new

scoring system which included histological grading known as "AGES". This scoring system denotes age of the patient, histological grade of the tumour, extension beyond thyroid capsule and size of the primary tumour. The "AMES" system can be applied preoperatively, as it does not require histology and we use it to risk-grade the patients who have a preoperative diagnosis. For patients who have the diagnosis made on paraffin section postoperatively, the "AGES" criteria can be used, which is dependent on histological grading. If papillary carcinoma has associated nodal metastasis when first diagnosed, a modified neck dissection is advised (3,15).

Medullary thyroid carcinoma is somewhat aggressive and multicentric (3) and total thyroidectomy is the treatment of choice (2,3,17,18). There were only four patients with medullary thyroid carcinoma in this study and all were managed by total thyroidectomy. Although 80% of patients with sporadic medullary thyroid carcinoma have unilateral disease (17) each patient should be regarded as a potential index case for the familial syndrome. Pheochromocytoma should be excluded by preoperative investigations in patients with MEN 2A and 2B and, if present, adrenalectomy should be performed prior to thyroidectomy. There is currently no proven place for adjuvant therapy in medullary thyroid carcinoma.

Anaplastic carcinoma grows rapidly and infiltrates into nearby structures. Occasionally surgical removal is possible by total thyroidectomy if there is no evidence of gross extra capsular invasion (3,19-21). Two patients in this series had total thyroidectomy and one had sub-total thyroidectomy. The other two patients did not return for total thyroidectomy. The rest only had biopsy as the disease was resectable.

The overall surgical complication rate of 34% was due to the inclusion of hypocalcaemia, which occurred in 19%. Hypocalcaemia following total thyroidectomy varies from 0-29% in the literature (1,2,15,22-24).

The importance of thyroid stimulating hormone (TSH) suppression after surgery by thyroxine administration has been emphasised by some because almost all differentiated thyroid carcinomas are TSH dependent (1,2,9,21,25). It has the advantage of minimal side effects and low cost (1,9,21). It has also been shown to improve recurrence and survival rates (4). Therapeutic radioactive iodine is preferred when metastatic disease is present (1,2,21,23,26). It has traditionally been used for follicular carcinoma although some authors have supported its use for all differentiated carcinoma (1,2,4,21,23,26). Thirty seven patients in this series were given radioactive iodine (papillary 4, follicular 33).

External beam radiotherapy is used selectively in well-differentiated carcinoma. It is recommended in patients with inoperable or residual disease that does not take up iodine as well as for skeletal metastases if radioiodine is not effective (2,4,21,27,28). While some authors have shown temporary response of anaplastic carcinoma with external beam radiotherapy (21,29), others have shown no benefit (3).

The overall five-year recurrence rate of 8% in this series (similar for both groups) was lower than the 18-24% reported in the literature(1,30). The development of local recurrence of well-differentiated thyroid carcinoma reportedly carries a 30-50% mortality rate(30). Our in-hospital mortality rate was 8% (10% for Africans and 0% for Indians). It is tempting to postulate that the high mortality rate among African patients was related to the high incidence of follicular carcinoma and anaplastic carcinoma in this population group which are in themselves more aggressive thyroid tumours.

In conclusion, we have shown that follicular carcinoma is the most common thyroid malignancy among Africans while it is the second most common thyroid malignancy after papillary carcinoma among Indians. The age at diagnosis of thyroid carcinoma and sex distribution compares to that in the west. Most patients in our practice present long after the development of symptoms. Uniform management of differentiated carcinoma is required so that long term studies can identify appropriate forms of treatment. Further research is required among African patients to determine reasons for the preponderance of follicular carcinoma.

ACKNOWLEDGEMENTS

To the Medical Superintendent of King Edward VIII Hospital for giving us permission to use patients' records from the hospital's medical registry and to publish these data.

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