Retrospective Analysis of Thyroid Cancer Patients

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Abstract

Background : Thyroid cancer is a spectrum of neoplasms and manifests in varied forms. The issues related to presentation, management and outcome of patients with thyroid malignancy are highlighted.

Methods : Retrospective analysis of 70 patients and survival analysis for event free survival was done.

Result : Papillary carcinomas constituted 88 percent followed by follicular cancers at nine percent of all cancers. Females were affected more than males in the ratio of 2.2: 1. Mean age of presentation for papillary cancer was 39 years and for follicular 50 years. Sixteen percent patients had regional and 10 percent distant metastases. Seventeen percent showed raised serum thyroglobulin and 29 percent had an abnormal whole body scan during the follow up. Relapse rate were similar in those receiving 30 mCi of radioiodine and in those receiving more than 30 mCi.

Conclusion : The study shows that tumour marker thyroglobulin has higher negative predictive value. Overall prognosis for differentiated thyroid cancers is good.

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Key Words : Thyroid cancer; Radioiodine therapy; Whole body scan

Introduction

Thyroid cancer is a spectrum of neoplasms ranging in pathogenicity from differentiated carcinoma thyroid with excellent prognosis at one end to anaplastic carcinoma thyroid, with a fatal outcome at the other [1]. Although thyroid cancer accounts for only 1% of all cancers, it is the commonest endocrine tumour. The estimated presence of palpable thyroid nodules in 4% of the adult population warrants that thyroid cancer should remain high on the clinician's list and thyroid nodules should be evaluated to rule out malignancy [2].

Though management of cancers of non-follicular origin is standardized, consensus is still lacking for differentiated cancers (papillary and follicular) of follicular cell origin. The favoured approach is to treat them with near total thyroidectomy along with radioiodine therapy and suppressive doses of thyroid hormones [3,4]. Since the differentiated thyroid carcinoma and its functioning metastases concentrate radioiodine, these tumours are amenable to radioiodine therapy. Radioiodine therapy has little role in the treatment of medullary and anaplastic carcinoma thyroid. Radioiodine is an effective and safe treatment modality for differentiated thyroid cancers and the reported incidence of complications has been low. Early complications include acute radiation sickness, sialoadenitis, pain, swelling and haemorrhage in metastases, precipitation of hyperthyroidism and bone

marrow suppression. Long-term complications seen after three months of initial radioiodine treatment are leukaemia, permanent bone marrow suppression, radiation pneumonitis, pulmonary fibrosis, and anaplastic transformation of differentiated thyroid cancer. However these side effects are infrequent and are common when more than 100 mCi of radioiodine is given [5].

The aim of this study was to analyze the clinical course of thyroid cancer in a heterogeneous population and to represent a cross-sectional view of current therapy. Our hospital treats patients who have been diagnosed elsewhere either on the basis of fine needle aspiration cytology (FNAC) or biopsy following lobectomy.

Material and Methods

This is a retrospective study of thyroid cancer patients and the median follow up period of these patients was 58 months (range, 4 to 348 months). Cases were registered only if tumour directed treatment was given. A total of 73 patients were registered, treated and being followed up. However, insufficient data was available for three patients and these were subsequently excluded from analysis.

Clinical stages of tumour were defined as localized (confined entirely to thyroid), regional (direct extension to surrounding tissue or regional nodal involvement), or distant (remote metastases or tumour cells growing in non lymphoid areas that were not contiguous with the normal thyroid gland). Tumours were divided into four histological categories; the

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papillary group including pure papillary adenocarcinoma, mixed papillary-follicular cancer and adenocarcinoma; the follicular including oxyphilic or Hurthle cell carcinoma; the medullary and anaplastic. Some subcategories were combined because of the well-known similarities in biologic behaviour.

Whole body evaluation for metastatic thyroid disease was first performed within two months of thyroidectomy. Thyroid replacement was withheld during this period to allow for endogenous thyroid stimulating hormone (TSH) stimulation of any remaining normal thyroid tissue in the thyroid bed and any functioning metastatic lesion. Siemens' Diacam Gamma Camera with high-energy collimator was used to obtain images. Dose of 2-4 mCi radioiodine was used and images obtained after 72 hours.

During followup, patients underwent complete physical examination, estimation of serum thyroglobulin, serum TSH, serum calcium, chest radiographs and whole body radioiodine scans. Our protocol is to repeat radioiodine scans at yearly intervals until they become negative and a follow up scan two years later. If the latter scan is negative, then further scans are obtained only at five yearly intervals unless clinical or other laboratory data (serum thyroglobulin, chest radiographs) indicate recurrence. A median dose of 30 mCi was given for ablation of residual thyroid. For patients presenting with regional lymph node metastases a median dose of 50 mCi was used. Higher doses were administered for distant metastases, which were 100 mCi for pulmonary and 150 mCi for brain metastases.

A database was created in MS Access and SPSS version 11.0 used for statistical analysis. Proportions, means, medians etc were calculated and suitable tests of significance carried out. Survival analysis was also carried out to get an overview of event free survival in these patients.

Results

Out of the 70 patients included, the male to female ratio was 1: 2.2 (22 males and 48 females). The majority of well differentiated malignancies manifested between second and fifth decades of life. Mean age at onset was 41 ± 11.7 years (median 40, range 16-66). Fifty three percent of the patients with papillary cancer were less than 40 years of age (mean 39 years) as compared to only 17 percent with those having follicular carcinoma (mean 50.3 years). However the difference was not statistically significant ($p=0.08$).

Table 1 shows that papillary carcinoma was the commonest, accounting for sixty-two cases (88%), followed by follicular carcinoma (9%) and medullary carcinoma (3%). No cases of anaplastic carcinoma were seen. Table 1 also depicts a comparison with the world literature [6]. Eighty seven percent males had papillary carcinoma as compared to 89 percent of females. The difference between males and females for the type of cancer was not statistically significant (p value = 0.87). The mainstay of diagnosis was fine needle aspiration cytology (FNAC). In patients on longer follow up the diagnosis was established on the final biopsy report following a hemithyroidectomy for a cold nodule, as FNAC was not widely available at that time.

Table 1

Distribution of malignant thyroid tumours amongst study group and comparison with world literature

Type of tumour	World literature [6] (%)	Our hospital (%)
Papillary carcinoma	60-80	88
Follicular carcinoma	5-25	9
Medullary carcinoma	5-10	3
Anaplastic carcinoma	4-10	0

Table 2

Profile of surgery

Type of surgery	Number of cases
Near total thyroidectomy	52
Completion thyroidectomy	5
Near total thyroidectomy with neck dissection	11
Total thyroidectomy	2

Surgery was carried out in all the cases. 52 (74%) patients had near total thyroidectomy and all the patients were put on suppressive doses of thyroid hormones. The details of surgery are given in Table 2. As a reflection of difference in the type of surgery carried out, all males had residual thyroid as compared to 87 percent females in the postoperative period. All these cases were given radioiodine therapy. Subsequent follow up showed 23 percent of males and 33 percent of females had residual, recurrent, or metastatic disease. Eight (11%) patients showed normal whole body scans carried out in the post surgical period. The remaining cases showed functional thyroid tissue in the neck requiring radioiodine ablation. The residual/recurrent/metastatic disease was identified by subsequent whole body scans which showed functional thyroid tissue in 18 (26%), 6 (9%) and 3 (4%) patients in the first second and third followup respectively.

In our study, patients receiving upto 30 mCi of radioiodine (62%) were compared with those receiving more than 30 mCi (38%) at first contact. On comparison it was seen that 53 percent of those receiving upto 30 mCi had relapse as compared to 47 percent of the other group. However this difference was not statistically significant ($p=0.140$).

Table 3 shows distribution of various parameters based on gender and age of patients. Of these 62 (88%) patients were given radioiodine therapy after surgery with doses ranging from 25-150 mCi. Dose of 30 mCi was used to ablate residual thyroid tissue where as higher doses were given to treat metastases and cancer recurrence. After the initial radioiodine therapy, 18 cases required subsequent radioiodine treatment during first, six in second and five in third followup respectively. A total of 20 (29%) cases had an abnormal whole body scan during the follow-ups. Males were given a median dose of 40 mCi on first follow up whereas females were given a radioiodine dose of 30 mCi ($p=0.02$). Though 33 percent of females had abnormal whole body scan during follow up as compared to 27 percent of males but this was not statistically significant ($p=0.78$).

Seven (10%) cases presented with distant metastases and

Table 3

Distribution of type of thyroid cancer, values of serum thyroglobulin, relapse and radio iodine (RAI) dose amongst study patients as per gender and age

	Papillary carcinoma (%)	Abnormal STG at first follow up (%)	Abnormal STG at fourth follow up (%)	Residual thyroid (%)	Relapse at first follow up (%)	Relapse at second follow up (%)	RAI dose (mCi) (Median)
Gender							
Male	87	11	25	100	23	8	40
Female	89	10	7	87	33	33	30
p value	0.87	1.00	0.16	0.26	0.69	0.18	0.02
Age							
≤ 40	97	11	12	90	24	27	30
> 40	47	10	14	94	36	17	30
p value	0.09	1.00	1.00	1.00	0.7	0.7	0.93

11 (16%) with regional lymph node metastases either at presentation or in the follow up period. The lungs were involved in five (7%) and brain metastases was seen in two (3%) cases. Ten percent of those with papillary cancer had distant metastases as compared to follicular carcinoma wherein 17 percent had distant metastases, however this difference was not statistically significant (p value = 0.78).

Serum thyroglobulin (STG) levels were raised in 12 (17%) cases when a cut off level of 10 ng/ml was taken. Almost similar proportion of males and females had abnormal STG at first contact. Higher proportion of males as compared to females had abnormal STG at fourth follow up; this was not statistically significant (p=0.84). Taking whole body scan as gold standard, serum thyroglobulin had a positive predictive value (PPV) of 27 percent but negative predictive value (NPV) of 69 percent.

Serum calcium levels were decreased in five (7%) cases requiring Vitamin D and calcium supplementation. Five percent of the female patients had low serum calcium levels in the post operative period, which increased to seven percent on fourth follow up. None of the male patients had low calcium levels. Only three percent of those undergoing near total thyroidectomy had low levels of serum calcium as compared to 17 percent of those with completion thyroidectomy and 14 percent with total thyroidectomy (p = 0.38). Only one case was detected to have recurrent laryngeal nerve palsy. An important finding was normal chest radiographs in all the cases.

Those cases requiring radioiodine therapy due to relapse were classified as having had an event and survival function (Kaplan-Meier) was carried out (Fig. 1). Overall 36 percent of the study participants had a relapse requiring radioiodine therapy. The mean event free survival amongst study participants was 141 months [Standard Error (SE) – 15, 95% Confidence Interval (CI), 112 – 170]. Survival functions were also carried out for males and females separately (Fig. 2). Amongst males, 32 percent had an event as compared to 38 percent females. The mean survival time, SE and 95% CI, amongst males and females was 93 months (12, 69 – 118) and 154 months (17, 121 – 188), respectively. However the difference in survival time between males and females was not statistically significant (p = 0.052).

Discussion

We had higher incidence (88%) of thyroid papillary carcinomas, similar to worldwide trend as iodine fortification of the salt have resulted in decreased prevalence of the iodine deficiency disorders. The ratio of papillary to follicular carcinoma is higher in areas not endemic for iodine deficiency. Various studies have examined the role of iodine prophylaxis on the morphology and the frequency of thyroid malignancies [7]. The gender distribution in our study is similar to that reported from other studies [2]. The mean age at diagnosis for papillary carcinoma was 39 years and for follicular was 50 years. This is in consonance with that reported in other studies [5]. Most of our patients underwent near total thyroidectomy. In our study three patients developed features of hypoparathyroidism and the complication rates with near total thyroidectomy were less as compared to completion and total thyroidectomy. The management of slow growing tumours is multidisciplinary and patients benefit from referral to a specialized centre [8-10].

Our study showed similar relapse rate in those receiving radioiodine upto 30 mCi and those who received more than 30 mCi. However, those who received a higher dose were the ones presenting with an aggressive disease. Studies are needed to compare the efficacy of these dosages but randomization will be fraught with ethical dilemmas. Some studies have examined the effect of the amount of the administered activity of radioiodine on the success of initial ablation in terms of outpatient administered activities of slightly less than 30 mCi. This was given in a single administration or at sequential time intervals so that the whole body burden of radioiodine never exceeded 30 mCi. When treatment was based on a radiation dose of at least 30000 cGy to the residual tissue, the success rate was similar to higher administered activities. Maxon HR et al [11], reported successful ablation in 74 percent of patients after the initial ablative therapy.

Fig. 1 : Survival function for all cases included in the study

In our series 12 (17%) cases showed raised serum thyroglobulin levels and 20 (29%) had an abnormal whole body scan on follow up. Our findings are at variance with the other studies, where it has been seen that the thyroglobulin level is more sensitive than the whole body scan in detecting persistent, recurrent, or metastatic disease [12]. The reasons for a negative thyroglobulin test in the setting of a positive whole body scan could be a tumour that does not synthesize thyroglobulin, a false lowering of the serum thyroglobulin in the presence of thyroglobulin antibodies or immunologically inactive thyroglobulin and inadequate thyroid hormone withdrawal at the time of testing. It has been estimated that the percentage of patients with metastatic disease and low or undetectable thyroglobulin levels of thyroid hormone suppressive therapy ranges from 1.3-9.2%, whereas 3.6-30% of these patients may have a low or undetectable thyroglobulin level during suppressive therapy [13]. This indicates that the technique of measuring serum thyroglobulin requires further refinement.

The chest radiographs were negative in all the patients although radioiodine whole body scans showed pulmonary metastases in five cases. The present study shows that serum thyroglobulin has a higher NPV as compared to PPV and whole body scans are a must for follow up of thyroid carcinoma patients. Differentiated thyroid cancers, which comprise more than 80% of all thyroid cancers, carry a good long term prognosis and residual/recurrent disease can be effectively treated with radioiodine.

Conflicts of Interest

None identified

Fig. 2 : Survival functions for males (M) and females (F) separately

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