Thyroid microcarcinoma during thyroidectomy

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ABSTRACT

Introduction: We aimed to retrospectively assess the prevalence of microcarcinoma in thyroidectomy specimens from a Greek population and the role of histopathology in determining management of these patients.

Methods: We used histopathological reports of thyroidectomies performed in a Greek general district hospital. The samples consisted of 191 thyroidectomies performed between January 1997 and July 2001. The female: male ratio was approximately 2:1 and the follow-up period was 327 weeks.

Results: There were 29 microcarcinomas (15.2 percent) with a female:male ratio of 6:1. The prevalence rate in cases with Hashimoto's thyroiditis was significantly higher compared to cases with other benign thyroid pathology (26.8 percent versus 11.9 percent, p-value equals 0.02). Eight microcarcinomas (27.6 percent) were multifocal. The histological type was that of papillary tumour in ten cases (34.5 percent) and follicular in 18 cases (62.1 percent). There were no deaths, recurrences or metastases during the follow-up period.

Conclusion: Our results suggest that incidental microcarcinomas are low-risk tumours that do not require routine further intervention. The latter may be necessary for tumours with poor differentiation or for non-incidental microcarcinomas.

Keywords: thyroid carcinoma, thyroid microcarcinoma, thyroidectomy

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INTRODUCTION

Thyroid microcarcinoma is defined as a malignant tumour of ≤ 1 cm in diameter.[1] Some authors have extended the definition to include tumours of up to 15 mm in diameter.[2,3] Such tumours can be discovered by neck ultrasonography or incidentally after histopathological examination of thyroidectomy specimens.[4,5] The latter are called "incidentalomas".[5] The prevalence varies; most autopsy studies place it in the range of 4.7%–9.9%,[6,7] but rates as high as 35%–36% have also been reported.[8] In thyroidectomy specimens, the prevalence ranges from 11% –35.3%.[3,4,9] A higher rate among male subjects has also been reported in the literature, with a male:female ratio ranging from 6:4 to 8:3.[6,7] There has been considerable debate in the literature about the significance of these occult tumours. Some authors believe that they should be treated as benign,[8] while others deem that aggressive management with radioiodine ablation of any thyroid tissue remnants is necessary.[5] We aimed to examine a Greek population to establish the characteristics of these tumours and the implications for subsequent management.

METHODS

Our materials consisted of the histopathological reports of thyroidectomies performed in the surgical department of a central Greek general district hospital located in the capital. We also assessed the relevant operating and patient notes from our archives. The samples consisted of 191 thyroidectomies performed by three different consultant firms between January 1997 and July 2001. The female:male ratio was approximately 2:1 in our samples (122 and 69, respectively) and the follow-up period was 327 weeks. Follow-up was clinical (six-monthly intervals). The surgical specimens were fixed in 10% buffered formaldehyde, adequately sampled, embedded in paraffin, and cut into sections 5 μm thick. The sections were then stained with haematoxylin-eosin. We decided to use the 15 mm maximum diameter cut-off for our study as we were particularly interested in the incidental nature of microcarcinomas rather than their size. A follicular tumour was considered to be a microcarcinoma when there was capsular or vascular invasion. We used the chi-square test. A p-value < 0.05 was considered to be statistically significant.

RESULTS

Of the 191 thyroidectomies, 16 (8.4%) were performed for clinically-suspected or histologically (fine-needle aspiration

[FNA]) confirmed cancer. 175 (91.6%) were performed for benign disease (e.g., goitre, solitary nodules), of which 41 (21.5%) were diagnosed postoperatively as Hashimoto's thyroiditis. There were 29 microcarcinomas (15.2%) discovered incidentally in the histopathological examination of the specimens, all less than 15 mm in diameter (range 0.1-15 mm). There were no incidental tumours of larger size. The female:male ratio was 6:1 (25 and four patients, respectively). The relevant procedures consisted of total thyroidectomy in 20 cases (69%), near-total thyroidectomy in seven (24.1%), sub-total thyroidectomy in one and unilateral lobectomy in one case. The indications for surgery and the prevalence of microcarcinoma are shown in Table I.

The prevalence rate of microcarcinoma in patients with Hashimoto's thyroiditis was the highest (26.8%), and when compared with other benign cases (11.9%), the difference was statistically significant ($p = 0.02$). A total of eight microcarcinomas (27.6%), were multifocal with 2–9 separate foci, 4/11 (36.6%) in Hashimoto and 4/18 (22.2%) in non-Hashimoto specimens. Of those tumours, seven (24.1%) involved both thyroid gland lobes. The histological type was that of papillary tumour in ten cases (34.5%), follicular in 18 cases (62.1%), and one (3.45%) was an incidental medullary tumour of 15 mm size in a thyroid gland excised for goitre (Table II). One of the tumours was of the tall-cell variant. There was one case of malignant infiltration of lymph nodes, but that was in a known cancer case. There was one additional case with extrathyroidal extension of the incidental carcinoma. It involved the tall-cell variant tumour, consisting of two separate foci of 5 and 7 mm, respectively. There were no deaths, recurrences or metastases during the follow-up period.

Table I. Primary indication for thyroidectomy and the relevant prevalence of microcarcinoma in specimens.

Primary indication	No. of patients with microcarcinoma (%)
Thyroid cancer	2/16 (12.5)
Solitary nodules	3/37 (8.1)
Goitre, total	24/138 (17.4)
Goitre (excluding Hashimoto's thyroiditis)	13/97 (13.4)
Hashimoto's thyroiditis #	11/41(26.8*)
All benign cases (excluding Hashimoto's thyroiditis)	16/134 (11.9*)
Total	29/191 (15.2)

* Statistically significant at $p < 0.05$ (chi-square test, $p = 0.02$)
\# Postoperative diagnosis

Table II. Histological type of incidental microcarcinoma

Histological type	No. of patients
Papillary	10
Follicular	18
Medullary	1

DISCUSSION

Our findings suggest a high prevalence of incidental microcarcinoma, frequently multifocal, in specimens removed for a benign or known malignant disease. We elected to include tumours of less than 15 mm in our study as our objective was to focus on their incidental nature. Three of the microcarcinomas and one of the foci in a multifocal tumour were 10–15 mm. Interestingly, our results demonstrated a higher rate of follicular rather than papillary tumours. This was also the case in a previous large study in Greece.[10] A moderate degree of iodine deficiency which is still persisting in Greece may be responsible, since it has been shown to increase the follicular/papillary tumour ratio.[11] Histological criteria may also play a role, as follicular tumours will often be reclassified as papillary on histological review.[12] Similar questions arise regarding our very high female/male (6:1) ratio, which contrasts with that in most other studies[6,7] but is similar with findings of other studies in Greece.[10] This ratio appears to be generally high in thyroidectomies, and thyroid diseases, in our population, as demonstrated by the 2:1 ratio of our initial sample.

The prevalence of microcarcinomas was particularly high in specimens with Hashimoto's thyroiditis, which has been demonstrated to be associated with Warthin-like papillary tumours.[13] In a series of 17 such tumours, a background of lymphocytic thyroiditis was identified. Seven cases had other microcarcinoma foci as well. This demonstrates a possible immune mechanism as a pathogenetic factor for development of thyroid tumours.[14] There were no deaths, recurrences or metastases among our patients, but it must be noted that our samples consisted of asymptomatic, incidental tumours. However, we had one case with malignant lymph node infiltration, but this was a known cancer case, as mentioned above. Studies that have demonstrated metastases or recurrences include incidental, known (by FNA) and suspected (lymph node involvement) microcarcinomas.[1,15-17] Nevertheless, even when symptomatic, non-incidental tumours are included in the analysis, and with follow-up periods of up to eight [1,14] or 20 years,[12] recurrence rate is low at 4%–6%,[1,15,16]

and related deaths are very rare,[15] even if the observation only is the chosen management option.[1]

Lymph node involvement at initial presentation is the strongest clinical predictor of recurrence, whereas the role of the extent of surgery or radioiodine treatment is conflicting.[1,15,16] Immunohistological positivity for Cyclin-D1,[18] Ki-67 and TGFbeta3[19] are also potential indicators of aggressiveness and metastasising behaviour. Tall-cell variants are examples of poor differentiation, which in turn is a strong predictor of aggressiveness and recurrence.[19] Incidental medullary tumours, on the other hand, seem to be sporadic[20] rather than familial, and not related to unfavourable outcomes. Such outcomes seem to be limited to symptomatic medullary microcarcinomas only.[21] In conclusion, we believe that incidental microcarcinomas are low-risk, "laboratory" tumours that do not routinely require further surgical, radiotherapeutic intervention or follow-up. Additional intervention may however be necessary for tumours with poor differentiation, evidence of extrathyroidal extension, presence of immunohistological aggressiveness markers, or non-incidental microcarcinomas. Regarding Hashimoto's thyroiditis and microcarcinoma, further research is needed to clarify the links between the two entities.

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