International Journal of Surgery 12 (2014) S98–S102

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Incidental carcinoma of the thyroid

Angela Pezzolla [a], Rinaldo Marzaioli [a], Serafina Lattarulo [a,*], Giovanni Docimo [b], Giovanni Conzo [c], Anna Ciampolillo [a], Graziana Barile [a], Ferdinando Massimiliano Anelli [a], Andrea Madaro [a]

[a] Department of Emergency and Organs Transplantation, University of Bari, Policlinico di Bari, P.zza Giulio Cesare 11, Bari, Italy
[b] Department of Surgery, Second University of Naples, Italy
[c] Department of Anesthesiologic, Surgical and Emergency Sciences, VII Division of General and Endocrine Surgery, Second University of Naples, Italy

ARTICLE INFO

Article history:
Received 23 March 2014
Accepted 3 May 2014
Available online 24 May 2014

Keywords:
Incidental carcinoma
Microcarcinoma
Thyroid

ABSTRACT

The diagnosis of incidental thyroid carcinoma in patients submitted to thyroidectomy for a benign disease is quite frequent. A retrospective analysis was performed on 455 patients submitted to surgical intervention in order to establish the incidence of this kind of carcinoma. Two hundred fifty-six patients (56%) were affected by benign disease (176 multinodular goiter, 12 uninodular goiter, 1 Plummer disease and 67 Basedow disease) and 202 (44%) by carcinoma. In 28 of 256 patients (11%), affected by benign disease, occurred a histological diagnosis of thyroid carcinoma, (10 papillary carcinoma, 1 follicular carcinoma, 29 papillary carcinoma follicular variant). In this study it's considered incidental thyroid carcinoma the one occurred in patients who never underwent Fine Needle Aspiration (FNA) and there were no suspicious features in all exams that may suggest the presence of carcinoma. Twenty-three of the 40 incidental carcinoma (57.5%) were microcarcinomas. Ten patients had a sincronous carcinoma. Actually, these patients are still in a follow up program and no recurrency of disease is occasionally observed. This study shows that the only way to put doubts on the real benignity of the disease is the fine needle aspiration; there are no other instruments that could identify the occurrence of the carcinoma. Moreover in the majority of cases the incidental carcinoma is a microcarcinoma, it doesn't reach significant volume, may be not centered by a FNA, but in most cases it's not really biologically aggressive.

1. Introduction

Thyroid nodular disease is extremely common; the incidence in the adult population of the United States varies from 2% to 4%, but is significantly higher in goitrogenic areas [1].

Nodules may occur as single or multiple lesion, some may be hypofunctioning compared to normal thyroid tissue, while others show a normal activity or develop an autonomous functioning, not subject to physiological regulation of the hypothalamic-pituitary-thyroid axis [2].

A small percentage of thyroid nodules is represented by malignancies: approximately 1 nodule of 20 (5%) is a cancer.

Carcinomas of the thyroid are about 1% of all malignancies [3,4], their annual incidence is 0.004% [4]. They are more frequent in females, and although the main age of onset is between 40 and 60 years, they can also arise in childhood and youth [3].

The incidence of thyroid carcinoma – particularly the follicular histotype – is higher in goitrogenic regions, while papillary forms are more common in areas where there are no conditions of iodine deficiency.

The incidental finding of thyroid carcinoma in goiters is, without doubt, an occurrence more common than in the past, due to the improvement of diagnostic imaging [5], greater accuracy of the histological technique and above all to the increased number of thyroid diseases needing surgical treatment.

2. Materials and methods

From January 2010 to June 2013, 455 patients (363 females and 92 males, mean age 56.98 years, range 15–83) underwent thyroid surgery. The operation performed was total thyroidectomy in 429 cases, lobectomy in 29.

Among the 455 observed patients 256 had a preoperative diagnosis of benign thyroid disease: goiter in 188 cases (176 multinodular, 12 uninodular), Plummer's disease in 1, and Basedow disease in 67. In 202 patients cytology led to the diagnosis of cancer

* Corresponding author.
E-mail address: s.lattarulo@virgilio.it (S. Lattarulo).

http://dx.doi.org/10.1016/j.ijsu.2014.05.041
1743-9191/

or suspicious malignant lesion. Only the 256 patients who underwent surgery for benign disease were included in this study.

All patients were studied by neck ultrasound prior to surgery, and submitted to a CT scan of the chest in the case of plunging goiter. In 11 patients a fine needle aspiration (FNA) was performed, excluding malignancy.

At the time of surgery all patients were euthyroid, and almost all with no evidence of chronic thyroiditis.

The histological examination of the specimen confirmed the diagnosis of benign disease in 228 patients (89%). In 28 patients (11%) the presence of 40 incidental carcinomatous lesions was detected (10 patients with synchronous carcinoma).

The majority of patients with incidental carcinoma underwent total thyroidectomy (27/28). In those previously submitted to lobectomy (1/28), completion thyroidectomy was performed.

Histology detected a papillary cancer in 10 patients (25%), follicular carcinoma in 1 (2.5%), follicular variant of papillary carcinoma in 29 (72.5%).

Referring to the "T" of TNM classification, we had 23 microcarcinoma, 2 T1 carcinoma, 3 T2 carcinoma and 12 T3 carcinoma. One of 12 patient with T3 carcinoma was T3N1.

Post-surgical treatments were entrusted to the endocrinologist consultant on the basis of the histological result. All the patients underwent to radioiodine metabolic therapy and were submitted to follow-up: in the first year after surgery annually dosage of thyroglobulin (TG), cervical ultrasound, and a progressive reduction of L-T4 dose leading from fully suppressive to half-suppressing effect (TSH levels maintained at 0.2–0.5 mU/l); further evaluation of TG after stimulation test with recombinant human Thyroid-Stimulating Hormone (rhTSH) was scheduled after 2 years.

At the moment, all patients are alive, apparently without local recurrence or systemic progression of disease, and are still in the course of follow-up.

3. Discussion

The thyroid carcinoma usually occurs as nodular disease. The etiology is likely to be multifactorial, resulting from the complex interaction between genetic, individual, and environmental risk factors.

Although the pathogenetic role of the ionizing radiations is currently well recognized [6], there is no significative correlation with prior radiotherapy if the thyroid tumor develops after the age of 35, since the carcinogenic potential of the radiation treatment, if performed at a later age, seems to decrease [7].

In about 3–5% of patients with thyroid carcinoma a family history for cancer of the thyroid is referred. Case in point is the association of medullary thyroid carcinoma with other endocrinopathies in MEN-2 polyglandular syndrome [8,9].

Most incidental thyroid cancers reported in literature are microcarcinomas. This term refers to a malignant lesion, predominantly papillary, smaller or equal to 1 cm in diameter [10].

In the last years a significant increase of this kind of neoplasm has been detected, probably due to the widespread of ultrasound examination as a first-level diagnostic tool in the study of thyroid diseases [11].

It is not yet been clarified whether the microcarcinoma is a distinct clinical entity characterized by a lower aggressiveness and lesser growth potential, or instead it represents a subgroup of differentiated thyroid carcinoma, diagnosed by chance when it is smaller than 1 cm, during its evolution towards a clinically evident cancer [12].

The prevailing current opinion is that the papillary microcarcinoma is a tumor characterized by an indolent trend of growth and a very favorable prognosis; despite the uncertainty about its natural history has caused the lack of univocal and standardized therapeutic approach [13,14].

Nevertheless in some authors' opinion, the papillary microcarcinoma is a nosological entity characterized by a heterogeneous clinical behavior, ranging from the small neoplastic outbreak accidentally discovered after surgery for benign thyroid diseases, to that of a cancer that is clinically manifested by the only presence of metastasis to lymph nodes of the neck or at a distance.

The tumor, however, has a good prognosis. Recurrences are mainly loco- regional and occur usually within the first 10 years of follow-up, with a prevalence oscillating between 1 and 10%. The rate of mortality for microcarcinoma is very low, and reported with a prevalence ranging between 0.2 and 2.2% [15].

Therefore, in patients at low risk of recurrence, as those with incidental microcarcinoma, cervical ultrasonography and, to a lesser extent, the basal dosage of serum TG may ensure a suitable surveillance, even in the absence of ablation of residual thyroid tissue. Moreover it is advisable to include in the protocol of controls clinical examination, serum dosage of FT3, FT4, TSH, TG and anti-TG antibodies (TGAb), in progress of hormone therapy [16–18].

In patients with medium/high risk of recurrence who underwent to ablative treatment of thyroid remnants, at a distance of approximately 12 months after the demonstration of complete ablation of thyroid tissue and undetectability of TG after maximum stimulation of the hypophysis, is advisable to perform a cervical ultrasound and the dosage of serum TG after stimulation of endogenous TSH or – even better – after exogenous stimulation with rhTSH.

The long-term follow-up of these patients shows that the risk of recurrence is less than 2%, and the relapsing lesion may be early detected by an ultrasonography of the neck [16].

Whilst our previous study showed a percentage of incidental carcinomas (18.2%) – higher than that of other experiences [19] – the current data, despite the greater number of patients (455 vs 240) report a lower value: 11%. This is due to the improvement and more extensive employ of preoperative diagnostic techniques, particularly the fine needle aspiration and its cytological interpretation.

This points out the importance of an accurate clinical and instrumental diagnostic of thyroid nodules to differentiate benign from malignant pathology.

For this purpose TSH, thyroid hormone, thyroglobulin, the presence or absence of autoantibodies are ineffective [20].

Other biomarkers are provided by clinical and laboratory research, aimed to the management of patients with thyroid neoplasms, applied in settings that vary from preoperative selection of thyroid nodules for surgery to postoperative follow-up.

In particular molecular markers of thyroid tumors, derived from genomic and proteomic methods, have been developed, but many of these are too complex or expensive for routine clinical use or are still poorly standardized [21–25].

One of the most interesting applications of biomarkers refers to the employ on needle aspiration specimens. Fifty potential thyroid tumor markers have been tested and five of these (galectin-3, telomerase, thyroid peroxidase, RET-PTC, and p53) showed relatively high accuracy for detecting malignancy in thyroid nodules with indeterminate FNAB findings [26].

Galectin-3, the only submitted to wide multicenter studies [27,28], usually is not expressed in normal thyroid tissue, while is over-expressed in thyroid malignancy. Therefore it is considered an accurate marker of early malignant transformation.

The highest value of specificity for galectin-3 to diagnose thyroid cancer nodules (97.2%) was shown using large needle aspiration (LNA), that ensures to the analysis a larger tissue substrate