

Incidental thyroid carcinomas. A retrospective study

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SUMMARY: Incidental thyroid carcinomas. A retrospective study.

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Aim. The aim of the present study is to report our series of incidental thyroid carcinomas in the last 15 years and their follow-up, discussing therapeutics indications and surgical choices.

Patients and methods. We have considered 1793 patients operated on Surgical Sciences Department of "Sapienza" University of Rome from January 1, 2001 to December 31, 2015. The study was conducted on 83 totally thyroidectomized patients with a real incidental thyroid carcinoma, by clinical, laboratory and instrumental controls. Whole-body scan was the most important test in postoperative evaluation.

Results. In our series, the incidence of incidental carcinomas was 4.62%. Compared to the total number of cancer patients, the percentage is 21,9%. In 15.66% of cases there was multifocality and in

7.23% also bilaterality. Regarding the histological type, in all cases they were papillary carcinoma. The size of the neoplastic lesions ranged from a minimum of 3 to a maximum of 10 mm. Whole-body scan revealed lymph node metastasis in 57.69% of patients.

Discussion. Comparing these data with our previous studies we have seen a significant increase in incidence of incidental thyroid carcinomas over the years. Our therapeutical choice is total thyroidectomy and completion thyroidectomy after lobectomy, because of a relevant percentage of multifocality and/or bilaterality of these tumors. Many Authors on the contrary prefer a more conservative approach invoking the good prognosis of these tumors. The 57.69% of lymph node metastasis at postoperative whole-body scan comfort us in our setting.

Conclusion. Incidental thyroid carcinomas are not uncommon. We consider only tumors until 1 cm in diameter. Multifocality and bilaterality are often present such as occult lymph node metastasis. Our therapeutical choice is total thyroidectomy in order to conduct a proper follow-up.

KEY WORDS: Incidental carcinoma - Microcarcinoma - Thyroid - Total thyroidectomy.

Introduction

The term "incidentaloma", coined by Anglo-Saxon authors to designate occasional adrenal hyperplasia lesions, is now currently used to indicate any mass, accidentally discovered with instrumental examinations (ultrasound, CT, PET/CT, MR) in the absence of specific symptomatology and regardless of the size of such lesions. The refinement of diagnostic imaging methods, even in animal models (1), has thus resulted in an increase in the incidence of such findings, especially in

thyroid diseases, while not allowing in most cases a safe diagnosis of nature (2-17).

If the term "incidental" adapts very well to fortuitously discovered adrenal or hepatic and renal lesions, as these organs are not easily clinically explored, in our opinion, occasional findings in an organ such as the thyroid that can easily be evaluated by a well-conducted objective examination, it is not the same thing.

Until a few years ago, we talk about "occult" carcinoma of the thyroid, to indicate what had been termed in previous ages as "occult sclerosing carcinoma" or "tumors encapsulated in sclerosis" (18, 19). The "occult" thyroid carcinoma is not uncommon (20, 21, 22) and it is defined as a neoplastic process with a diameter equal to or less than 1 cm (1.5 cm for some Authors (23)), in the presence of hematogenic or lymphatic metastases, in the absence of documented clinical signs of thyroid disease and with certain pathological features comprising: 1. unmodified gland profile; 2. intact thyroid capsule; 3. mono or multi-

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microfocality; 4. absence of a own capsule; 5. frequent desmoplastic reaction (24, 25).

Until a few years ago, incidental carcinomas were classified in a single group with occult carcinomas, solely according to their size, although in the absence of precessive metastasis. In fact, the differential feature between incidental carcinomas and occults carcinomas is to be always an occasional finding, during surgery for benign pathologies or as a confirmation of the definitive histological examination on the operative specimen, without any evidence of remote metastasis. Briefly, incidental thyroid carcinomas would be occult carcinomas that have not yet metastasized.

It is then argued if incidental carcinomas also include the carcinomas discovered at the definitive histological examination, after total thyroidectomy for multinodular goiter (26-33) or during treatment of an unrelated head and neck cancer (34). There is no doubt that the latter are also an occasional finding within parenchymas where multinodularity and poor response to medical therapy become responsible for an inalienable surgical choice.

It is also true that histologic positivity for cancer is almost always related to one of the many nodules echographically visible and clinically palpable and hence the incidentality of the finding is solely due to the defect of preoperative definition of the nature of each single nodular lesion.

We believe that in the incidental carcinoma group we must consider all those tumors that exhibit the character of occasionality of the finding and, in accordance with international literature, we cannot confer the incidental title to a thyroid carcinoma that has a diameter greater than 1 cm.

The aim of the present study is to report our series of incidental thyroid carcinomas in the last 15 years and their follow-up, discussing therapeutics indications and surgical choices.

Patients and methods

We have considered 1793 patients operated on Surgical Sciences Department of "Sapienza" University of Rome from January 1, 2001 to December 31, 2015.

In 379 cases (21.14%), surgery was performed for neoplastic diseases. The remaining 1414 patients (78.86%) were operated for benign pathology. Of the 379 thyroid cancers, 197 (51.98%) were taken to surgery already with preoperative, presumed or certain diagnosis of neoplasia.

Of the remaining 182 patients undergoing total thyroidectomy for cancer, 19 had precessive laterocervical lymph node metastases of an occult carcinoma. Of these, 15 patient had a carcinoma of 0.9 cm in diameter

and therefore classified in all respects as an occult. The others had a diameter larger than one centimeter. In these patients we performed a laterocervical functional node dissection and none of these were included in the study group.

Except the 19 patients with laterocervical lymph node metastases, among the remaining 163 cancer patients, in 17 the neoplasia was discovered at the frozen section examination on the nodule for which they had been sent to surgery. Even though the neoplasia had a size of less than 1 cm in 5 of these patients. None of these were included in the study group.

Of the 146 remaining patients, 18 were a totalization of a previous lobectomy for benign pathology, in which histologic examination of thyroid lesions, clinically and instrumentally evident, had been negative, and the definitive histological examination on the operative specimen revealed an unknown primary carcinoma of different origin than thyroid. These patients were also excluded from the "incidental" carcinomas group.

The remaining 128 patients, on the other hand, were subjected to total thyroidectomy for widespread benign pathology, finding an unknown primary carcinoma only at the definitive histological examination.

Of these 128, in 45 cases the neoplasia had a diameter greater than 1 cm. These were also excluded from the study group. There are therefore 83 patients in whom a total thyroidectomy with preoperative diagnosis of multinodular goiter has been performed, in which the histologically definitive examination on the operative specimen showed the existence of an "incidental" carcinoma with a diameter less than 1 cm. Only the latter have been the subject of this study.

The follow-up protocol, in addition to clinical, ultrasound and laboratory controls, provided a whole-body scan scintigraphy in the absence of levotiroxine therapy and eventually the radiometabolic treatment with I^{131} .

Results

In our series, the incidence of incidental carcinomas was 83 cases out of 1793 patients (4.62%). Compared to the total number of cancer patients, the percentage is 21,9%. Out of 83 patients 70 were women (84.33%) and 13 men (15.67%). The mean age was 48.9 years and localization was in the right thyroid lobe in 49 cases, in the left lobe in 31 and in the isthmus in 3 cases.

In 13 cases (15,66%) there was multifocality and in 6 of these also bilaterality (7.23%). Regarding the histological type, in all cases it was papillary carcinoma. The size of the neoplastic lesions ranged from a mi-

nimum of 3 to a maximum of 10 mm in diameter.

As for the follow-up, 5 patients died for causes not related to thyroid neoplasia. The other 78 patients were all alive and performed whole-body scan scintigraphy 40 days after surgery, in the absence of levotiroxine therapy. Thirty-three patients were free from any secondary location and no additional treatment was performed. In the other 45 (57.69%), small areas of radioiodine uptake in the laterocervical and recurrent lymph nodes have been highlighted and all these patients were sent to I^{131} therapy. In 29 patients (64.44%), scintigraphy after radiometabolic therapy showed the disappearance of iodine uptake areas and subsequent annual scintigraphic controls were negative. However, in 16 patients (35.56%), a second administration of I^{131} was required to see all areas of iodine uptake disappear. All 78 patients were also clinically and ecographically monitored at 3, 6 and 12 months after surgery, and then every 1 year, without showing recurrence of cancer, and monitored for plasma thyroglobulin levels which were found to be always in normal range, as well as radiological control of chest.

We compared the data of this experience with those derived from a previous study conducted in 1995 by our School on 440 thyroid cancers from November 1970 to December 1994 (35). This study had shown an incidence of occult carcinomas (less than 1 cm in diameter) equal to 8.63% (38 out of 440) of all neoplasms. Of these patients, only 12 (2.72%) could be classified as incidental carcinomas being the other 26 patients with laterocervical lymph node metastases. We cannot compare data on the incidence of incidental carcinomas discovered after total thyroidectomy for benign diseases because until 1986 we did not ordinarily performed total thyroidectomy for benign pathology.

However, it is evident from the comparison of the data for the two different periods of our case series, the net increase in the incidence of "incidental" carcinomas from 1986 to today.

Discussion

The incidence of incidental carcinoma of the thyroid varies depending on whether the clinical or pathological aspect is preferred. Thyroid cancer has a variable morbidity, depending on the ethnological group and geographical location, from 1 to 7×10^5 . Clinically it is therefore extremely rare. In contrast, many pathological studies account for an incidence from 6% to 24% to 35.6% in Harac (1984), 45.2% in Pagni (2014) and 59% in Woolner (1960) (36-39). In a 2016 Greek study (40) a thyroid microcarcinoma was discovered incidentally in 81.8% of patients undergoing surgery for other pathology non-related to thyroid malignancy, with

35.8% of multifocality and 10.7% of lymph node involvement. Also in the United States, pathological studies on autopsy series showing an incidence of incidental thyroid carcinomas ranging from 5% to 13%, in patients deceased for other causes so to suggest a number of 10 to 30 million occult thyroid cancer patients in that country. Other authors believe that thyroid carcinomas are not recognized in more than 20% of cases even in autopsy research and that they are recognized throughout life in no more than 15% of affected patients (41). In Italy it is reasonable to assume that the incidence is between 1% and 5%. Despite this high incidence, clinically manifest thyroid carcinoma is relatively rare, as they occur with an incidence of 20-30 cases per million inhabitants per year. This seems to show that only one occult cancer per 100 becomes clinically manifest. The incidence also varies in relation to the histological type and the type of thyroid disease associated. Papillary forms would appear to be much more frequent than follicular ones (42).

Multifocality would be present from 18% to 58% of cases, often associated with bilaterality. Concerning associated thyroid diseases, multinodular goiter appear to have the highest incidence, from 4% to 17% (43, 44). In Graves, the incidence varies from 0.5% to 1.8% (45-49). The incidence of carcinomas in the cervico-mediastinal goiter compared with benign thyroid cervical-mediastinum disease, is around 12.1% (50, 51). The association with parathyroid diseases (52-56) and lymphocytic thyroiditis (57, 58) is also described.

From the theoretical point of view, the unambiguous interpretation of data and findings so different between clinical and autopsy studies can be explained by the theory that the presence of neoplastic outbreaks within the thyroid tissue and subsequent extinction of neoplastic cells within the gland is an histologically normal growth event. The clinical manifestation would only be realized sporadically in cases where the neoplastic microscopic cells, released from any control (immunologic, hormonal), evolve volumetrically or with lymph node or distance dissemination. Consequently, incidental carcinoma of the thyroid is considered by some Authors as a particular entity whose problem would be dissociated from that of larger and/or clinically evident carcinomas, giving this type of cancer a "paraphysiological" connotation that would not affect the life expectancy of these patients. In our view, the assessment of the potentiality of a neoplasm cannot be based on its size as the biological (local and remote) aggressiveness is a trait of both small and large tumors. Incidental carcinomas therefore should be considered as equal and univocal entities with thyroid cancer and should be treated as such.

Our previous studies (59-78) have convinced us that the choice of the intervention in case of accidental car-

cinoma detection cannot be made on partial gland ablation, but must provide total thyroidectomy. The problem with the choice of intervention does not obviously include incidental carcinomas discovered after total thyroidectomy for multinodular goiter, but only the very small number of cases where discovery of incidental carcinoma is performed at the final histological examination after lobectomy. This finding imposes, in our opinion, the totalization of the previous partial thyroidectomy. This setting in the surgical indication finds its justification in some specific considerations, first of all the high incidence of multifocality and bilaterality of neoplastic lesions. This phenomenon does not seem to be entirely justified by the anatomopathological hypothesis previously described which would like the “histologically physiological” presence of neoplastic out-breaks in the thyroid tissue. In fact, the maximum percentage of these findings in not selected subjects is about 36% versus a much higher percentage (58%) of neoplastic focal lesions in the contralateral lobe after total thyroidectomy for cancer. Our experience only partly confirms the literature on multifocality and bilaterality as the percentage of multifocality was lower (15.66%), albeit slightly, compared with that reported by other authors, and only in 7.23% we observed bilaterality of neoplastic lesions. However, the data resulting from postoperative scintigraphic controls (57.69% of lymph node metastasis detected) gives us the validation of our approach and some authors agree with us (23, 79-82). On the contrary some Authors do not share this setting (83-91) and others suggest a stratification of the risk of recurrence based on the presence of BRAF mutation, extrathyroidal extension, lateral neck lymph node metastases, multifocality, TSH levels, molecular markers, high metabolic tumor volume and tumor stage (92-102).

We think that the choice of total thyroidectomy allows, in the post-operative period, to point out remote metastasis by means of whole-body scintigraphy, which can be obtained only in the absence of residual glandular tissue, while allowing radiometabolic treatment with I^{131} and ultimately resulting in an intervention not only useful, but necessary for the proper diagnostic-therapeutic follow-up of these patients. In contrast to the advocates of conservative surgery, it should be recalled that in our series, the gland portion most frequently affected by the neoplasm was the posteromedial one located in the proximity of the point where the recurrent nerve enters the larynx and more precisely, in that portion of the gland that is preserved as a residue in case of non-radical thyroid surgery, as well as the pyramidal lobe, in which incidental carcinomas are described (103, 104). Supporters of partial thyroidectomy for incidental carcinoma claim that the motivation of their surgical choice, is a possible de-

finite postoperative hypoparathyroidism or the possibility of surgical lesions of the inferior laryngeal nerve. These risks, which are always present in thyroid surgery, as demonstrated by our experience (105, 106, 107), are exceeded by a regulated surgical technique that involves the preparation of the inferior laryngeal nerves along the entire cervical tract and the ligation of the inferior thyroid artery on its branches, near the thyroid capsule. In addition, with regard to the complications of total thyroidectomy, it should be considered that it is certainly more risky a redo surgery on a minimal glandular stump, in a scar tissue residual at first intervention, rather than total ablation. In cases where we must perform a completion thyroidectomy after lobectomy, the risks associated with recurrent nerve dissection and parathyroid preservation do not increase, since we can perform an operation in a surgical field not compromised by a previous surgery.

With regard to total thyroidectomy for benign pathology, more and more Authors are convinced of the validity of the rational assumptions of this surgical choice. To the functional, anatomopathological and clinical motivations that have pushed us, together with others, to support total thyroidectomy also for non-neoplastic disease, an oncological consideration should be added to the results of the present study considering that 4.62% of the total thyroidectomies performed for benign pathology showed the presence of an unknown neoplastic disease. This percentage of tumor incidence in multinodular goiters, in line with the data reported in the literature, would not be unexpected, although significantly higher than that recorded by our previous experience. Moreover the fact that 57.69% of these patients already had unrecognized laterocervical lymph node metastasis evidenced by post-operative whole-body scan, is certainly a data that even the most vigorous advocates of conservative interventions must consider.

Conclusion

Incidental thyroid carcinomas are not uncommon. We consider only tumors until 1 cm in diameter. Multifocality and bilaterality are often present such as occult lymph node metastasis. Our therapeutical choice is total thyroidectomy in order to conduct a proper follow-up. After lobectomy we are in favor of completion thyroidectomy even if in very low-risk cases a conservative approach is possible.

Disclosure

The Authors have no conflict of interest or any financial support.

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